ORIGINAL ARTICLE

Comparison of Modified ROX Index Score and ROX Index Score for Early Prediction of High Flow Nasal Oxygen Therapy Outcome in Patients with Acute Respiratory Failure: A Prospective Observational Cohort Study

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Abstract

Background: We compared the modified ROX index and ROX index scores in earlier predictions of high-flow nasal oxygen (HFNO) therapy outcomes in patients with acute respiratory failure.

Methods: We conducted a prospective observational study on 151 acute respiratory failure patients initiated on HFNO therapy. The primary objective of this research was to compare the modified ROX index and ROX index to investigate which score predicted HFNO treatment outcome earlier.

Results: The modified ROX index score had better predictive power than the ROX score at different time points, especially one hour following the start of HFNO therapy (AUC 0.790; 95% CI: 0.717–0.863; $p < 0.001$). For the ROX Index at 1 hour, the ideal cut-off value for HFNO outcome was 4.36 (sensitivity: 72.6%, specificity: 53.9%), and for the modified ROX index at 1 hour, it was 4.63 (sensitivity: 74.2%, specificity: 69.7%). The presence of various comorbidities didn't show any change in ROX-HR cut-off values.

Conclusion: The modified ROX index is a better predictor of the success of HFNO therapy than the ROX index. Furthermore, the presence of any comorbidities did not affect modified ROX index cut-off values or the outcome of HFNO therapy.

Keywords: Acute hypoxemic respiratory failure, High flow nasal oxygen, Hypoxia, Intensive care, Non-invasive ventilation.

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Highlights

- Predicting high-flow nasal oxygen (HFNO) therapy outcomes helps make early treatment choices while improving care in patients with acute respiratory failure.
- We examined the modified ROX index and ROX index in early HFNO therapy outcomes in patients with acute respiratory failure.
- The modified ROX index is an early predictor of the success of HFNO therapy outcomes compared to the ROX index.

Introduction

High-flow nasal oxygen therapy uses a specialized nasal cannula to supply heated, humidified oxygen at high flow rates (20–60 L/min). It significantly boosts patient comfort in various clinical settings, including intensive care units, emergency rooms, and general wards. It also efficiently improves oxygenation and minimizes the labor of breathing.[1] In acute respiratory failure (ARF), HFNO therapy assists in avoiding invasive mechanical ventilation and lowers associated hazards. Its advantages include enhanced patient tolerance, lessened respiratory effort, and adequate oxygen supply. The capacity to modify a fraction of inspired oxygen (FiO_2) enables HFNO therapy to offer specialized respiratory support. It is a crucial non-invasive option in respiratory treatment due to its broad uses, which include acute respiratory distress syndrome, exacerbation of chronic obstructive pulmonary disease, and pneumonia.[2] The wide range of applications and clinical benefits of HFNO therapy make it an essential tool for respiratory support.[3]

High-flow nasal oxygen therapy outcomes must be predicted to make early treatment decisions, improve patient care, and limit unnecessary therapies. It may help healthcare professionals to allocate resources wisely, customize management strategies, and, if necessary, adopt alternative interventions.

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The ROX Index Score is computed by multiplying the respiratory rate (RR) in breaths per minute by the ratio of oxygen saturation (SpO_2) to the fraction of inspired oxygen (FiO_2).[3] It gives a number representing the patient's oxygenation level and breathing effort.

A modified version of the ROX Index Score (RIS), the Modified ROX Index Score (MRIS), also takes into account heart rate (HR).[4] The goal of this change is to improve the accuracy of predicting therapy outcomes by considering the patient's cardiovascular status. The Modified ROX Index score, also known as ROX-HR, calculated from the ratio of respiratory rate to heart rate and pulse oximetry/FiO_2 to respiratory rate, showed promise in predicting HFNO therapy outcomes earlier than the traditional ROX Index score.[5–7]

MRIS seeks a more complete evaluation of the patient's physiological response to HFNO therapy by considering respiratory and cardiovascular parameters. The critical distinction between MRIS and RIS is adding heart rate (HR) to the computation.

