Role of Respiratory Rate Oxygenation (ROX) Index in Predicting Outcomes of Non-Invasive Ventilation in Patients with Acute Hypercapnic Respiratory Failure

Gamal Agmy[1], Manal A. Mahmoud[1], Kholoud Zakaria[*2], Mohamed F. Adam[1]
[1]Department of Chest Diseases and Tuberculosis, Assiut University Hospitals, Faculty of Medicine, Assiut University, Assiut, Egypt
[2] Department of Chest Diseases, Al-Mabarra Hospital, Assiut, Egypt
***Corresponding Author:* Kholoud Zakaria**
E-mail: khloud011172@med.au.edu.eg

Abstract:

Background and Aim: Non-invasive ventilation (NIV) plays a vital role in managing acute hypercapnic respiratory failure, yet its failure remains a major clinical challenge. Early identification of patients at risk of NIV failure is essential to prevent delays in invasive mechanical ventilation. The ROX index, calculated as the ratio of SpO_2/FiO_2 to respiratory rate, has emerged as a potential non-invasive tool for guiding clinical decision-making. This study evaluated the predictive value of the ROX index in determining the success of non-invasive ventilation in patients with acute hypercapnic respiratory failure.

Methods: A prospective observational study was conducted on 100 adult patients admitted to the respiratory intensive care unit with acute hypercapnic respiratory failure requiring NIV. ROX index and arterial blood gases were recorded at baseline and multiple time points (1, 12, 24, 36, and 48 hours).

Results: NIV was successful in 80% of patients, while 20% experienced failure. The ROX index was significantly higher at all time points in the successful group ($p < 0.001$). An ROX index < 5.11 and a baseline respiratory rate > 28 breaths/min were identified as independent predictors of NIV failure. At a cut-off point of < 5.19, the ROX index had an overall diagnostic accuracy of 87.2% in predicting NIV failure.

Conclusion: The ROX index serves as a straightforward and practical bedside parameter for assessing the likelihood of noninvasive ventilation (NIV) success in patients presenting with acute hypercapnic respiratory failure. Regular evaluation of the ROX index can support timely clinical decisions regarding the need for endotracheal intubation.

Keywords: ROX index; Non-invasive ventilation; Respiratory failure.

Introduction

Noninvasive ventilation (NIV) has been shown to reduce the need for endotracheal intubation, thereby decreasing dependence on invasive mechanical ventilation in patients with acute respiratory failure. Despite these advantages, NIV failure remains a significant concern, particularly in specific patient subgroups. Notably, patients who fail NIV have been reported to experience a two- to six-fold increase in mortality compared to those with successful NIV outcomes **[1, 2]**.

Delayed intubation in the context of NIV failure further exacerbates this risk, underscoring the importance of early identification of high-risk patients and timely transition to invasive mechanical support when necessary. Clinical monitoring of patients receiving noninvasive oxygenation strategies typically involves evaluation of respiratory rate and oxygenation indices, such as the PaO_2/FiO_2 ratio. A decline in these parameters may signal the need for escalation of respiratory support **[3]**.

Respiratory Rate–Oxygenation (ROX) index is a simple, noninvasive tool to assess the likelihood of success with noninvasive oxygen therapies [4]. ROX index has already been employed in subjects with COVID-19 treated with HFNC as well as with NIV to early identify those at high risk of failure, with good results [5-7]. Still, different cut-offs have been adopted by different studies. In the current study, we aimed to evaluate the ability of the ROX index to predict the success of non-invasive ventilation in patients with respiratory failure.

Patients and Methods:

Study Design and Setting

A prospective study was conducted at the Department of Chest Disease and Tuberculosis. It was done between June 2022 and January 2024.

Inclusion Criteria

The study enrolled a patient who was admitted to RICU with acute hypercapnic respiratory failure requiring NIV support.

Exclusion Criteria

Any patient with one or more of the following criteria was excluded: acute hypoxemic respiratory failure, absolute indication for intubation, contraindication to NIV like untreated pneumothorax, pneumothorax with air leak, or tracheostomy, central causes of hypercapnic respiratory failure, and/or disturbed conscious level or GCS < 12.

All patients signed informed consent. The study was approved by Assiut Faculty of Medicine, Institutional Review Board (IRB no: 17101300/ 2023).

