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PREDICTING SUCCESS OF HIGH FLOW NASAL CANNULA IN PNEUMONIA PATIENTS WITH HYPOXEMIC RESPIRATORY FAILURE: THE UTILITY OF THE ROX INDEX

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ABSTRACT

Purpose

To describe early predictors and to develop a prediction tool that accurately identifies the need for mechanical ventilation (MV) in pneumonia patients with hypoxemic acute respiratory failure (ARF) treated with HFNC.

Materials and methods

Four year prospective observational two-center cohort study including patients with severe pneumonia treated with HFNC. HFNC failure was defined as need for MV. ROX index was defined as the ratio of SpO_2/F_IO_2 to respiratory rate.

Results

One hundred and fifty-seven patients were included of whom 44 (28.0%) eventually required MV (HFNC failure). After 12 hours of HFNC treatment, the ROX index demonstrated the best prediction accuracy (area under the ROC curve 0.74 [95%CI 0.64-0.84]; $p<0.002$). The best cutoff point for the ROX index was estimated to be 4.88. In the Cox's proportional hazards model, a ROX index ≥4.88 measured after 12 hours of HFNC was significantly associated with a lower risk for MV (HR 0.273 [95%CI 0.121-0.618]; $p=0.002$), even after adjusting for potential confounding.

Conclusions

In patients with ARF and pneumonia, the ROX index can identify patients at low risk of HFNC failure in whom therapy can be continued after 12 hours.

KEYWORDS

High flow nasal cannula, nasal high flow, pneumonia, acute respiratory failure, hypoxemia, oxygen therapy.

INTRODUCTION

Heated humidified high flow nasal cannula (HFNC) has been described as a safe and useful therapy for hypoxemic acute respiratory failure (ARF) patients). Compared with conventional oxygen therapy, it may improve comfort and oxygenation (2, 5, 8, 9). It has also been shown that it may decrease the need for mechanical ventilation (MV) in ARF lung transplant patients readmitted to the ICU (3) and may decrease reintubation rates as well (9). More recently, the first large randomized control trial comparing the effectiveness of conventional oxygen therapy, noninvasive ventilation (NIV) combined with HFNC, and HFNC alone in hypoxemic ARF (1) demonstrated that HFNC alone reduced need for MV in the most severe ($PaO_2/F_IO_2 \leq 200$mmHg) subgroup of patients. HFNC patients also had the higher 90-day survival rate of the entire cohort.

However, one of the most challenging decisions in the management of ARF patients is to decide when to move from a spontaneous breathing oxygenation therapy to invasive MV (10). In this regard, although HFNC may avoid further need for MV in some patients with ARF (1, 3), it may unduly delay initiation of MV in others and worsen their outcome, (11) as already evidenced for NIV (12–15). Therefore, to identify and describe accurate early predictors of the need for MV in spontaneously breathing patients with ARF is of special interest.

Some clinical or oxygenation variables have been associated with HFNC failure and subsequent need for MV. For example, absence of oxygenation improvement (5,16) or significant decrease in the respiratory rate and persistence of thoracoabdominal asynchrony (5) were early indicators of treatment failure. They were however not discriminant enough to unequivocally identify patients that would require subsequent intubation. In addition to respiratory parameters, presence of additional organ failures

such as hemodynamic (3, 4, 16) or neurological failure has also been considered as a significant determinant of HFNC failure.

Indexes are commonly and widely used to help or guide physicians in the bedside decision-making process of patients' management. This is particularly true in critically ill patients to predict their probability of death (17, 18), assess their systemic severity (19) or the severity of some specific diseases, such as lung injury (20) or pneumonia (21, 22). Because the latter is by far the main indication for HFNC (1, 3, 5, 6, 16), the aim of the present study was to describe a feasible and reliable easy-to-use index that accurately predicted the need for MV in patients with pneumonia and hypoxemic ARF treated with HFNC.

MATERIAL AND METHODS

Study design

This is a two-center prospective observational cohort study performed over a four-year period (from 2009 to 2012), including patients with pneumonia admitted to the 32-bed medico-surgical ICU of Vall d'Hebron University Hospital, Barcelona (Spain) and the 12-bed medico-surgical ICU of Louis Mourier University Hospital, Colombes (France), who were treated with HFNC (*Optiflow™, Fisher & Paykel, New Zealand*). Some patient data was extracted from previously published prospective observational studies (4–6). Local Ethics Committee approved the studies and patient's informed consent was obtained before inclusion.

