

Comparison of Predictive Validity of the ROX Index and the m-ROX Index for the HFNC Outcome in ICU Patients with AHRF

Dan-Dan Liu^{1,2}, Jia-Li Pan^{1,2}, Ming-Yue Miao^{2,3}, Yue-Fu Wang^{1,2}, Hong-Liang Li^{2,3}, Jian-Xin Zhou²

¹Department of Surgical Intensive Care Unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, 100038, China.

²Emergency and Critical Care Medical Center, Beijing Shijitan Hospital, Capital Medical University, Beijing, 100038, China.

³Department of Intensive Care Unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, 100038, China.

First author

Dan-Dan Liu, Emergency and Critical Care Medical Center, Department of surgical intensive care unit, Beijing Shijitan Hospital, Capital Medical University, Beijing, 100038, China.
Email: ldd3967@163.com

Corresponding author

Jian-Xin Zhou, Emergency and Critical Care Medical Center, Beijing Shijitan Hospital, Capital Medical University, Beijing, 100038, China.
Email: zhoujx@icloud.com

Abstract

Objective:

To compare the predictive validity of ROX index and m-ROX index for high-flow nasal cannula (HFNC) outcomes in patients with acute hypoxia respiratory failure (AHRF) admitted to the intensive care unit (ICU).

Methods:

All adult patients who received HFNC therapy due to AHRF at Beijing Shijitan Hospital's ICUs from May 2022 to May 2024 were analyzed. Heart rate, peripheral oxygen saturation, fraction of inspiration oxygen, and respiratory rate were collected at 0.5 hours, 6 hours, 12 hours, 18 hours, and 24 hours after HFNC initiation through electronic medical records to calculate the ROX index and m-ROX index. Predictive validity of the two indices to HFNC outcome were analyzed by ROC curve, and the diagnostic efficacy in actual clinical application was compared through clinical decision curve analysis(DCA).

Results:

After 1:1 PSM matching, a total of 100 patients were included in the analysis, with 50 patients in the succeed group and 50 in the failed group. ROC analysis revealed that the predictive validity of both the ROX index(AUROC 0.76, cut-off value 5.7,sensitivity 0.88, specificity 0.57) and m-ROX index (AUROC 0.79, cut-off value 7,sensitivity 0.78, specificity 0.77) after 6 hour of HFNC initiation were acceptable, and improved over time. No statistical difference in predictive validity between the two indices($p>0.05$). The cut-off value for the ROX index varied at subsequent monitoring points(H12: 6.9; H18: 6.25; H24: 6.25), whereas the cut-off values for the m-ROX index remained relatively stable(H12: 7; H18: 7; H24: 6).

DCA analysis demonstrated that both indices exhibited strong predictive validity within the threshold probability range of 0.3 to 1.0. At a threshold probability of 0.6, the m-ROX index displayed equivalent predictive validity to that of the ROX index.

Conclusions: both ROX index and m-ROX index had strong predictive validity for the HFNC outcome.

Key words: high flow nasal cannula, acute hypoxia respiratory failure, ROX index, m-ROX index

Introduction

The high-flow nasal cannula (HFNC) is extensively utilized in patients experiencing acute hypoxic respiratory failure (AHRF), particularly during and following the COVID-19 pandemic [1]. Studies have shown that, in subgroups of patients with arterial partial pressure of oxygen/fraction of inspiration oxygen ($\text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$) and/or those who cannot tolerate non-invasive mechanical ventilation or standard oxygen therapy, HFNC could improve clinical outcomes such as decrease in length of mechanical ventilation, rates of intubation, and mortality [2,3]. The primary issue in managing HFNC in AHRF patients is the prediction of success and/or failure of HFNC.

Apart from simple indices such as respiratory rate (RR) and tidal volume, an integrated index of ROX (first proposed by a 4-year multi-centre study, defined as the peripheral oxygen saturation (SpO_2)/ FiO_2 /RR) has been introduced to predict the outcome of HFNC [4-7]. The studies showed a moderate-to-good prediction efficacy of ROX in identifying patients at a higher risk of HFNC failure. Additionally, the optimal cut-off value was diverse in the above mentioned studies.