The modified ROX Index score shows promise as a predictive tool for HFNO therapy outcomes. However, additional research is required to confirm its efficacy, identify the best cut-off values, and consider various aspects, including comorbidities. We hypothesized that MRIS could predict HFNO therapy outcomes in ARF patients earlier than the ROX index.

Methods

This prospective observational cohort study was conducted in the intensive care unit of a tertiary care hospital from October 2021 to June 2023. Adult patients aged between 18 and 85 years diagnosed with acute respiratory failure and initiated HFNO therapy were recruited. Institutional ethics committee clearance (AIIMS/IEC/2021/3576) was obtained, and written consent was obtained from patient relatives. We excluded patients with cardiogenic pulmonary oedema, Glasgow Coma Scale (GCS) < 12; presence of any cardiac arrhythmia; recent nasal bleed; cerebrospinal fluid (CSF) rhinorrhea; patients cycled between HFNC and NIV; and patients with "Do Not Intubate" (DNI) order.

Based on the patient presentation, information was gathered for their demographics, diagnoses, and comorbid conditions. At particular time intervals (1, 2, 4, 6, 12, 18, 24, and 48 hours), clinical data comprising heart rate (HR), respiratory rate (RR), oxygen saturation (SpO_2), fraction of inspired oxygen (FiO_2), and SF ratio (SpO_2/FiO_2) were obtained before and after the start of HFNO therapy. Data were collected by a treating clinician who was not a part of the study.

Patients were started on HFNC therapy (Fisher & Paykel Healthcare, Auckland, New Zealand) at a flow rate of 40 L/min, and FiO_2 was adjusted by aiming for a SpO_2 level above 92%. As needed, the flow was steadily increased, reaching a maximum of 60 L/min. HFNO therapy flow was constantly monitored, and once the required FiO_2 level remained below 40%, it was decreased to below 40 L/min. Patients were monitored for 48 hours. Continuation or termination of HFNO treatment was dependent on the intensivist's clinical assessment.

The ROX index score was calculated by multiplying the respiratory rate (RR) in breaths per minute by the ratio of oxygen saturation (SpO_2) to the fraction of inspired oxygen (FiO_2). The Modified ROX index score was calculated by dividing the ROX index score by heart rate and multiplying it by a factor of 100.

Success for the HFNO therapy was defined as a transfer to lower oxygen therapy within 48 hour, with no requirement for intubation or non-invasive ventilation (NIV). HFNC therapy failure was defined as the need for intubation or NIV within 48 hour due to respiratory reasons, omitting patients who switched between HFNC and NIV.

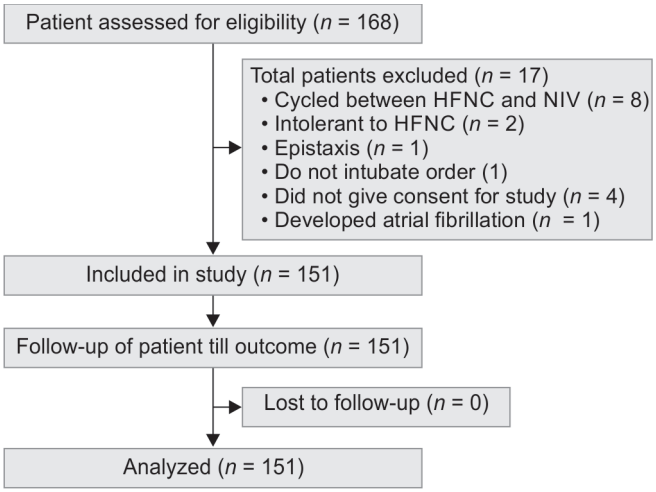

Fig. 1: Strengthening the reporting of observational studies in epidemiology (STROBE) diagram

The primary outcome of the present study was a comparison of MRIS and RIS to see which score has efficacy in predicting the outcome of HFNO therapy earlier. The secondary outcomes were to determine if any comorbid conditions or vasopressor support leads to a change in MRIS cut-off values and the clinical outcome of HFNO therapy. Goh et al. have reported sensitivity values between 55 and 85% for RIS and MRIS in predicting HFNO therapy success. Considering a 75% sensitivity, 75% specificity, and 50% prevalence, we estimated a sample size of 151 patients at 95% CI, 10% precision, and 5% dropout rate.