Patients

All patients admitted to the ICU with pneumonia and treated with HFNC were included. Pneumonia was diagnosed according to IDSA/ATS 2007 guidelines (23). Non-inclusion criteria were age younger than 18 years old, indication for immediate MV (24) upon admission and absence of commitment to pursue full life-support. Patients electively intubated for diagnostic or therapeutic procedures (fibrobronchoscopy, surgery) were also not included. Patients were followed until death or hospital discharge.

Data collection

Demographic variables and severity scores were recorded at the moment of inclusion. APACHE II (17) was calculated in the first 24h of ICU admission. SOFA (19) score was recorded once a day during the first 5 days of HFNC therapy. We also recorded Pneumonia Severity Index (PSI) (22) and type of pneumonia (community acquired (23)

vs health-care associated (25). To assess radiologic severity, chest -X-ray findings were evaluated at the beginning of HFNC therapy. Clinical respiratory and pulmonary gas exchange variables in patients with arterial line were recorded 2h, 6h, 12h, 18h and 24h after initiation of HFNC therapy. After the first 24h, the same variables were recorded once daily until HFNC withdrawal. Failure of HFNC was defined as subsequent need for invasive MV because in the participating units, NIV is not used as second line ventilatory support in case of HFNC failure where tracheal intubation is the preferred option and thus performed if necessary. The presence of an organ failure before and during HFNC therapy was also registered. Briefly, shock was defined as need for vasopressors (3), renal failure was defined as increased serum creatinine x 1.5 and/or urine output <0.5ml/kg/h during 6 hours (26). ARDS was defined according to the Berlin definition (27) with the presence of bilateral infiltrates in Chest X ray, no evidence of heart failure, but modified by using the ratio SpO_2/F_IO_2 < 315 to assess hypoxemia (28). We also recorded length of HFNC therapy, MV, and ICU and hospital stay; and survival.

Device description and management

The HFNC device (Optiflow™ system, MR850 heated humidified RT202 delivery tubing, and RT050/051 nasal cannula; Fisher and Paykel Healthcare Ltd, Auckland, New Zealand) consists of a low resistance nasal cannula that can deliver up to 60L/min of totally conditioned (37ºC and 100% of relative humidity) gas admixture. It was initiated with a minimum flow of 30L/min with a fraction of inspired oxygen (F_IO_2) of 1. Then, F_IO_2 was set to maintain a pulse oximetry (SpO_2) above 92% and flow rate was set according to the physician judgment. The parameters used to assess the level of respiratory support provided were F_IO_2 and total flow delivered, adjusted to the

individual patient's needs. The parameters used to assess respiratory failure were respiratory rate (RR), SpO_2/F_IO_2 ratio and arterial carbon dioxide ($PaCO_2$). The criteria for intubation and MV (1, 4) were decreased level of consciousness (Glasgow coma score <12), cardiac arrest/arrhythmias and severe hemodynamic instability (norepinephrine >0.1µg/kg/min) or persisting or worsening respiratory condition defined as at least two of the following criteria: failure to achieve correct oxygenation (PaO_2 <60mmHg despite HFNC flow ≥30L/min and F_IO_2 of 1), respiratory acidosis ($PaCO_2$ >50mmHg with pH <7.25), RR >30bpm or inability to clear secretions.

ROX Index description

The index predicting the need for MV was calculated from the measured respiratory variables assessing respiratory failure that significantly differ among groups (success *vs* failure). It aimed to obtain an additive effect, increasing their capacity to discriminate between patients who would succeed on HFNC and those who would fail. In the numerator were placed the variables with a positive association with HFNC success, such as oxygenation, assessed by the ratio SpO_2/F_IO_2. In contrast, RR was placed in the denominator as it has an inverse association with HFNC success. We used the name ROX (Respiratory rate-OXygenation) for the index, as the ratio of SpO_2/F_IO_2 to RR.