Sample Size Calculation

Based on the frequency of failure with NIV, which was 5-61% **[8]**, a sample size equal to 93 patients was required with the following assumptions: 5% alpha error, confidence interval of 95%, and power of the study 80%. To avoid dropout, we recruited a total of 100 patients with respiratory failure requiring NIV support.

Methodology

All patients were subjected to thorough history taking and clinical evaluation. The following data were collected: age, sex, occupation, smoking history, body mass index, and comorbidities. In addition, laboratory data included complete blood count, INR, liver function tests, creatinine, urea, sodium, and potassium. Arterial blood gases and vital signs were assessed at baseline and 1st, 12th, 24th, 36^{th,} and 48th hr after NIV.

Non-invasive Ventilation:

Patients received NIV using ICU ventilators (Dräger, Hamilton, or Engström) via CPAP interface, with initial settings of 8 cmH_2O pressure support and 5 cmH_2O PEEP. Settings were titrated to achieve tidal volumes of 6–8 mL/kg and $SpO_2 \geq 92\%$.

NIV was administered for at least 12 hours per day, alternating with oxygen via a Venturi mask (8–10 L/min) to maintain SpO_2 between 90% and 92%. Patients were positioned with head-of-bed elevation to 45°, and ABGs were monitored every 12 hours or as clinically indicated. Weaning from NIV to conventional oxygen therapy (4–10 L/min) was considered once RR < 25 breaths/min, $SpO_2 \geq 90\%$, and $FiO_2 \leq 0.5$.

NIV outcomes were recorded as [9]:

- NIV failure was defined as requiring intubation or dying during NIV
- NIV success was defined by the avoidance of endotracheal intubation with clinical and ABG improvement.

ROX Index Assessment

It was assessed at baseline and 1st, 12th, 24th, 36^{th,} and 48th hr after NIV. It was calculated as the ratio of (SpO_2/FiO_2) to RR multiplied by 100 **[10]**.

Daily clinical evaluations were performed during morning ICU rounds to assess patient status, including improvement or deterioration under oxygen therapy. For patients requiring intubation and mechanical ventilation, the underlying indication and timing were systematically recorded.

Complications related to noninvasive ventilation (NIV), as well as its duration, were carefully monitored. The length of ICU stay and the overall hospitalization period were documented. Patient satisfaction with respiratory support was assessed using the Modified Borg Scale (MBS) **[11]** and the Visual Analogue Scale (VAS) **[12]**.

Severity Assessment

This was done using the Acute Physiology and Chronic Health Examination-II (APACHE-II) score.

Statistical Analysis

Data were collected and analyzed using SPSS (Statistical Package for the Social Sciences, version 20; IBM Corp., Armonk, NY). The Shapiro–Wilk test was employed to assess the normality of data distribution. Quantitative variables were presented as mean ± standard deviation (SD) and compared using the Student's t-test. Categorical (nominal) variables were reported as counts (n) and percentages (%) and analyzed using the Chi-square (χ^2) test. Predictors of NIV success were identified through logistic regression analysis. The optimal cut-off value of the ROX index for predicting NIV success was determined using receiver operating characteristic (ROC) curve analysis. A confidence level of 95% was applied, and a p-value of < 0.05 was considered statistically significant.

Results

The current study enrolled 100 patients with respiratory failure (RF); Out of those patients, 20/100 patients had failed NIV and required MV, while 80/100 (80%) patients had successful NIV (figure 1).

