

Research Article

Predictive Accuracy of the ROX Index and HACOR Score for Non-Invasive Respiratory Support Failure in Critically Ill Patients: a Prospective Comparative Study

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Abstract

Background: Early identification of noninvasive respiratory support failure may help avoid delayed intubation. This study compared the predictive performance of the ROX index and HACOR score in critically ill patients with acute hypoxemic respiratory failure.

Methods: This prospective comparative study included 200 adults receiving high-flow nasal cannula or noninvasive ventilation. ROX and HACOR were calculated at initiation and after 2 hours. The primary outcome was endotracheal intubation within 48 hours.

Results: Support failure occurred in 75 (37.5%) patients. At 2 hours, ROX was lower and HACOR higher among patients requiring intubation. ROX showed greater discrimination than HACOR (AUROC 0.705 vs 0.604; $p=0.008$). After adjustment, higher 2-hour ROX remained associated with lower odds of failure (adjusted OR 0.79 per point, 95% CI 0.69-0.92; $p=0.002$), whereas HACOR was not independently associated with outcome.

Conclusion: Two-hour ROX outperformed HACOR for predicting early support failure.

Keywords: ROX Index, HACOR Score, High-Flow Nasal Cannula, Noninvasive Ventilation, Intubation.

INTRODUCTION

Acute hypoxemic respiratory failure is one of the most common reasons for admission to intensive care and often necessitates escalation of oxygen therapy or ventilatory support. High-flow nasal cannula (HFNC) and noninvasive ventilation (NIV) can be used to maximize oxygenation and minimize the need for immediate endotracheal intubation in the right patient. In the FLORALI trial, HFNC was shown to be associated with better 90-day survival than standard oxygen or NIV in patients with acute hypoxemic respiratory failure, but there was no significant difference between the groups in the primary intubation outcome [1]. NIV is also a well-established method of acute respiratory support in a number of clinical indications, and its efficacy is very dependent on the correct selection of patients and close monitoring [2].

The main problem with noninvasive respiratory support is the failure to recognize an inadequate response before significant deterioration occurs. There have been associations with poor outcomes when intubation is delayed following failure of HFNC. Kang et al. reported significantly higher mortality rates in the ICU for patients who were intubated after 48 hours of failed HFNC compared to those intubated earlier, and fewer ventilator-free days and lower rates of successful ventilator weaning [3]. It is clinically important, therefore, to identify patients at high risk of treatment failure within the first hours of support.

The respiratory rate-oxygenation (ROX) index was created as a simple bedside index that combines peripheral oxygen saturation, inspired oxygen concentration and respiratory rate. Roca et al. in the original study of patients

with acute hypoxemic respiratory failure due to pneumonia who received HFNC, found that a ROX score of ~ 4.88 at 12 hours was useful in predicting the outcome of HFNC, with higher scores associated with a greater likelihood of avoiding intubation [4]. It was subsequently validated in a multicentre study, which showed that its discriminatory performance improved with time, from an AUROC of 0.679 at 2 hours, to 0.703 at 6 hours and 0.759 at 12 hours. An elevated ROX value ≥ 4.88 at these time points was consistently linked to reduced risk of subsequent intubation [5].

Evidence from wider populations has been largely supportive of ROX as a helpful, but not perfect, predictor. In a systematic review and meta-analysis of patients with pneumonia and acute hypoxemic respiratory failure, ROX was found to have clinically relevant discrimination for HFNC outcome, and to show significant inter-study variation in optimal ROX thresholds and timing [6]. This variability implies that the dynamic assessment and validation of the tool in other patient groups may be more informative than using a single universal cut-off.

For patients treated with NIV, the heart rate, acidosis, consciousness, oxygenation, and respiratory rate (HACOR) score was developed to identify early treatment failure. The original HACOR score was derived and validated in hypoxemic patients undergoing NIV. The score had an AUROC of 0.88 for NIV failure at one hour, and a score >5 defined a high-risk population; in high-risk patients who went on to fail NIV, earlier intubation was associated with lower hospital mortality [7]. Unlike ROX, HACOR also includes arterial pH, neurological status, heart rate, oxygenation and respiratory frequency, which may reflect a wider range of physiological decline.