Statistical Analysis

Quantitative variables were expressed as mean and standard deviation or median and interquartile range if normality criteria, as tested with Kolmogorov-Smirnov test, were not met. Categorical variables were expressed as frequencies and percentages. Continuous variables were compared using the Student *t* test or U-Mann Whitney test, as appropriate. Differences in categorical variables were assessed with Chi square or

Fisher exact test, as appropriate. To assess the accuracy of different variables for correctly classifying patients who would succeed or fail on HFNC, receiver operating characteristic curves (ROC) were performed and the area under the curves were calculated (AUROC). The optimal threshold of continuous variables was chosen to maximize the sum of sensitivity and specificity. According to the cut-point described in the ROC curve analysis for ROX index, Kaplan-Meier curves were used to determine the probability of MV for patients with higher ROX index and those with lower ROX index. These curves were compared using the log-rank test. To identify if the ROX index was associated with higher need for MV, Cox's proportional hazards modeling was chosen, while simultaneously adjusting for other covariates. Variables with p value <0.2 in the univariate analysis were considered as potential covariates. We also adjusted by severity scores (APACHE and PSI). In order to prevent model overfitting, we introduced all potential confounding one at a time. A two-sided p value of 0.05 or less was considered statistically significant. Statistical analyses were performed using the SPSS statistical package (version 20.0; SPSS Inc, Chicago, IL).

RESULTS

General characteristics of the included population

One hundred fifty seven patients with pneumonia were treated with HFNC, after having received conventional oxygen therapy. Baseline characteristics of the study population upon ICU admission are presented in Table 1. Forty-four (28.0%) patients required subsequent intubation and mechanical ventilation and were categorized as HFNC failure. HFNC failure patients had a greater extent of disease on chest X-ray and a higher SOFA score. Moreover, they were less likely to suffer from chronic respiratory disease. At HFNC onset, there was a trend towards a higher prevalence of shock (6 [13.6%] vs 7 [6.1%] patients; p=0.127) and renal failure (16 [36.4%] vs 29 [25.4%] patients; p=0.158) in patients who failed HFNC compared to those patients who succeeded. None of the patients were treated with non-invasive ventilation after HFNC failure. Three patients received NIV prior to HFNC which had been introduced because of NIV intolerance. One patient received NIV after the acute phase of respiratory failure, as part of his long term home treatment. No further differences were observed during HFNC treatment.

Respiratory variables during HFNC treatment: the ROX index

Only 92 patients have an arterial line at the beginning of HFNC therapy; all of them were monitored using SpO_2 and RR. HFNC success patients had higher SpO_2/F_IO_2 and lower RR at 12h and 18h of HFNC onset, respectively (Table 2). Significant differences were observed in ROX index after 12h of HFNC treatment between success and failure HFNC patients (Table 2). The differences increased throughout the study period. Their accuracy to predict further need for MV was assessed calculating the AUROC (Table 3). None of the variables analyzed at 2 or 6 hours after HFNC had good predictive

capacity for MV (AUROC<0.7). After 12 hours of HFNC treatment, ROX index demonstrated the best prediction accuracy (AUROC 0.74). Moreover, its accuracy was better at 18 and 24 hours, respectively. Using the ROC curve, the best cutoff point for the ROX index at 12 hours was estimated to be 4.88. A ROX index ≥4.88 at 12 hours after HFNC onset, has a sensitivity of 70.1%, a specificity of 72.4%, a positive predictive value of 89.4%, a negative predictive value of 42%, a positive likelihood ratio of 2.54 and a negative likelihood ratio of 0.41 in predicting treatment failure. Interestingly, among those patients who were still on HFNC after 18 hours, the median change of ROX index between 18 and 12 hours in patients who succeeded was higher (0.37 [-0.57 – 1.64] vs -0.19 [-1.04 – 0.21]; p=0.014).

Time to intubation, length of HFNC therapy and outcome

The median duration of the HFNC therapy in success and failure groups was 3 (2-6) days and 1 (1-4) days, respectively (p<0.001). Of note, almost 70% of the patients were intubated after at least 12h hours of HFNC use. HFNC was not associated to any intolerance or side effect. Hospital and ICU mortality and length of stay were higher in the HFNC failure group (Table 1 SDC). To assess if time to intubation could have influenced outcomes, we divided patients who failed in two different groups. Firstly, we considered patients intubated during the first 48h of treatment and secondly, patients intubated after 48h of HFNC therapy. Among all patients who failed on HFNC, 12 (27.3%) were intubated after 48 hours of treatment. These patients were comparable in terms of organ failure and pneumonia severity with those who were intubated during the first 48 hours of HFNC treatment. Furthermore, no differences were observed between groups in length of stay, nor in mortality (Table 2 SDC).