The ROX index is designed to assess the outcome of HFNC therapy using simple and readily available clinical parameters. In ICU, vital signs monitored at the bedside include heart rate (HR), RR, SpO_2 , and blood pressure. However, despite continuous monitoring, these data often exhibit a poor normal distribution [8], which may account for the variability in cut-off values of the ROX index reported in previous studies. In cases of acute hypoxia, HR tends to increase alongside changes in SpO_2 and RR [9]. HR can serve as an important indicator for risk stratification across various clinical scenarios, including sepsis and COVID-19 patients. Furthermore, models that incorporate temperature, blood pressure, and partial pressure of carbon dioxide (PaCO_2) can be utilized for prognostic evaluation and guiding fluid resuscitation efforts [10,11]. The combination of HR, RR, and SpO_2 within this index may also hold predictive value regarding the prognosis of patients in surgical ICUs [12].

In studies of HFNC, there is an index combined three vital signs (HR, RR and SpO_2). A modified ROX incorporating heart rate ($\text{ROX-HR} \times 100$) has recently been introduced to improve diagnostic performance in detecting HFNC failure [13]. Limited data have shown that the modified-ROX (m-ROX) index might be a promising tool in the early identification of HFNC failure [13,14].

Hence, we hypothesized that the m-ROX index would have the same diagnostic validity as the ROX index for the HFNC outcome in the ICU, and tested in this study.

Materials and Methods

This retrospective study analyzed all adult patients with AHRF who received HFNC therapy and remained in the ICU for more than 24 hours at Beijing Shijitan Hospital, Capital Medical University between May 2022 and May 2024. Ethical approval was obtained from the Ethics Committee of Beijing Shijitan Hospital, Capital Medical University. Given the nature of this study, the informed consent process was waived.

Inclusion criteria were: patients aged 18 years or older who received HFNC therapy due to AHRF and had an ICU length of stay (LOS) of at least 24 hours. Exclusion criteria were: patients who refused

tracheal intubation after HFNC failure, patients who were discharged voluntarily or received palliative care, and patients with incomplete data.

The primary endpoint was the outcome of HFNC therapy. HFNC failure was defined as the need to switch to invasive or non-invasive mechanical ventilation.

Data were collected from the electronic medical record system and included the following: patient baseline characteristics (age, gender, diagnosis, concurrent chronic diseases, and whether surgery was performed); HR, SpO₂, FiO₂, and RR at 0.5, 6, 12, 18, and 24 hours after HFNC initiation. The ROX index and modified ROX (m-ROX) index were calculated using the average of 10 consecutive values obtained after stabilization of HR, SaO₂, and RR. The arterial blood gas analysis indicators (PaCO₂, PaO₂, and lactate (Lac)) were assessed at the corresponding monitoring time points. Additionally, data on FiO₂ and flow rate of HFNC were collected. Furthermore, outcomes of HFNC therapy (categorized as success or failure) along with other prognostic indicators were also documented (length of hospital stay, ICU LOS, HFNC therapy time, mechanical ventilation time, 28-day mortality, and 60-day mortality).