The HACOR concept has since been developed. Duan et al. assessed an updated score which added baseline clinical parameters to the original physiological parameters in a large prospective multicentre study. The new model was more successful in predicting NIV failure, especially after 1–2 hours of support [8]. These results further support the need to perform an early reassessment rather than relying only on measurements taken at the start.

ROX and HACOR were developed for different forms of noninvasive respiratory support and are very different in complexity. ROX uses only routine non-invasive measurements, while HACOR uses arterial blood gas and neurological data. There is limited direct comparative data

between the two scores in heterogeneous critically ill patients who are treated with either HFNC or NIV. In addition, it remains unclear whether the measurements taken early after treatment initiation offer greater discrimination than baseline values in a heterogeneous population of patients with acute hypoxemic respiratory failure.

The present study thus compared the predictive value of the ROX index and the HACOR score at the time of initiation and 2 hours after the start of noninvasive respiratory support in critically ill adults with acute hypoxemic respiratory failure. Their predictive accuracy for endotracheal intubation within 48 hours was assessed overall and according to respiratory-support modality, as well as the independent association of the two-hour scores after adjustment for the severity of illness and clinical diagnosis.

PATIENTS AND METHODS

Study design and participants

A prospective observational comparative study was conducted in the adult intensive care unit of Medicovert Hospitals, Hyderabad, India, during 2026. Eligible patients were consecutive patients ≥ 18 years old with acute hypoxemic respiratory failure requiring high-flow nasal cannula (HFNC) or noninvasive ventilation (NIV; continuous or bilevel positive airway pressure). Patients who needed immediate endotracheal intubation, who had a do-not-intubate or other treatment-limitation order, who had a pre-existing tracheostomy, who were only receiving noninvasive support for routine post-extubation prophylaxis, who had prolonged support before referral, or who had unavailable measurements or unavailable 48-hour outcome ascertainment were excluded. A total of 200 patients met the analytical criteria out of 218 screened. HFNC/NIV was not allocated by randomisation but depended on the clinical condition. Each patient contributed a single index episode of respiratory support.

Clinical assessment and respiratory-support measurements

Demographic data, smoking history, comorbidities, primary respiratory diagnosis, Sequential Organ Failure Assessment (SOFA) score at admission, Acute Physiology and Chronic Health Evaluation II (APACHE II) score (when available), use of vasopressors and serum lactate levels were recorded. The settings for HFNC flow and NIV mode and pressure were recorded where appropriate. Physiological parameters measured at the time of initiation of support (T0) and about 2 hours

later (T2h) included heart rate, respiratory rate, blood pressure, peripheral oxygen saturation (SpO₂), fraction of inspired oxygen (FiO₂), arterial pH, PaO₂, PaCO₂, and Glasgow Coma Scale (GCS) score. The mean arterial pressure was calculated as (systolic pressure + 2 × diastolic pressure)/3, while the PaO₂/FiO₂ and SpO₂/FiO₂ ratios were obtained using values measured at the same time. FiO₂ was represented as a decimal fraction. The analytical cohort had complete measures required for both scores and the primary endpoint.

Calculation of ROX and HACOR scores

The ROX index was calculated as (SpO₂ [%]/FiO₂)/respiratory rate (breaths/min). The original five-component HACOR score (range 0–25) comprised heart rate, arterial pH, consciousness, oxygenation, and respiratory rate. Heart rate >120 beats/min contributed 1 point; otherwise, 0. Arterial pH contributed 0, 2, 3, or 4 points for ≥7.35, 7.30–<7.35, 7.25–<7.30, and <7.25, respectively. GCS of 15, 13–14, 11–12, and ≤10 contributed 0, 2, 5, and 10 points; PaO₂/FiO₂ of ≥201, 176–200, 151–175, 126–150, 101–125, and ≤100 mmHg contributed 0, 2, 3, 4, 5, and 6 points; and respiratory rates of ≤30, 31–35, 36–40, 41–45, and ≥46/min contributed 0, 1, 2, 3, and 4 points. ROX and HACOR were calculated at T0 and T2h. Changes were defined as the 2-hour value minus the baseline value.