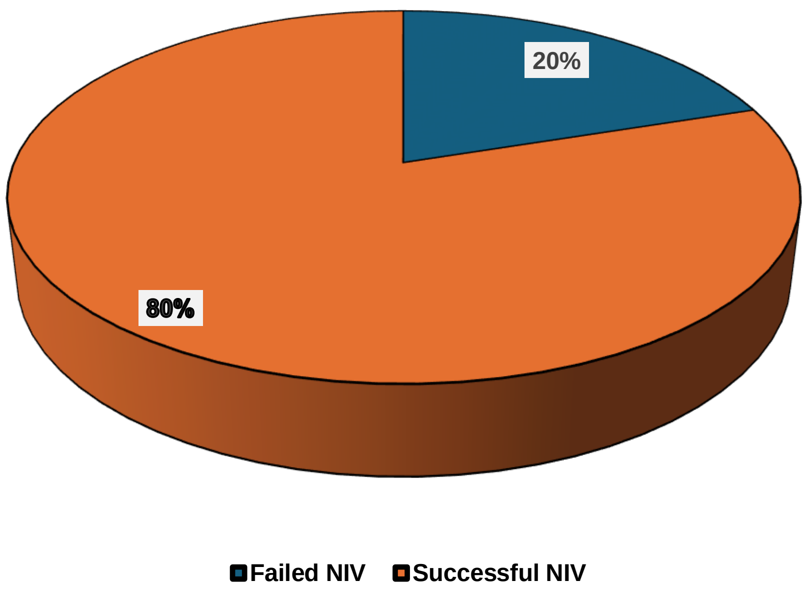

Figure 1: Outcome of NIV in the current study. NIV: non-invasive ventilation

Baseline data of the study patients based on the outcome of NIV (Table 1):
The failed NIV group had a significantly higher mean age (61.30 ± 9.11 vs. 55.22 ± 5.34 (years); p < 0.001). Other baseline data were comparable between both groups.

Table 1: Baseline data of the study patients based on the outcome of NIV

	Successful NIV (n= 80)	**Failed NIV (n= 20)**	***P* value**
Age (years)	55.22 ± 5.34	61.30 ± 9.11	**< 0.001**
Sex			0.62
Male	48 (60%)	11 (55%)	
Female	32 (40%)	9 (45%)	
Boyd mass index (kg/m^2)	27.06 ± 5.21	28.01 ± 4.44	0.09
Smoking status			0.63
Current smoker	40 (50%)	10 (50%)	
Ex-smoker	20 (25%)	7 (35%)	
Non-smoker	20 (25%)	3 (15%)	
Previous admission	8 (10%)	3 (15%)	0.34
Comorbidities			
Diabetes mellitus	30 (37.5%)	9 (45%)	0.11
Hypertension	32 (80%)	8 (40%)	0.67
Cardiac disease	25 (31.3%)	7 (35%)	0.31
Kidney disease	4 (5%)	2 (10%)	0.09
Hepatic disease	8 (10%)	2 (10%)	0.34
Underlying diseases			0.09
COPD	40 (50%)	9 (45%)	
Overlap syndrome	20 (25%)	4 (20%)	
OHS	14 (17.5%)	4 (20%)	
Bronchiectasis	6 (7.5%)	3 (15%)	

Data expressed as mean (SD) frequency (percentage). **NIV:** non-invasive ventilation; **COPD:** chronic obstructive pulmonary disease; **OHS:** obesity hypoventilation syndrome

Laboratory data among the patients based on outcome:

There was a significantly lower serum albumin level among patients with failed NIV. The failed NIV group had a significantly higher APACHE-II score (51.12 ± 13.11 vs. 32.56 ± 10.34; *p* < 0.001).

Hemodynamic changes among studied patients based on outcome:

Both groups had comparable hemodynamic changes but lower RR in the successful NIV group at the 24th hr and 48th hr of ventilation. Also, the successful NIV group had better parameters of ABGs at different times of assessment.

ROX index assessment in patients based on outcome (Table 2, Figure 2):

Patients with successful NIV had significantly higher ROX at a different assessment (*p* < 0.001).

Table 2: ROX index assessment in studied patients based on outcome

ROX index	Successful NIV (n= 80)	Failed NIV (n= 20)	*P* value
Baseline	5.22 ± 1.50	3.44 ± 1.21	< 0.001
At 2nd hr	6.30 ± 1.29	3.70 ± 2.11	< 0.001
At 4th hr	6.89 ± 1.09	4.22 ± 1.87	< 0.001
At 6th hr	6.45 ± 1.22	3.83 ± 1.21	< 0.001
At 12th hr	7.01 ± 1.45	3.65 ± 1.20	< 0.001
At 24th hr	7.23 ± 0.66	4.40 ± 1.21	< 0.001
At 48th hr	7.80 ± 0.50	3.32 ± 1.05	< 0.001

Data expressed as mean (SD). *P* value was significant if < 0.05. **NIV:** non-invasive ventilation