Statistical analysis

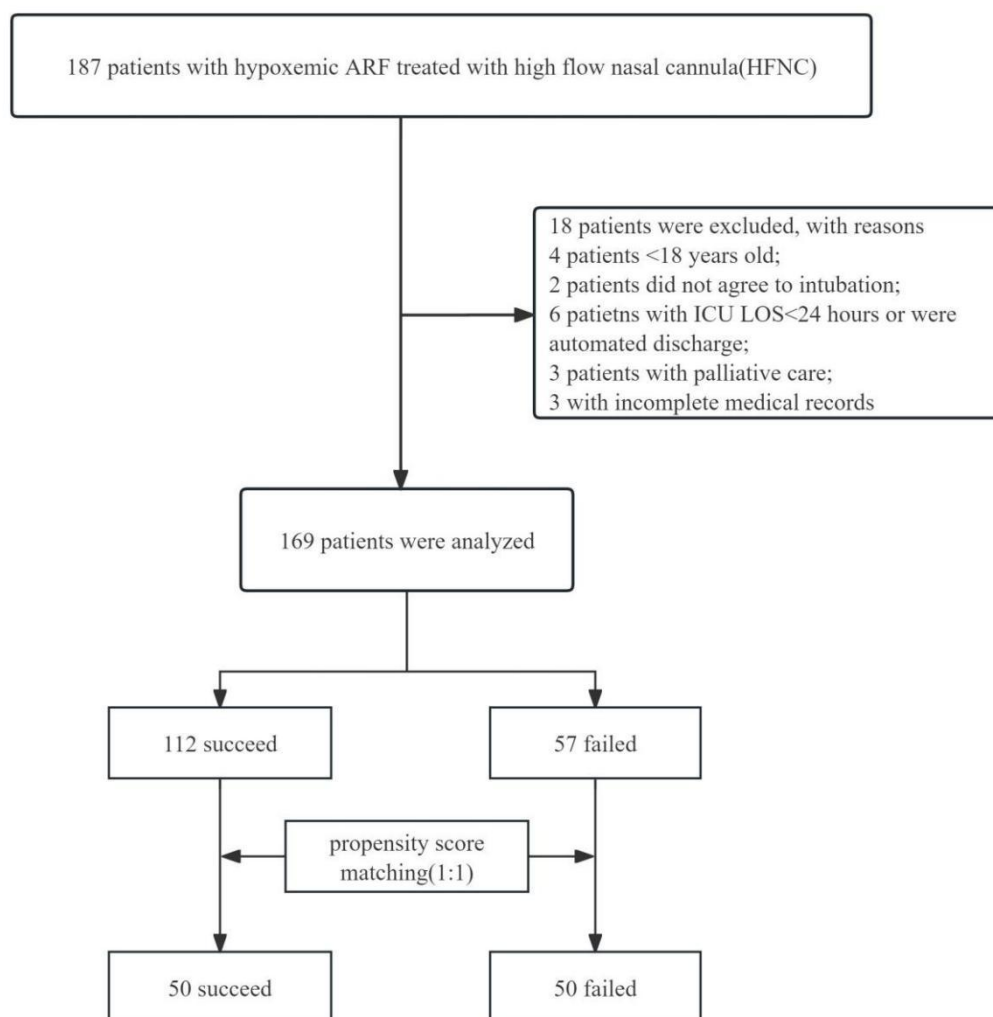
The data were analyzed using R. The Kolmogorov-Smirnov test was employed to assess the normality of continuous variables. Continuous variables with a normal distribution were presented as mean $\pm$ standard deviation (SD), while those with a non-normal distribution were presented as median and interquartile range (IQR). Categorical data were summarized as frequency and percentage. Propensity score matching (PSM) was performed to minimize the bias in this retrospective analysis. PSM was conducted using age and APACHE II score as covariates, employing the nearest neighbor matching method at a 1:1 ratio and a caliper value of 0.1. The standardized mean difference (SMD) was calculated to evaluate the balance of covariates between the groups before and after matching. SMD is defined as the absolute value of the difference in means or proportions divided by the square root of the pooled variance [15]. An SMD < 0.25 indicates an acceptable balance of baseline covariates between the two groups [16].

For statistical comparisons, continuous variables with a normal distribution were analyzed using independent t-test, while non-normal distribution variables were analyzed using non-parametric tests. Categorical data were compared using the χ^2 test or Fisher's exact test. The area under the ROC curve (AUROC), threshold, sensitivity, specificity, NPV and PPV of the two indices were evaluated through ROC curve analysis. Additionally, the diagnostic efficacy of the two indexes in real-world clinical application was compared using clinical decision curve analysis (DCA).

Results

A total of 187 patients with AHRF were admitted to the ICU and received HFNC therapy during the selected research period. After excluding 18 patients (4 under the age of 18, 2 who refused endotracheal intubation, 6 who were discharged voluntarily or stayed in the ICU for less than 24 hours, 3 who received palliative care, and 3 with incomplete case data), 169 patients (112 in the HFNC success group and 57 in HFNC failure group) were included. Following 1:1 matching, a total of 100 patients (50 in the HFNC success group and 50 in HFNC failure group) were included in the final analysis (Fig. 1).

Fig. 1 Flow diagram of the study participant



Before PSM, significant differences were observed in age, patient source, and APACHE II score. After PSM, the SMD of age and internal medicine patients was less than 0.25, and the SMD of APACHE II score and postoperative surgical patients decreased, indicating that the baseline data of patients after matching were within an acceptable balance. Among the 100 patients finally included in the analysis, there were 50 patients in the HFNC success group, including 29 (58%) internal medicine critical patients and 21 (42%) postoperative surgical patients; there were 50 patients in the HFNC failure group, including 41 (82%) internal medicine critical patients and 9 (18%) postoperative surgical patients. The HFNC failure group had a higher proportion of patients from internal medicine sources. Compared with the HFNC failure group, the HFNC success group had fewer cases of acute kidney injury (17 cases (34%) vs 37 cases (74%), $p < 0.01$), received HFNC therapy for a longer duration (89 (45 - 173.5) hours vs 41 (0.5 - 136) hours, $p < 0.04$), had a shorter ICU stay (6 (1 - 12) days vs 15 (1 - 33) days, $p < 0.01$), and exhibited lower mortality rates (28-day mortality : 8%(4 cases) vs 38%(19 cases), $p < 0.01$; 60-day mortality: 14%(7 cases) vs 46%(23 cases), $p < 0.01$). [Table 1](#) shows the baseline characteristics of the patients included in the analysis before and after PSM at the time of ICU admission.