Study outcomes

The primary outcome was failure of noninvasive respiratory support, which was defined as endotracheal intubation and invasive mechanical ventilation within 48 hours after starting HFNC or NIV. Escalation from HFNC to NIV without intubation was not defined as failure. For patients who had the primary outcome, time from initiation of support to intubation was recorded. Secondary outcomes were ICU, hospital and 28-day mortality, length of stay in the ICU and hospital, duration of noninvasive support and escalation from HFNC to NIV. The 2-hour score assessments were the primary diagnostic exposures, while baseline scores and early changes were secondary predictors.

Statistical analysis

Data for continuous variables were presented as mean ± SD or median [IQR] and for categorical variables as n (%). Welch's t test or Mann–Whitney U test was used for continuous variables, and χ² or Fisher's exact test was used for categorical variables to compare success and failure groups.

Receiver operating characteristic analysis was used to assess the diagnostic performance of ROX and HACOR at baseline and 2 hours for predicting intubation within 48 hours. ROX was reverse-coded because lower scores represent a higher risk of failure. The AUROCs were calculated with 95% bootstrap confidence intervals, exploratory cut-offs were determined by the Youden index, and paired AUROCs were compared by the DeLong test.

Multivariable logistic regression models were used to assess 2-hour ROX and HACOR, both after adjustment for age, admission SOFA score, respiratory-support modality and primary diagnosis. Odds ratios were reported with 95% confidence intervals. Modality-specific AUROCs and Kaplan–Meier assessment of intubation-free survival were performed for exploratory analyses. Available observations were analyzed without imputation. All tests were two-sided and p<0.05 was considered significant.

RESULTS

Participant characteristics

Of 218 patients screened, 200 were included in the analysis; 125 (62.5%) did not require invasive ventilation and 75 (37.5%) underwent intubation within 48 hours of starting noninvasive respiratory support. High-flow nasal cannula (HFNC) was used in 105 (52.5%) patients and noninvasive ventilation (NIV) in 95 (47.5%). Pneumonia was the most frequent diagnosis, accounting for 82 (41.0%) patients. Compared with the success group, patients experiencing support failure had greater admission illness severity and more frequent vasopressor use (Table 1).

Physiological response and score distributions

At two hours, respiratory rates and oxygen requirements remained higher among patients who subsequently required intubation. ROX was lower and HACOR was higher in the failure group, with overlapping individual score distributions (Figure 2). The change in ROX over the first two hours differed between groups, whereas change in HACOR did not show a statistically significant between-group difference (Table 2).

Diagnostic discrimination

At two hours, ROX showed greater discrimination for 48-hour support failure than HACOR (AUROC 0.705 versus 0.604; paired DeLong z = 2.65, p = 0.008). ROC curves are shown in Figure 1, with detailed operating characteristics, study-derived thresholds, and paired comparisons presented in Tables 3 and

4. Improvement in discrimination from baseline to two hours was observed for ROX but not HACOR.

Adjusted associations and clinical outcomes

In separate multivariable models, higher two-hour ROX remained associated with lower odds of support failure, whereas the corresponding association for HACOR was not statistically

significant after adjustment. Baseline SOFA score was associated with support failure in both models (Table 5). Exploratory modality-specific analyses showed broadly similar AUROCs for ROX within HFNC and NIV groups (Table 6). ICU length of stay was longer among patients requiring intubation, and 28-day mortality occurred in 12 (6.0%) patients overall.