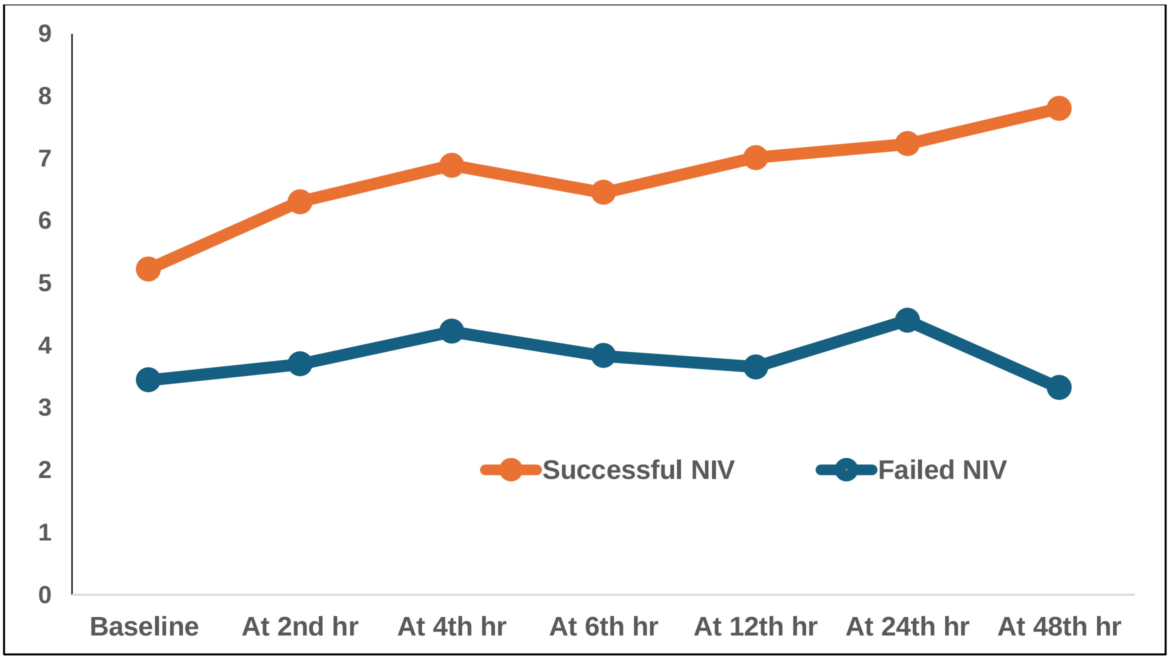

Figure 2: ROX index in studied patients based on outcome. **NIV:** non-invasive ventilation

Comfortability and Length of stay (LOS) and complications (Table 3):
Patients with successful NIV had better VAS (2.42 ± 0.65 vs. 5.42 ± 1.50; $p < 0.001$) and MBS (3.33 ± 0.50 vs. 6.01 ± 0.60; $p < 0.001$) with lower LOS. Both groups reported comparable complications.

Table 3: Comfortability, LOS, and complications in patients based on the outcome

	Successful NIV (n= 80)	**Failed NIV (n= 20)**	***P* value**
Visual analogue scale	2.42 ± 0.65	5.42 ± 1.50	< 0.001
Modified Borge scale	3.33 ± 0.50	6.01 ± 0.60	< 0.001
Hospital stay (day)	8.55 ± 2.22	15.45 ± 3.45	< 0.001
Complications			
Nasal ulceration	8 (10%)	3 (15%)	0.09
Leak	4 (5%)	2 (10%)	0.22
Nasal dryness	4 (5%)	1 (5%)	---
Retained secretion	3 (3.8%)	1 (5%)	0.07
Outcome			< 0.001
Alive	80 (80%)	15 (75%)	
Died	0	5 (25%)	

Data expressed as mean (SD) frequency (percentage). *P* value was significant if < 0.05.

Indications of MV among the studied patients with failed MV:

Indications of MV in patients with failed NIV were respiratory distress (30%), hypercapnia (25%), hemodynamic deterioration (20%), cardiopulmonary arrest (20%), and disturbed consciousness (5%)

Predictors of failure of NIV in patients with respiratory failure (Tables 4-5, Figure 3):

Predictors of failure of NIV in patients with RF were only baseline RR > 28 c/min and ROX index < 5.11. At a cut-off point < 5.19, it was found that the ROX index had 80% sensitivity and 89% specificity with 87.2% overall accuracy in the prediction of failed NIV in patients with RF.