Table 1. Baseline characteristics of patients with AHRF treated with HFNC before and after propensity score matching

Variables	Before propensity score matching			After propensity score matching		
	HFNC succeed group(n=112)	HFNC failed group(n=57)	SMD	HFNC succeed group(n=50)	HFNC failed group(n=50)	SMD
Age (years)	65(46-84)	75(60-90)	0.4	77(59-90)	78(61-90)	-0.04
Sex (male,%)	68(60.7%)	33(57.9%)	0.025	35(70%)	31(62%)	0.05
Patients						
Medical patients, n(%)	48(42.9%)	48(84.2%)	-0.58	29(58%)	41(82%)	-0.14
Surgery patients, n(%)	64(57.1%)	9(15.8%)	0.47	21(42%)	9(18%)	0.35
Comorbidities						
Hypertension, n(%)	70(62.5%)	37(64.9%)	-0.015	38(76%)	32(64%)	0.07
Diabetes mellitus, n(%)	43(38.4%)	23(40.4%)	-0.03	25(50%)	20(40%)	0.1
CHD, n(%)	61(54.5%)	47(82.5%)	-0.16	33(66%)	42(84%)	-0.09
COPD, n(%)	17(15.2%)	17(29.8%)	-0.3	9(18%)	11(22%)	-0.08
APACHE II at ICU admission	6(4-10)	8(4-12)	-0.35	7±2	8(5-11)	-0.28

AHRF:acute hypoxic respiratory failure; HFNC:high flow nasal cannula; CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; APACHE II:Acute Physiology and Chronic Health Evaluation II score.

The predictive validity of the ROX index and m-ROX index for HFNC outcomes (success/failure) was analyzed in two stages: Firstly, the AUROC, threshold, sensitivity, specificity, PPV and NPV were analyzed through ROC. Second, the predictive ability of the two indices in clinical settings was evaluated through DCA.

ROC analysis revealed that the predictive validity of the ROX index and m-ROX index for HFNC outcomes in patients with AHRF was relatively low at H0.5(0.5 hours after HFNC initiation), with AUROC values of 0.51 and 0.53, respectively. The predictive ability improved to an acceptable level at H6 (AUROC_H6: ROX 0.76, m-ROX 0.79). The AUROC of both indices progressively increased over time and stabilized within the range of 0.8 and 0.9, indicating enhanced predictive performance. A comparison of the AUROC values demonstrated that p-values at all monitoring points exceeded 0.05, suggesting no statistically significant difference in the diagnostic accuracy of the two indices regarding HFNC outcomes. (Table 2).

Table 2. The AUROC of each prediction points

Time point	ROX index AUROC(95%CI)	m-ROX index AUROC(95%CI)	P-value (ROX versus m-ROX)
0.5h	0.51(0.41-0.61)	0.53(0.43-0.63)	0.34
6h	0.76(0.66-0.84)	0.79(0.69-0.86)	0.19
12h	0.92(0.85-0.97)	0.84(0.77-0.89)	0.78

18h	0.97(0.9-0.99)	0.98(0.92-0.99)	0.2
24h	0.99(0.95-1)	0.99(0.95-1)	0.96

AUROC: Area Under the Receiver Operating Characteristic Curve

The cut-off value, sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) derived from ROC analysis at each monitoring point are presented in Table 3. At H6, the cut-off value of the ROX index was 5.7 (sensitivity 0.88, NPV 0.83, specificity 0.57, PPV 0.67), while the cut-off value of the m-ROX index was 7 (sensitivity 0.78, NPV 0.87, specificity 0.77, PPV 0.8). The cut-off value of the ROX index exhibited variability at subsequent monitoring points (H12: 6.9, H18: 6.25, H24: 6.25), whereas the cut-off value of the m-ROX index remained relatively stable across these intervals (H12: 7, H18: 7, H24: 6). Notably, both sensitivity and specificity demonstrated a gradual increase over time.