Tables

Table 1. Baseline demographic and clinical characteristics

Characteristic	Success (n = 125)	Failure (n = 75)	Statistic	p
Age (years)	57.3 ± 15.8	59.6 ± 14.1	t=-1.05	0.293
BMI (kg/m ²)	26.1 ± 3.9	26.3 ± 3.9	t=-0.36	0.723
Sex			χ²=0.19	0.659
Male	72 (57.6)	40 (53.3)	—	—
Female	53 (42.4)	35 (46.7)	—	—
Primary diagnosis			χ²=8.78 (permutation)	0.178
Pneumonia	52 (41.6)	30 (40.0)	—	—
ARDS	14 (11.2)	19 (25.3)	—	—
Sepsis-associated hypoxemia	17 (13.6)	10 (13.3)	—	—
Cardiogenic pulmonary edema	16 (12.8)	5 (6.7)	—	—
COPD exacerbation with hypoxemia	9 (7.2)	5 (6.7)	—	—
Aspiration	10 (8.0)	4 (5.3)	—	—
Other	7 (5.6)	2 (2.7)	—	—
Respiratory support			χ²=2.03	0.154
HFNC	71 (56.8)	34 (45.3)	—	—
NIV	54 (43.2)	41 (54.7)	—	—
Diabetes mellitus	42 (33.6)	21 (28.0)	χ ² =0.45	0.504
COPD history	25 (20.0)	14 (18.7)	χ ² =0.00	0.963
Chronic heart disease	26 (20.8)	13 (17.3)	χ ² =0.17	0.678
Vasopressor use	7 (5.6)	12 (16.0)	χ ² =4.75	0.029
Admission SOFA	5.1 ± 2.0	6.5 ± 2.2	t=-4.39	<0.001
APACHE II	14.9 ± 5.0	16.8 ± 6.1	t=-2.24	0.027
Serum lactate (mmol/L)	1.5 [1.1–1.9]	1.7 [1.2–2.2]	U=3618.0	0.035

Values are mean ± SD, median [IQR], or n (%). For binary variables, the reported category is "Yes." APACHE II was available in 118/125 and 72/75 patients, and lactate in 121/125 and 73/75. Between-group tests were Welch t,

Mann–Whitney U, χ² or permutation χ² as indicated. ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; SOFA, Sequential Organ Failure Assessment.

Table 2. Physiological measures, score evolution and selected clinical outcomes

Parameter	Success (n = 125)	Failure (n = 75)	Statistic	p
At initiation (T0)				
Heart rate (beats/min)	104.6 ± 12.4	106.0 ± 15.1	t=-0.67	0.503
Respiratory rate (breaths/min)	27.6 ± 4.3	30.0 ± 4.0	t=-3.93	<0.001
FiO ₂ (fraction)	0.55 ± 0.10	0.60 ± 0.10	t=-3.53	<0.001
PaO ₂ /FiO ₂ (mmHg)	170.3 ± 34.0	162.8 ± 36.5	t=1.45	0.149
Arterial pH	7.37 ± 0.04	7.36 ± 0.04	t=0.68	0.495
ROX index	6.7 ± 2.1	5.6 ± 1.6	t=4.21	<0.001

HACOR score	4.0 ± 2.6	4.7 ± 2.7	t=-1.82	0.070
At 2 hours (T2h)				
Heart rate (beats/min)	100.4 ± 15.2	103.8 ± 16.6	t=-1.47	0.144
Respiratory rate (breaths/min)	24.8 ± 5.2	27.9 ± 4.6	t=-4.35	<0.001
FiO ₂ (fraction)	0.50 ± 0.10	0.56 ± 0.10	t=-4.38	<0.001
PaO ₂ /FiO ₂ (mmHg)	201.9 ± 45.1	180.1 ± 46.7	t=3.23	0.002
Arterial pH	7.38 ± 0.05	7.37 ± 0.04	t=1.48	0.140
ROX index	8.5 ± 3.3	6.5 ± 2.3	t=5.08	<0.001
HACOR score	2.5 ± 2.5	3.5 ± 2.8	t=-2.52	0.013
Change from baseline				
ΔROX (T2h – T0)	1.9 ± 1.7	1.0 ± 1.0	t=4.80	<0.001
ΔHACOR (T2h – T0)	-1.5 ± 1.8	-1.2 ± 1.9	t=-1.07	0.286
Clinical outcomes				
ICU stay (days)	7.4 [6.0–8.8]	11.2 [9.6–12.9]	U=1140.5	<0.001
28-day mortality, n (%)	3 (2.4)	9 (12.0)	OR 0.18	0.011

Continuous variables are mean ± SD or median [IQR]. Between-group comparisons used Welch t or Mann–Whitney U tests; 28-day mortality used Fisher’s exact test. Δ denotes the two-

hour minus baseline value. A positive ΔROX represents improvement, whereas a negative ΔHACOR represents improvement. FiO₂ is reported as a decimal fraction.