Statistical Analysis

Data was entered into Microsoft Excel and analyzed using the statistical package for the social sciences (SPSS) version 23. The continuous parametric data was reported as mean and standard deviation, while non-parametric data were reported as median. Nominal data was described using frequency and percentages and analyzed using the Chi-Square test or Fisher's Exact test as appropriate. Ordinal data were described using Median and IQR and analyzed using the Mann–Whiteney *U* test. A receiver operating characteristics (ROC) curve analysis was done to ascertain the predictive ability of RIS and MRIS, and cut-offs were determined using Youden's index method. A *p*-value of less than 0.05 was considered statistically significant.

Results

Initially, 168 patients were enrolled in the study; however, 17 patients were excluded for a variety of reasons: 8 patients were cycled between HFNO and NIV, two patients were intolerant to HFNO, one patient was terminated due to nose bleed, one patient had a DNI order, four patients relatives did not give consent for enrollment in the study, and one patient developed atrial fibrillation while in the intensive care unit (ICU) (Fig. 1). Finally, HFNO therapy was given to the remaining 151 patients. The most prevalent comorbidity among them was hypertension (46.35%), followed by diabetes (41.72%). Pneumonia was the most frequent etiology (54.96%) in the patients (Table 1).

Table 1: Patient's demographic data

Parameter	*Value*
Age (years)	60.15 ± 19.18
Weight (kg)	63.42 ± 10.76
Male	107 (70.86%)
Female	44 (29.13%)
Comorbidity	
HTN	70 (46.35%)
DM	63 (41.72%)
CAD	24 (15.89%)
CKD	15 (9.93%)
COPD	14 (9.27%)
AIDS	2 (1.32%)
Diagnosis	
Pneumonia	92 (54.96%)
ARDS	55 (36.42%)
Pulmonary edema	3 (1.98%)
Need for vasopressor support	
Yes	35 (23.17%)
No	116 (76.82%)
Clinical outcome of HFNC therapy	
Success	62 (41.05%)
Failure	89 (58.94%)

AIDS, acquired immune deficiency syndrome; ARDS, acute respiratory distress syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension

Over two-thirds of the patients required a FiO_2 of more than 50% at the beginning of HFNO therapy, with the median FiO_2 requirement being 45%. Before the start of HFNO therapy, the median respiratory rate (RR) was 26 breaths per minute. Thirty-five patients needed vasopressor assistance while receiving HFNC therapy. Of 151 patients, 62 (41.05%) of HFNO therapy were successful, while 89 (58.94%) failed and necessitated intubation.

Higher RIS and MRIS values were associated with HFNO therapy success, suggesting that patients with higher scores had better outcomes. HFNO failure was associated with lower median RIS and MRIS values compared to HFNO therapy success at different time intervals, suggesting a possible association between lower index values and HFNO therapy failure (Table 2).

The predictive abilities of MRIS and RIS at 1st hour for HFNO success were assessed. MRIS at 1 hour showed significant prediction with an area under the curve (AUC) of 0.790 (95% CI: 0.717–0.863, $p < 0.001$), indicating better performance than RIS at 1 hour, which had an AUC of 0.701 (95% CI: 0.617–0.786, $p < 0.001$) (Fig. 2). The ideal cut-off for RIS at 1 hour was determined as 4.36, with a sensitivity of 72.6% and a specificity of 53.9%. For MRIS at 1 hour, the ideal cut-off was 4.63, with a sensitivity of 74.2% and specificity of 69.7%.

The AUC for RIS and MRIS scores significantly differed at multiple follow-up times. At most intervals (1st, 2nd, 4th, and 6th), MRIS demonstrated higher AUC values than RIS. This indicates that MRIS had superior classifying power for predicting HFNO therapy outcomes at these intervals. However, there was no statistically significant difference between RIS and MRIS AUC values at the 12th, 24th, and 48th hours (Table 3). There was no significant difference in HFNO therapy outcomes in individuals with and without various

Table 2: ROX index score and MRIS in HFNO therapy success and failure groups at various time intervals