Table 4: Predictors of failure of NIV in patients with respiratory failure

	Odd's ratio	**95% Confidence interval**	***P* value**
Age > 60 years	0.76	0.55- 1.45	0.33
APACHE-II > 15	1.34	0.50- 2.01	0.70
Low serum albumin	1.09	0.30- 2.18	0.45
Baseline RR > 28 c/min	2.11	1.50- 4.22	0.01
ROX < 5.11	3.45	2.80- 8.19	< 0.001

P value was significant if < 0.05. **RR:** Respiratory failure

Table 5: Accuracy of ROX index in prediction of failure of NIV

	Indices
Sensitivity	80%
Specificity	89%
Positive predictive value	70%
Negative predictive value	92%
Accuracy	87.2%
Cut-off point	< 5.19
Area under curve	0.738
P value	0.038

P value was significant if < 0.05. **AHRF:** Acute hypoxemic respiratory failure

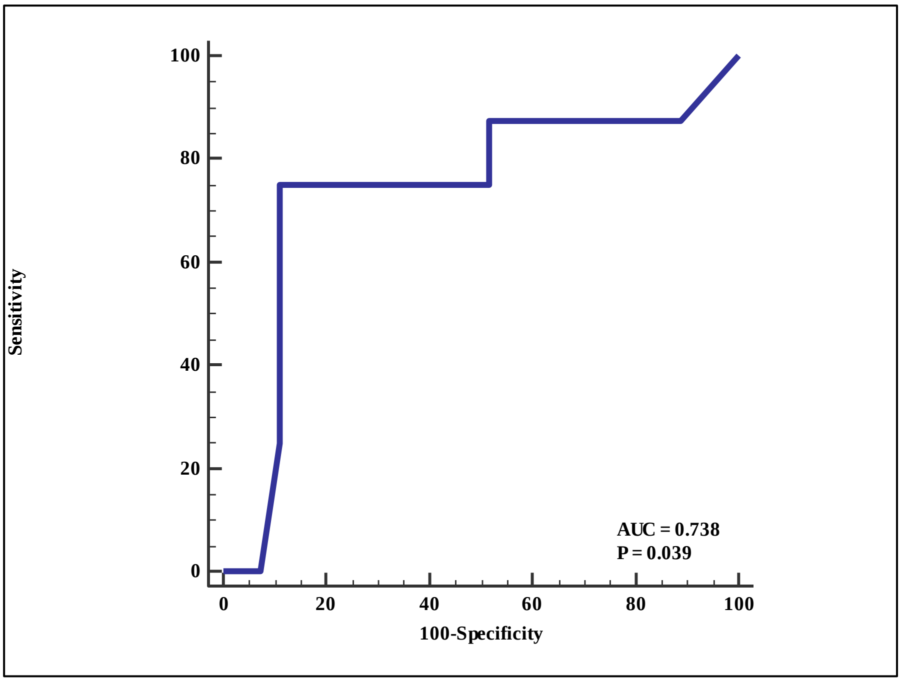

Figure 3: Accuracy of ROX index in prediction of failed non-invasive ventilation. **AUC:** area under the curve

Discussion

The ROX index is a non-invasive, bedside monitoring tool used to guide non-invasive oxygen therapy in patients with hypoxemic respiratory failure. It was initially developed to predict the success of high-flow nasal cannula (HFNC) therapy in patients with pneumonia admitted to the intensive care unit (ICU) **[13]**.

In this prospective observational study, we evaluated the prognostic value of the ROX index in predicting the outcome of noninvasive ventilation (NIV) in patients presenting with acute hypercapnic respiratory failure. A total of 100 patients were included to assess the diagnostic accuracy of the ROX index in forecasting NIV success or failure. Of these, 80 patients (80%) responded favorably to NIV and were managed without the need for endotracheal intubation, while 20 patients (20%) exhibited clinical deterioration and subsequently required transition to invasive mechanical ventilation (IMV). These findings underscore the potential of the ROX index as a bedside tool for the early identification of patients at risk for NIV failure.

The frequency of NIV failure observed in our study was consistent with that reported in the literature, where the failure rate in patients with acute respiratory failure ranges from 12% to 65% **[14-16]**.