Table 3. Diagnostic accuracy for predicting intubation within 48 hours

Predictor	AUROC (95% CI)	Cutoff	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	Youden J
ROX baseline	0.668 (0.600–0.739)	≤ 6.20	76.0	54.4	50.0	79.1	0.304
HACOR baseline	0.590 (0.514–0.675)	≥ 5	61.3	60.8	48.4	72.4	0.221
ROX at 2h	0.705 (0.637–0.773)	≤ 7.03	74.7	67.2	57.7	81.6	0.419
HACOR at 2h	0.604 (0.531–0.684)	≥ 3	62.7	57.6	47.0	72.0	0.203
ΔROX	0.681 (0.608–0.751)	≤ 0.95	66.7	67.2	54.9	77.1	0.339
ΔHACOR	0.543 (0.457–0.624)	≥ -2	78.7	28.0	39.6	68.6	0.067

Thresholds maximize Youden’s index in this cohort and are exploratory. Lower ROX or ΔROX and higher HACOR or ΔHACOR indicate greater failure risk. The positive outcome is

endotracheal intubation within 48 hours. AUROC, area under the receiver operating characteristic curve; PPV/NPV, positive/negative predictive value.

Table 4. Paired AUROC comparisons using DeLong’s test

Paired comparison	AUROC 1	AUROC 2	Difference	z	p
ROX 2h vs HACOR 2h	0.705	0.604	+0.101	2.65	0.008
ROX baseline vs HACOR baseline	0.668	0.590	+0.078	2.12	0.034
ROX baseline vs ROX 2h	0.668	0.705	-0.037	-2.10	0.036
HACOR baseline vs HACOR 2h	0.590	0.604	-0.014	-0.53	0.596

Difference is AUROC of Score 1 minus AUROC of Score 2; paired two-sided DeLong tests use the same participants.

Table 5. Multivariable predictors of 48-hour support failure

Predictor	Adjusted OR (95% CI)	z	p
Model A: ROX at 2 h			
ROX at 2 h, per point	0.79 (0.69–0.92)	-3.09	0.002
Age, per 10 years	1.13 (0.92–1.38)	1.19	0.235
SOFA, per point	1.20 (1.02–1.42)	2.20	0.028
NIV vs HFNC	1.72 (0.91–3.25)	1.66	0.096
Pneumonia vs other diagnoses	0.95 (0.49–1.84)	-0.15	0.884

Cardiogenic edema vs other	0.76 (0.23–2.55)	-0.44	0.660
Model B: HACOR at 2 h			
HACOR at 2 h, per point	1.09 (0.97–1.23)	1.43	0.153
Age, per 10 years	1.12 (0.92–1.36)	1.09	0.275
SOFA, per point	1.31 (1.12–1.53)	3.42	<0.001
NIV vs HFNC	1.50 (0.80–2.79)	1.27	0.203
Pneumonia vs other diagnoses	0.92 (0.48–1.76)	-0.24	0.807
Cardiogenic edema vs other	0.58 (0.18–1.85)	-0.92	0.360

Separate logistic models each included age, admission SOFA, support modality, and diagnosis-group indicators (pneumonia; cardiogenic pulmonary edema), using other diagnoses as reference. Model A AUROC =

0.746, McFadden $R^2 = 0.129$; Model B AUROC = 0.699, McFadden $R^2 = 0.094$. Intercepts omitted. OR >1 indicates higher odds of support failure.