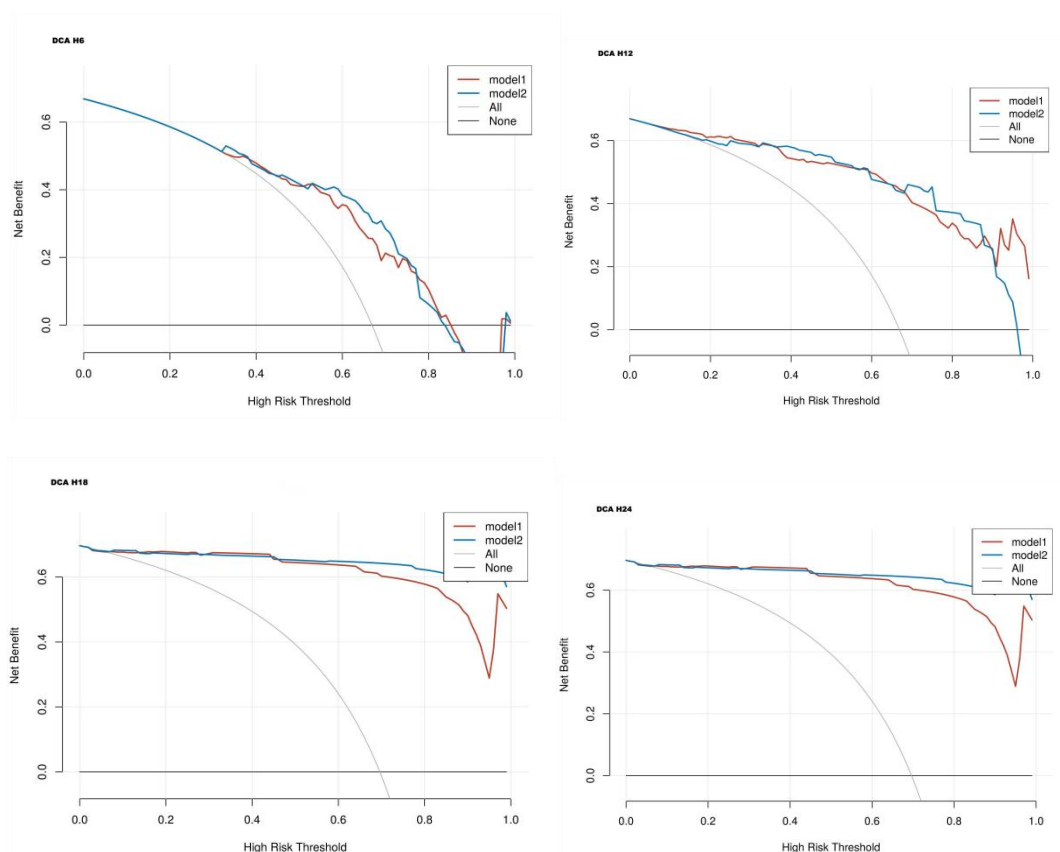
Table 3. Other discriminations of the ROX and m-ROX index

Time point	ROX index					m-ROX index				
	Cut-off value(95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV	Cut-off value (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV
0.5 h	8.9(7.8-10)	0.78(0.64-0.89)	0.38 (0.25-0.53)	0.55 (0.46-0.64)	0.63 (0.52-0.74)	12(8-16)	0.92 (0.8-0.98)	0.26 (0.15-0.4)	0.54 (0.49-0.59)	0.76 (0.7-0.82)
6h	5.7(4.8-6.6)	0.88(0.76-0.96)	0.57 (0.42-0.72)	0.67 (0.61-0.73)	0.83 (0.78-0.88)	7(5.9-8.1)	0.78 (0.64-0.89)	0.77 (0.62-0.88)	0.8 (0.75-0.85)	0.87 (0.81-0.93)
12h	6.9(5.9-7.9)	0.85 (0.72-0.94)	0.86 (0.72-0.95)	0.86 (0.79-0.93)	0.85 (0.79-0.91)	7(6-8)	0.87 (0.74-0.95)	0.84 (0.69-0.93)	0.84 (0.79-0.89)	0.85 (0.77-0.93)
18h	6.25 (5.1-7.35)	0.96 (0.85-0.99)	0.95 (0.81-0.99)	0.94 (0.88-0.99)	0.96 (0.89-0.99)	7(5.8-8.2)	0.91 (0.79-0.98)	1 (0.9-1)	0.95 (0.9-1)	0.96 (0.9-1)
24h	6.25(5.2-7.3)	0.98(0.88-1)	1(0.9-1)	1(0.89-1)	0.98 (0.93-1)	6(5.1-7.1)	0.98(0.88-1)	1(0.9-1)	1(0.89-1)	0.98(0.93-1)

PPV:Positive Predictive Value;NPV: Negative Predictive Value.