The failed NIV group had a higher mean age with lower serum albumin and a higher APACHE-II score. In agreement with the current study, many previous studies reported older age among the NIV group **[17-20]**. Also, other studies noticed lower albumin with a higher APACHE-II score with failed NIV **[21-24]**

Also, the successful NIV group had better VAS and MBS with shorter LOS and comparable complications. **Arsude et al. (2019)** stated that patients with successful NIV had better dyspnea score as assessed by

MBS**[9]**. Many studies proved such findings regarding satisfaction and LOS **[25-27]**.

Indications for MV were respiratory distress (30%) and hypercapnia (25%). In a similar study by Salwa et al. (2019), 58.33% of patients with acute hypercapnic respiratory failure (AHRF) who failed NIV did so due to inability to alleviate dyspnea and ABG values, 25% due to excessive secretions, and 16.67% due to hemodynamic instability **[28]**.

We found that the successful NIV group had significantly higher ROX at a different assessment ($p < 0.001$). Predictors of failure of NIV in patients with RF were only baseline RR > 28 c/min and ROX index < 5.11. With ROC curve analysis, at a cut-off point < 5.19, the ROX index had 87.2% overall accuracy in the prediction of failed NIV in patients with RF.

Recently, **Lijović et al. (2025)** confirmed that this index is better than other indices, with an AUC of 0.63 **[29]**. Also, another study stated that the 94% accuracy of an index with AUC was 0.974 **[30]**.

This study is subject to several limitations that should be considered when interpreting the findings. First, the relatively small sample size and the single-center nature of the study may limit the external validity and generalizability of the results to broader patient populations and varied clinical settings. Second, while the ROX index offers a valuable tool for guiding respiratory management, noninvasive ventilation (NIV) represents a dynamic and continuously evolving intervention.

Therefore, reliance on static or infrequent ROX index measurements may not fully capture the patient's trajectory, potentially delaying necessary escalation to invasive mechanical ventilation. Lastly, variability in clinical judgment may have influenced outcomes, as some treating physicians may have relied on the ROX index at isolated time points rather than incorporating serial measurements, which could have impacted the timing of intubation decisions. However, being a randomized trial, this remains a significant strength of the study. Furthermore, our study provides valuable insight into the context of our local healthcare setting.

Conclusion

The ROX index is a practical and reliable bedside tool with strong predictive value for detecting NIV failure in patients with acute respiratory failure. Its early application can support timely decisions about intubation, potentially reducing complications and improving patient outcomes. However, larger multicenter studies are needed to validate these results and standardize their clinical use.

References

1. Ruzsics I, Matrai P, Hegyi P, et al. Noninvasive ventilation improves the outcome in patients with pneumonia-associated respiratory failure: systematic review and meta-analysis. J Infect Public Health. 2022;15(3):349-59.
2. Bongiovanni F, Michi T, Natalini D, et al. Advantages and drawbacks of helmet noninvasive support in acute respiratory failure. Expert Rev Respir Med. 2023;17(1):27-39.
3. Frat JP, Ragot S, Coudroy R, et al. Predictors of intubation in patients with acute hypoxemic respiratory failure treated with a noninvasive oxygenation strategy. Crit Care Med. 2018;46(2):208-15.
4. Roca O, Caralt B, Messika J, et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Respir Crit Care Med. 2019;199(11):1368-76.
5. Calligaro GL, Lalla U, Audley G, et al. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: a multi-centre prospective observational study. EClinicalMedicine. 2020;28:100570.
6. Zucman N, Mullaert J, Roux D, et al. Prediction of outcome of nasal high flow use during COVID-19-related acute

hypoxemic respiratory failure. Intensive Care Med. 2020;46:1924-6.