RIS and MRIS at different time interval	*HFNC Success/failure*					
	Failure			*Success*		
	Median	*First quartile*	*Third quartile*	*Median*	*First quartile*	*Third quartile*
RIS at 1 h	4.3	3.5	4.9	5.2	4.3	6.7
MRIS at 1 h	4.0	3.4	4.8	5.9	4.6	7.0
RIS at 2 h	4.1	3.4	4.6	5.1	4.4	6.5
MRIS at 2 h	3.9	3.2	4.5	6.3	4.7	7.3
RIS at 4 h	3.8	3.5	4.5	5.9	4.7	7.5
MRIS at 4 h	3.7	3.2	4.3	6.8	5.3	8.6
RIS at 6 h	3.7	3.2	4.4	6.2	5.3	7.8
MRIS at 6 h	3.5	3.0	4.2	6.6	5.4	8.8
RIS at 12 h	3.7	3.3	4.3	6.6	5.6	8.8
MRIS at 12 h	3.5	3.1	4.1	7.6	6.3	9.5
RIS at 18 h	3.5	3.1	3.9	7.6	5.8	9.2
MRIS at 18 h	3.3	2.8	3.7	8.5	5.9	10.4
RIS at 24 h	3.5	3.2	3.8	8.3	6.9	10.2
MRIS at 24 h	3.3	2.9	4.0	8.8	7.1	11.0
RIS at 48 h	3.5	3.2	3.9	9.5	7.7	11.1
MRIS at 48 h	3.3	3.0	3.9	10.0	8.6	12.9

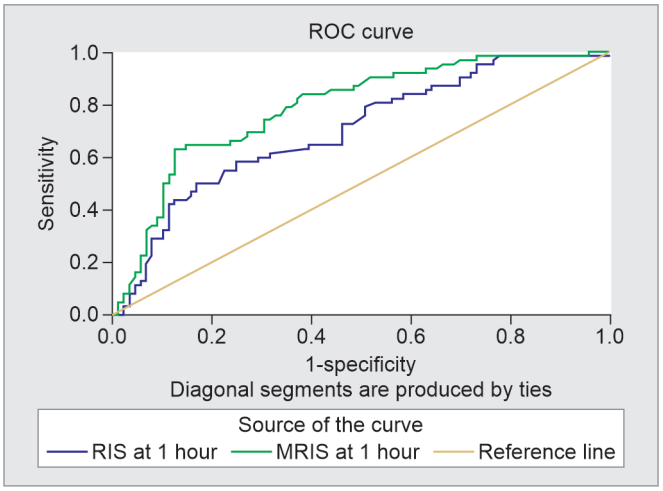

Fig. 2: ROX index score and MRIS after 1 hour of HFNO therapy

Table 3: ROC curve for ROX index score and MRIS according to HFNC outcome

Time interval	*Area under the curve (95% CI)*		*p-value*
	ROX	*ROX-HR*	
1 h	0.701 (0.617–0.786)	0.790 (0.717–0.863)	<0.001
2 h	0.769 (0.693–0.845)	0.827 (0.760–0.895)	0.001
4 h	0.834 (0.766–0.902)	0.885 (0.828–0.942)	0.003
6 h	0.865 (0.798–0.932)	0.895 (0.838–0.951)	0.029
12 h	0.877 (0.809–0.944)	0.899 (0.838–0.960)	0.060
18 h	0.930 (0.878–0.982)	0.953 (0.908–0.998)	0.064
24 h	0.929 (0.867–0.991)	0.906 (0.832–0.980)	0.349
48 h	0.970 (0.919–1.020)	0.970 (0.924–1.015)	1.000

comorbidities. However, individuals receiving vasopressor support had a higher proportion of treatment failure compared to those without vasopressor support ($p < 0.001$).

The multivariate linear regression analysis showed that age is consistently and significantly associated with decreased RIS and MRIS values at all time intervals. In contrast, sex was not a statistically significant covariate for either the RIS or MRIS score.

Discussion

In this study, we compared the usefulness of the Modified ROX Index score and the ROX Index score in predicting the results of HFNO therapy in patients with acute respiratory failure.