Table 6. Exploratory diagnostic discrimination by respiratory-support modality

Modality	Score at 2 h	n	Failures, n (%)	AUROC (95% CI)
HFNC	ROX 2h	105	34 (32.4)	0.712 (0.598–0.808)
HFNC	HACOR 2h	105	34 (32.4)	0.597 (0.469–0.726)
NIV	ROX 2h	95	41 (43.2)	0.706 (0.601–0.801)
NIV	HACOR 2h	95	41 (43.2)	0.603 (0.495–0.722)

Stratum-specific AUROC confidence intervals were obtained by stratified resampling. HFNC and NIV represent clinically selected treatment

modalities; between-modality differences were not formally tested.

Figures

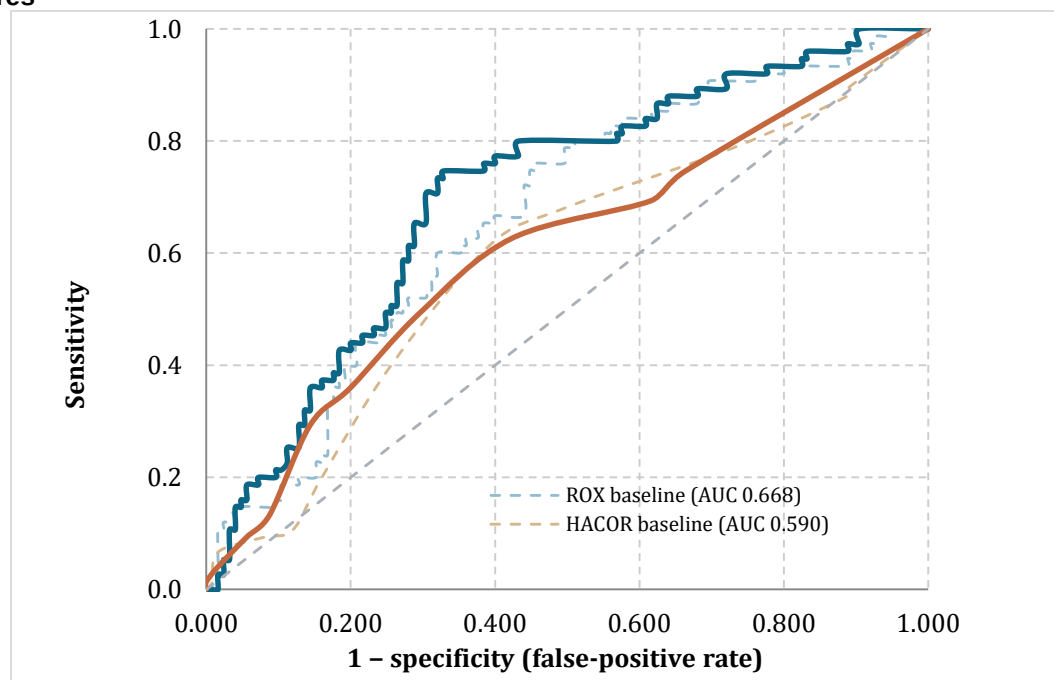


Figure 1. ROC curves of baseline and two-hour ROX index and HACOR score for predicting invasive intubation within 48 hours.

The ROC curves compare discrimination at initiation and two hours after starting respiratory support. A higher ROX score indicates lower failure risk and is reverse-coded

for the ROC analysis; a higher HACOR score indicates higher failure risk. The dotted line denotes chance discrimination.

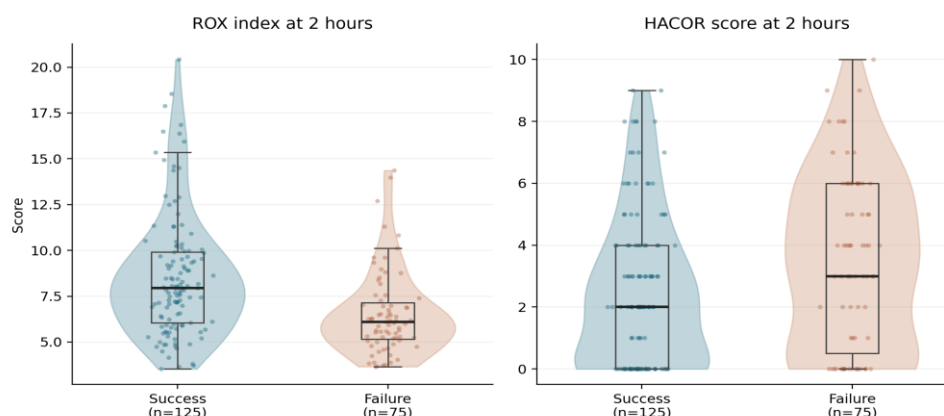


Figure 2. Distribution of two-hour ROX and HACOR scores by 48-hour respiratory-support outcome.