The predictive validity of the ROX index and the m-ROX index in actual clinical practice was verified through DCA comparison (Fig. 2). Given the poor predictive validity indicated by the AUROC at H0.5, DCA analysis was not conducted for this parameter. The results demonstrated that within the threshold probability range of 0.3 to 1.0 at H6, the curves of both parameters were positioned above both the All line and the None line, indicating strong predictive capability. As monitoring time progressed, there was a gradual enhancement in predictive ability. When comparing these two parameters, the DCA curves at all monitoring points revealed that, at a probability threshold of 0.6, the m-ROX index exhibited predictive validity comparable to that of the ROX index.

Fig 2. DCA curve of ROX index and m-ROX index at H6, H12, H18 and H24



Model 1: ROX index, model 2: m-ROX index, DCA: decision curve analysis

Among the patients included in the analysis, 30% were postoperative surgical patients. Subgroup analyses were performed based on the classification of medical critical care and postoperative surgical patients. In the HFNC success group, the duration of HFNC for postoperative surgical patients was shorter compared to that for medical critical care patients (48 (0.5 - 135.5) hours vs 105.5 (21.75 - 189.25), $p = 0.06$); although this difference did not reach statistical significance. At H6, PaCO₂ levels were significantly lower in postoperative surgical patients than in medical critical care patients (41.7 ± 11 vs 39 ± 6 , $p = 0.02$), and a similar trend was observed at H18 (41.85 ± 9.8 vs 39 ± 6.6 , $p = 0.04$). No statistically significant differences were found in other baseline indicators such as PaO₂, SpO₂/FiO₂ ratios, ROX index, m-ROX index, or Lac levels. Consequently, no further subgroup analysis was conducted regarding the comparative predictive validity of ROX and m-ROX indices for postoperative AHRF patients.([supplemental table: S1](#)).

Discussion

This study demonstrated that m-ROX index exhibited equivalent predictive validity compared to the ROX index for the HFNC outcomes in ICU patients with AHRF. The cut-off value of the ROX index was higher than that reported in previous studies, whereas the cut-off value of the m-ROX index were relatively stable compared to the ROX indices at each monitoring time point.

The reasons for the m-ROX index exhibiting comparable predictive validity to the ROX index and maintaining a relatively stable cut-off value may be as follows:

The heart and lungs are closely interconnected. Hypoxia caused by respiratory dysfunction, such as pneumonia, can induce hemodynamic changes in the heart, influencing parameters such as heart rate, preload, contractility, and afterload. Variations in cardiac load may either exacerbate or alleviate

preexisting respiratory dysfunction[17]. The patients included in this study were elderly (mean age 77 years [range 59-90] in the HFNC success group; mean age 78 years [range 61-90] in the HFNC failure group) and exhibited a high prevalence of chronic diseases, including hypertension (70%), coronary artery disease (75%), diabetes mellitus (45%), and chronic obstructive pulmonary disease (20%). Furthermore, there was a significant incidence of complications such as acute kidney injury (54%). All of these factors represent risk factors for new cardiovascular events or exacerbation of existing cardiovascular conditions during AHRF[18,19]. Among potential cardiovascular events, changes in heart rate are particularly sensitive indicators. This may explain why the m-ROX index demonstrates comparable predictive validity to the ROX index and maintains a relatively stable cut-off value at each monitoring time points. The m-ROX index, which incorporates heart rate, not only enhances actual clinical predictive accuracy but also effectively mitigates threshold variability—highlighting its potential utility in clinical practice.

This study showed that the cut-off value of ROX index were 5.7 at H6, 6.9 at H12, 6.25 at H18, and 6.25 at H24, which were higher than the threshold of 4.88 in previous study[3]. Recent studies have also reported cut-off values exceeding 4.88 [20, 21]. The reasons for this discrepancy may be as follows:

1. Roca O et al. focused on severe cases of AHRF caused by pneumonia. In contrast,, approximately 30% of the patients in our study were postoperative surgical patients who either had no pulmonary infection or only mild infections before surgery. Consequently, their oxygenation metrics were likely superior to those observed in patients suffering from severe pneumonia included in Roca O et al.'s investigation.

2. In our study, most postoperative patients underwent abdominal surgeries with an average HFNC duration of 48 hours (ranging from 0.5 to 135.5 hours), coinciding with the acute postoperative phase. It is hypothesized that these patients developed acute respiratory distress syndrome (ARDS) secondary to complications of abdominal surgery. Following resolution of the underlying cause (acute surgical stress), along with early mobilization and effective circulatory management, improvements in lung ground-glass opacities and overall oxygenation indicators were observed. These findings explain the close alignment of our thresholds with those reported in recent studies involving COVID-19 patients[22]. The pathophysiological alterations in both conditions are comparable—primarily characterized by interstitial changes that hinder oxygen transfer into the blood vessels, which further clarifies why our determined threshold exceeds that associated with AHRF resulting solely from uncomplicated pneumonia.