Initially introduced by Roca et al.,[8] the ROX index was considered a helpful assessment tool derived from non-invasive measurements and calculated as SpO_2/FiO_2 divided by respiratory rate. It provides a valuable indicator of oxygenation and respiratory effort. Goh et al.[4] conducted a study to assess the potential of the MRIS for early prediction of outcomes in patients receiving HFNO therapy. They concluded that the MRIS was superior to the RIS for early prediction of HFNO therapy outcome. We also observed similar results.

A previous study by Kansal et al.[9] study concluded that the ROX index might be more diagnostically accurate by including heart rate. An elevated heart rate is frequently seen as a reaction to heightened sympathetic drive during increased breathing. Tachycardia is a typical compensatory cardiovascular reaction to sustain cardiac output in situations of severe hypoxemia.

The evaluation of the RIS and MRIS in our study revealed that higher values were generally associated with HFNO therapy success, consistent with previous studies conducted by Goh et al.,[4] Li et al.,[10] and Webb et al.[11] These studies demonstrated the predictive capabilities of the ROX index and its modified versions in determining HFNO outcomes. However, our study expanded on these findings by examining the performance of the MRIS specifically at various time intervals. We observed that the AUC for MRIS was significantly higher than RIS up to 6 hour. This suggests that the MRIS has better predictive ability than the RIS during these intervals. However, there was no statistically significant difference between RIS and MRIS AUC values at the 12th, 18th, 24th, and 48th hours, indicating comparable performance between the two indexes at those time points.

In the present study, the efficacy of MRIS for prediction of HFNO outcome was earliest after 1 hour of initiation of therapy, which was found to be 2 hours in the previous study done by Goh et al.[4] According to a first study done on the ROX index by Roca et al.,[8] the cut-off values of ROX at 2 and 6 hours were 2.85 and 3.47, with good sensitivity (>95%) but poor specificity (<15%). When changes were added to the ROX index by adding heart rate into the equation, the modified ROX index cut-off values at 2 and 6 hours were found to be 4.5 and 5.0 with better specificity of 88% but less sensitivity of 34%. We also found higher sensitivity and specificity of MRIS than RIS for up to 6 h.

Our study results showed that the MRIS at 1 hour had a higher AUC than the RIS at 1 hour, indicating it to be a better indicator for HFNO therapy outcome as early as after 1 hour of HFNO initiation. It was found that RIS at 1 hour, the ideal cut-off is 4.36, where sensitivity is 72.6% and specificity is 53.9%, and MRIS at 1 hour, the ideal cut-off is 4.63, where sensitivity is 74.2% and specificity is 69.7%. In another study by Webb et al.[11] in the pediatric ICU population, an ROX-HR value of <3.0 was significantly associated with a higher risk of HFNO failure at 1 hour and 6 hours. Studies done by Li et al.[10] and Kansal et al.[9] used a different version of the Modified ROX index as mROX and Delta POX HR, which incorporated P/F ratio instead of S/F ratio into the equation, which required an invasive technique of repeated arterial blood sampling at regular intervals.

We also found that the presence or absence of particular comorbidities did not significantly affect the MRIS capacity to predict outcomes. However, we found an association between vasopressor support and the success of HFNO therapy, with vasopressor support recipients more likely to experience HFNO treatment failure.

The present study shows that the Modified ROX Index score can accurately predict the outcome of HFNO therapy. The results emphasize that it is critical to consider heart rate while evaluating oxygenation and respiratory effort.[12,13] However, this study had certain limitations. As this was a single-center study, the generalizability of the findings to other healthcare settings may be limited.

Partial pressure of oxygen (PaO_2) was not considered part of the modified ROX index equation. Additional studies are required to confirm these results in bigger and more varied patient populations.

Conclusion

The MRIS has higher efficacy in the early prediction of HFNO therapy outcomes as early as 1 hour into the initiation of therapy than the ROX Index score. The result of HFNO therapy has a negative relation in patients with ongoing vasopressor support. Furthermore, the presence of comorbidities does not have any effect on the MRIS cut-off value or the outcome of HFNO therapy.

Authors Contributions

Conceptualization: AGS,AS. Methodology: SM,AS, NK, SG. Formal analysis and investigation: SM, TM Writing—initial draft preparation: AGS, AS, NK, KK and TM. Writing—review and editing: all the authors. Supervision: PB,SG.

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