Violin plots show the distributions of individual scores with overlaid boxplots (medians and interquartile ranges) and patient observations. Lower ROX values and higher HACOR values were observed among patients who required invasive intubation within 48 hours.

DISCUSSION

Among the 200 patients who received noninvasive respiratory support in this prospective comparative study of critically ill patients, 37.5% needed intubation within 48 hours. The main result was that the ROX index at 2 hours had a higher AUROC than the HACOR score (0.705 vs 0.604; $p=0.008$) for discriminating support failure. ROX discrimination improved significantly from baseline to 2 hours, while HACOR discrimination did not show much improvement over time. Each 1-point increase in 2-hour ROX was independently associated with reduced odds of failure (adjusted OR 0.79), and HACOR was not independently associated with outcome. ROX discrimination was seen within both HFNC and NIV subgroups.

The results are similar to those of Praphruekit et al., who performed a prospective study of 75 ED patients with acute hypoxemic respiratory failure (AHRF) who received HFNC. Treatment failed in 30.7%, and ROX was significantly superior at 1 hour, 2 hours and 6 hours; the AUROCs were 0.784 for ROX and 0.690 for HACOR at 2 hours. ROX was still independently associated with the success of HFNC, and its performance was further improved after 6 hours, with the AUROC being 0.853 [9]. The present results corroborate this finding in HFNC and demonstrate similar ROX discrimination in patients on NIV.

There has also been evidence of the use of ROX during NIV. In a study of 441 patients who were receiving NIV for COVID-19 pneumonia, Anand

et al. found that 59.4% of these patients failed NIV. A ROX >4.47 was an independent predictor of a significantly decreased risk of failure (OR 0.15), and age >60 years and SOFA score also remained significant. The AUC for ROX discrimination rose from 0.84 on day 1 to 0.94 on day 3, whereas HACOR rose from 0.79 to 0.92 [10]. While the population and timing of assessments in both studies were very different from those used in our study, both studies indicate that ROX can be a prognostic tool during NIV and not limited to the use of HFNC.

But not every comparison is in ROX's favour. Uysal et al. performed a prospective study of 127 patients with acute hypoxemic respiratory failure who were treated in the ED with NIV alone; 52.0% failed NIV within 24 hours. At 1 hour, HACOR had an AUC of 0.878, which was better than baseline HACOR, ROX-based measures, and change in ROX. A HACOR score >5 had a sensitivity of 96.7% and a negative likelihood ratio of 0.05 [11]. This is in contrast to our results, which demonstrated only modest 2-hour HACOR discrimination, and HACOR was not statistically significant after adjustment. The discrepancy may be due to differences in treatment modality, definition of failure, disease spectrum, timing and prevalence of acidosis or altered consciousness.

The performance of HACOR may also vary according to the clinical phenotype. Chong et al. reported a failure rate of 24.4% for 221 patients with acute cardiogenic pulmonary edema who were treated with NIV. The AUC of a HACOR score >5 at 1 hour was 0.73, with 53.7% sensitivity and 83.2% specificity. Importantly, other variables were also found to contribute to failure risk, such as acute coronary syndrome, acute kidney injury, underlying heart failure, and the ROX index [12]. Cardiogenic pulmonary oedema was a

minority of cases in our cohort, and pneumonia and ARDS occurred more often; therefore, a score heavily weighted towards acidosis and consciousness may not have been as discriminatory across this diverse group.