7. Leszek A, Wozniak H, Giudicelli-Bailly A, et al. Early measurement of ROX index in intermediary care unit is associated with mortality in intubated COVID-19 patients: a retrospective study. J Clin Med. 2022;11(2):365.
8. Ozyilmaz E, Ugurlu AO, Nava S. Timing of noninvasive ventilation failure: causes, risk factors, and potential remedies. BMC Pulm Med. 2014;14:19.
9. Arsude S, Sontakke A, Jire A. Outcome of noninvasive ventilation in acute respiratory failure. Indian J Crit Care Med. 2019;23(12):556-60.
10. Junhai Z, Jing Y, Beibei C, et al. The value of ROX index in predicting the outcome of high flow nasal cannula: a systematic review and meta-analysis. Respir Res. 2022;23(1):33.
11. Roca O, Riera J, Torres F, et al. High-flow oxygen therapy in acute respiratory failure. Respir Care. 2010;55(4):408-13.
12. Heller GZ, Manuguerra M, Chow R. How to analyze the Visual Analogue Scale: Myths, truths, and clinical relevance. Scand J Pain. 2016;13(1):67-75.
13. Roca O, Messika J, Caralt B, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. J Crit Care. 2016;35:200-5.
14. Carteaux G, Millán-Guilarte T, De Prost N, et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. Crit Care Med. 2016;44(2):282-90.
15. Tonelli R, Fantini R, Tabbì L, et al. Early inspiratory effort assessment by esophageal manometry predicts noninvasive ventilation outcome in de novo respiratory failure. A pilot study. Am J Respir Crit Care Med. 2020;202(4):558-67.
16. Mercurio G, D'Arrigo S, Moroni R, et al. Diaphragm thickening fraction predicts noninvasive ventilation outcome: a preliminary physiological study. Crit Care. 2021;25(1):219.
17. Duan J, Yang J, Jiang L, et al. Prediction of noninvasive ventilation failure using the ROX index in patients with de novo acute respiratory failure. Ann Intensive Care. 2022;12(1):110.
18. Custodero C, Gandolfo F, Cella A, et al. Multidimensional prognostic index (MPI) predicts non-invasive ventilation failure in older adults with acute respiratory failure. Arch Gerontol Geriatr. 2021;94:104327.
19. Burns KE, Stevenson J, Laird M, et al. Non-invasive ventilation versus invasive weaning in critically ill adults: a systematic review and meta-analysis. Thorax. 2022;77(8):752-61.
20. Shu W, Guo S, Yang F, et al. Association between ARDS etiology and risk of noninvasive ventilation failure. Ann Am Thorac Soc. 2022;19(2):255-63.
21. Antonelli M, Conti G, Esquinas A, et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med. 2007;35(1):18-25.
22. Wang H, Zhao QY, Luo JC, et al. Early prediction of noninvasive ventilation failure after extubation: development and validation of a machine-learning model. BMC Pulm Med. 2022;22(1):304.
23. Di Costanzo D, Mazza M. Noninvasive Ventilation Success, and Failure Risk Factors: The Role of Upper Airways. In: Upper Airway Disorders and Noninvasive Mechanical Ventilation: Rationale and Approaches. Springer; 2023:117-29.
24. Ismail HGA, Mohammadien HA, Ahmed KH, et al. Non-Invasive Ventilation in Patients with Acute

Hypoxemic Respiratory Failure. Sohag Med J. 2024;28(3):25-41.

25. Smith TA, Davidson PM, Lam LT, et al. The use of non-invasive ventilation for the relief of dyspnoea in exacerbations of chronic obstructive pulmonary disease; a systematic review. Respirology. 2012;17(2):300-7.
26. Sehgal IS, Kalpakam H, Dhooria S, et al. A randomized controlled trial of noninvasive ventilation with pressure support ventilation and adaptive support ventilation in acute exacerbation of COPD: a feasibility study. COPD. 2019;16(2):168-73.
27. Barrett NA, Hart N, Daly KJ, et al. A randomised controlled trial of non-invasive ventilation compared with extracorporeal carbon dioxide removal for acute hypercapnic exacerbations of chronic obstructive pulmonary disease. Ann Intensive Care. 2022;12(1):36.
28. Salwa AG, Romeh OA, Youssef MM, et al. Effectiveness of Noninvasive Ventilation in Acute Respiratory Failure. Med J Cairo Univ. 2019;87(March):713-22.
29. Lijović L, Radočaj T, Kovač N, et al. Predictive performance of ROX index and its variations for NIV failure. Med Intensiva (Engl Ed). 2025; In press.
30. Mamdouh OM, Ahmed AES, Hashem AZA, et al. Performance of different dynamic oxygenation indices incorporating heart rate to predict non-invasive ventilation outcomes in hypoxemic respiratory failure. Egypt J Bronchol. 2024;18(1):103.