The results indicated that as the monitoring duration extended, the diagnostic efficacy of both the ROX index and m-ROX index progressively improved. However, if HFNC is administered continuously for 18 hours, 24 hours, or longer, the probability of treatment failure becomes significantly reduced unless new-onset infection or ARDS occurs. This study aims to investigate the early predictive capabilities of both indices regarding HFNC outcomes in order to mitigate adverse prognoses associated with delayed intubation and mechanical ventilation. The optimal monitoring time frame should ideally fall within 12 hours following initiation of HFNC. Therefore, further analysis concerning the cut-off value for the ROX index and m-ROX index through large-scale studies remains necessary.

Limitation:

This study was a single-center research that analyzed both critically ill patients with internal medical conditions and postoperative surgical cases. The management of fluids and anti-infection treatments for these two kinds patients could not be standardized, which might impact the accuracy of the results. Future large-scale studies focusing on patients with a single etiology is needed.

References

1. Crimi C, Pierucci P, Renda T, Pisani L, Carlucci A. High-Flow Nasal Cannula and COVID-19: A Clinical Review. *Respir Care*. 2022 Feb;67(2):227-240.
2. Frat JP, Ragot S, Girault C, Perbet S, Prat G, Boulain T, et al. Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial. *Lancet Respir Med*. 2016 Aug;4(8):646-652.
3. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015 Jun 4;372(23):2185-96.
4. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, 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 Oct;35:200-5.
5. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy. *Am J Respir Crit Care Med*. 2019 Jun 1;199(11):1368-1376.
6. Zhou X, Liu J, Pan J, Xu Z, Xu J. The ROX index as a predictor of high-flow nasal cannula outcome in pneumonia patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *BMC Pulm Med*. 2022 Apr 1;22(1):121.
7. Junhai Z, Jing Y, Beibei C, Li L. The value of ROX index in predicting the outcome of high flow nasal cannula: a systematic review and meta-analysis. *Respir Res*. 2022 Feb 17;23(1):33.
8. Maslove DM, Dubin JA, Shrivats A, Lee J. Errors, Omissions, and Outliers in Hourly Vital Signs Measurements in Intensive Care. *Crit Care Med*. 2016 Nov;44(11):e1021-e1030.
9. Siebenmann C, Lundby C. Regulation of cardiac output in hypoxia. *Scand J Med Sci Sports*. 2015 Dec;25 Suppl 4:53-9.
10. Bhavani SV, Robichaux C, Verhoef PA, Churpek MM, Coopersmith CM. Using Trajectories of Bedside Vital Signs to Identify COVID-19 Subphenotypes. *Chest*. 2024 Mar;165(3):529-539.
11. Bhavani SV, Semler M, Qian ET, Verhoef PA, Robichaux C, Churpek MM, et al. Development and validation of novel sepsis subphenotypes using trajectories of vital signs. *Intensive Care Med*. 2022 Nov;48(11):1582-1592.
12. Blackburn HN, Clark MT, Moorman JR, Lake DE, Calland JF. Identifying the low risk patient in surgical intensive and intermediate care units using continuous monitoring. *Surgery*. 2018 Apr;163(4):811-818.
13. Goh KJ, Chai HZ, Ong TH, Sewa DW, Phua GC, Tan QL. Early prediction of high flow nasal cannula therapy outcomes using a modified ROX index incorporating heart rate. *J Intensive Care*. 2020 Jun 22;8:41.
14. Ruangsomboon O, Jirathanavichai S, Phanprasert N, Puchongmart C, Boonmee P, Thirawattanasoot N, et al. Ratio of Oxygen Saturation to Inspired Oxygen, ROX Index, Modified ROX Index to Predict High Flow Cannula Success in COVID-19 Patients: Multicenter Validation Study. *West J Emerg Med*. 2023 Apr 28;24(3):511-521.
15. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.
16. Linden A, Samuels SJ. Using balance statistics to determine the optimal number of controls in matching studies. *J Eval Clin Pract*. 2013;19(5):968-975.
17. Hamahata N, Pinsky MR. Heart-Lung Interactions. *Semin Respir Crit Care Med*. 2023 Oct;44(5):650-660.
18. Desai A, Aliberti S, Amati F, Stainer A, Voza A. Cardiovascular Complications in Community-Acquired Pneumonia. *Microorganisms*. 2022 Nov 2;10(11):2177.
19. Dandel M. Heart-lung interactions in COVID-19: prognostic impact and usefulness of bedside echocardiography for monitoring of the right ventricle involvement. *Heart Fail Rev*. 2022 Jul;27(4):1325-1339.
20. Lee YS, Chang SW, Sim JK, Kim S, Kim JH. An Integrated Model including the ROX Index to Predict the Success of High-Flow Nasal Cannula Use after Planned Extubation: A Retrospective Observational Cohort Study. *J Clin Med*. 2021 Aug;10(16):3513.