Early reassessment of ROX has been shown time and time again in populations treated with HFNC. Zucman et al. analysed 62 patients with COVID-19-associated acute hypoxemic respiratory failure who were treated with nasal high flow; 39 of 60 evaluable patients ended up on mechanical ventilation. Within the first 4 hours, a ROX ≥ 5.37 was associated with a lower subsequent intubation risk (HR 0.59), AUROC 0.75 and specificity 83% [13]. Likewise, in a study by Chandel et al., 272 patients who received HFNC for COVID-19 respiratory failure were studied and 60.3% were successfully weaned. A ROX value >3.0 at 2, 6, and 12 hours was 85.3% sensitive for subsequent HFNC success [14]. The present finding of more useful data from reassessment after the start of support is supported by these data.

However, the optimum time and threshold seems to depend on the population. Ferrer et al. conducted a prospective study of 85 patients who were treated with HFNC for SARS-CoV-2 pneumonia, with 55.3% of those patients experiencing treatment failure. ROX at 24 hours had the highest AUROC of 0.826, and a cutoff of 5.35 was the most discriminatory with 91% sensitivity and 79% specificity and was the strongest predictor in multivariable analysis [15]. The threshold of ROX ≤ 7.03 derived in our study may not be directly comparable with later thresholds derived in pneumonia-dominant populations, and should be considered cohort specific.

Lemiale et al. demonstrate the pitfalls of using a universal ROX threshold in 302 immunocompromised patients who were receiving HFNC. Intubation was performed in 38.1%, and 6-hour ROX was significantly lower in intubated patients, but had only moderate discrimination (AUROC 0.623). The previously suggested threshold of 4.88 had low sensitivity and specificity, but higher ROX was still independently associated with lower odds of intubation (OR 0.89) [16]. This heterogeneity further emphasizes the importance of using ROX as a dynamic risk marker, not simply as a binary trigger for intubation.

The observed improvement in ROX from baseline to 2 hours is also clinically relevant. The patients who went on to success experienced a greater increase in ROX than those who failed, while there was no significant

difference between the groups with regard to change in HACOR. Improvement may be due to a decrease in the FiO_2 requirement and respiratory rate at the same time, due to the integration of both parameters in ROX. However, several HACOR components, such as consciousness and arterial pH, are relatively stable in patients with predominantly hypoxemic, as opposed to hypercapnic, respiratory failure and may not be as responsive to scoring during the short term.

Severity of illness was still significant when both bedside scores were used. In both multivariable models, admission SOFA was significantly associated with support failure, and patients who failed support were more likely to require vasopressors, to have longer ICU stays, to have higher APACHE II scores, and to die within 28 days. This means that the results of ROX or HACOR should not be considered in isolation from the overall clinical setting. Underlying organ dysfunction and diagnosis remain important in escalation decisions, although bedside scores may help to guide early reassessment.

The present study has several strengths: prospective data collection, calculation of both scores at the same time in the same patients, direct paired comparison of AUROCs, and inclusion of both HFNC and NIV. Using separate adjusted models also decreased the collinearity between competing scores. Some limitations are: single-centre design, non-random allocation of respiratory-support modality, heterogeneous causes of hypoxemic respiratory failure, and derivation of thresholds within the same cohort. Only a 2-hour early reassessment was prespecified, and later changes could not be assessed. In addition, the definition of support failure was limited to intubation within 48 hours, and outcomes could vary if mortality or subsequent intubation are included in composite failure endpoints.

The results are overall favorable for the use of the ROX index as a readily available bedside tool for risk stratification during noninvasive respiratory support. Its discrimination was superior to HACOR in this cohort, improved after 2 hours and was similar within HFNC and NIV groups, suggesting potential use outside its original HFNC application. However, the moderate AUROC and inter-population variability suggest that ROX is not a substitute for clinical assessment and accepted measures of illness severity.

CONCLUSION

The ROX index assessed two hours after initiation of noninvasive respiratory support showed better discrimination for 48-hour intubation than the HACOR score and remained independently associated with support failure after adjustment for clinical severity and diagnosis. Early reassessment of ROX may therefore provide a simple adjunct for identifying patients at increased risk of noninvasive respiratory support failure.

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