21. Rodriguez M, Thille AW, Boissier F, Veinstein A, Chatellier D, Robert R, et al. Predictors of successful separation from high-flow nasal oxygen therapy in patients with acute respiratory failure: a retrospective mono-center study. *Ann Intensive Care*. 2019 Sep 11;9(1):101.
22. Girault C, Bubenheim M, Boyer D, Declercq PL, Schnell G, Gouin P, et al. ROX index performance to predict high-flow nasal oxygen outcome in Covid-19 related hypoxemic acute respiratory failure. *Ann Intensive Care*. 2024 Jan 18;14(1):13.

Supplemental table S 1. Respiratory variables of HFNO success group comparing medical ICU patients and surgical ICU patients

Variable	Time(h)	Medical patients	Surgical patients	P value
PaCO ₂ , mmHg	0.5h	39.9(28.8-51)	40.4±6.1	0.9
	6h	39.55 (29.6-49.5)	40.55 (48.75-32.35)	0.96
	12h	39.15 (31.7-46.6)	39 (27.43-50.57)	0.34
	18h	39.35(31.67-47.03)	37.25(22.7-51.8)	0.04
	24h	39.65(32.42-46.88)	37.05(23.5-50.6)	0.03
PaO ₂ , mmHg	0.5h	88.1±21.7	77.85(60.72-94.98)	0.2
	6h	87.95(70.85-105.05)	85.5(60.83-110.17)	0.3
	12h	89.5(64.65-113.75)	89.45(55.18-123.72)	0.5
	18h	97(80.35-113.65)	92.95(60.6-145.3)	0.15
	24h	97.7(81.7-113.7)	93.55(62.97-124.13)	0.15
SpO ₂ /FiO ₂	0.5h	186.2(101.5-270.9)	187.8(108.5-267.1)	0.8
	6h	190.6±62.3	195.9(116.6-275.2)	0.16
	12h	194(115-273)	197(113.1-280.9)	0.8
	18h	230.5(165.2-295.8)	232.9(101.9-363.9)	0.65
	24h	244.3(187.1-301.5)	244.5(142.3-346.7)	0.37
PaO ₂ /FiO ₂	0.5h	166.1(86.2-246)	158.6(68.2-249)	0.9
	6h	185.6±71.2	197±74	0.3
	12h	191.7(109-274.4)	207.6(89.9-325.3)	0.92
	18h	230.9(152.8-309)	211(110.3-311.7)	0.4
	24h	234.3(153.4-315.2)	217.8(138.8-296.8)	0.37
ROX index	0.5h	6.6(2.9-10.3)	7.6±2.8	0.47

	6h	8.2±3.2	8.9(4.8-13)	0.08
	12h	9.3±3.9	10.3(4.4-16.2)	0.66
	18h	12.1(7-17.2)	12.6(4-21.2)	0.9
	24h	12.9(7.7-18.1)	12.9(5.2-20.6)	0.75
m-ROX index	0.5h	0.07(0.02-0.12)	0.07(0.02-0.12)	0.98
	6h	0.09(0.04-0.14)	0.1±0.04	0.18
	12h	0.1(0.03-0.17)	0.12(0.04-0.2)	0.62
	18h	0.16±0.07	0.17(0.04-0.3)	0.67
	24h	0.17(0.11-0.23)	0.18(0.05-0.31)	0.57
Lactate, mmol/L	0.5h	1.8(0.6-3)	1.9(0.7-3.1)	0.37
	6h	1.8±0.7	1.8(0.8-2.8)	0.58
	12h	1.6(1.1-2.1)	1.5(0.4-2.6)	0.6
	18h	1.5(0.9-2.1)	1.4(0.4-2.4)	0.18
	24h	1.4(0.9-2.1)	1.3(0.5-2.1)	0.19