Analysis of variables related with need for MV

Kaplan-Meier plots showing the probability of MV according to the ROX group were shown in Figure 2. Patients with ROX index score ≥4.88 after 12 hours of HNFC were less likely to need MV (p=0.001). To assess the association of the ROX index at 12h of HFNC therapy and other covariates in the risk of MV in patients treated with HFNC, a Cox's proportional hazards model was performed (Table 4). A ROX index ≥4.88 measured after 12 hours of HFNC was consistently associated with a lower risk for MV, even after adjusting for potential confounding. We have also constructed a Cox model with the three variables that were significantly associated with the risk of MV: ROX, gender and chronic respiratory disease. This Cox model yielded similar results, with the ROX index the only variable associated with the risk of mechanical ventilation (data not shown).

Patients intubated within the first 12 hours of HFNC therapy.

Patients who were intubated within the first 12 hours of HFNC treatment were also analyzed separately. Compared to those who succeeded, they had more frequently a viral pneumonia and a greater chest X-ray involvement (Table 3 and 4 SDC). Finally, patients who were intubated in the first 12 hours of treatment were compared to those who failed after 12 hours of HFNC. Patients intubated in the first 12 hours were more likely to have a chronic respiratory disease and tended to be more affected in the chest X ray (Table 5 SDC). However, no differences were observed in respiratory variables or ROX index (Table 6 SDC).

DISCUSSION

In the present study we describe a feasible and easy-to-use index defined as the ratio of SpO_2/F_IO_2 to RR. When measured 12 hours after HFNC onset, a ROX index≥4.88 is a determinant of HFNC success in patients with pneumonia, even after adjustment for potential confounding. Finally, it should be noted that intubation after more than 48 hours of HFNC treatment was not associated with a worse prognosis.

This is a key issue, because unduly delaying intubation with HFNC might run the same risk of increasing mortality as has been shown with NIV(8,28). Hence, to be able to accurately identify patients that can be maintained under HFNC (without exposing them to unnecessary risks) and those that need to be intubated is a crucial point.

Previous studies have shown that oxygenation improvement (5, 16), significant decrease in RR and abolition of thoraco-abdominal asynchrony (5) were indicators of HFNC success. On the other hand, presence of an additional organ failure was associated with a higher risk of HFNC failure (3, 4, 16). However, most of these variables were analyzed in small sample size studies that included heterogeneous populations of ARF patients. In this study, we present the ROX index that, when measured 12 hours after HFNC onset in a large cohort of patients with severe pneumonia is a better predictor of treatment success compared with SpO_2/F_IO_2 or RR alone. Furthermore, patients who had a ROX index ≥4.88 after 12 hours of HFNC therapy were less likely to be intubated, even after adjusting for potential covariates.

When comparing our patients intubated before and after 48 hours of HFNC, we found no differences in mortality or ICU LOS. Similar results were previously reported in a cohort of lung transplant recipients who were readmitted to the ICU due to ARF (3). In contrast, a recent retrospective, single centre study dealing with patients with ARF using propensity score analysis suggested that patients who were intubated more than

48h after HFNC therapy onset presented higher ICU mortality and lower weaning success and ventilator-free days (11). However, several limitations regarding the study were issued following its publication (29) and substantial differences with our study should be taken into account. First, they included patients with different ARF etiologies and some of them were treated in general wards where close general and respiratory monitoring cannot be performed as closely as in the ICU. Second, patients of the late group were treated for a median of more than 5 days with HFNC before intubation and it is not clear if intubation criteria were met sometime before intubation was ultimately performed or not. Third, no data was provided regarding need for vasopressors, or duration of ARF prior to intubation, variables that have been shown to be predictors of HFNC failure (3, 4, 16). Likewise, no data on flow rates applied to the patients was given, even though the benefits of HFNC are clearly related to the level of flow delivered (30, 31). Thus, the possibility that some patients may have been undertreated cannot be ruled out. Finally, acute-on-chronic respiratory failure was an independent risk factor for ICU mortality and hypercapnic failure as a cause of intubation was almost three times more frequent in the late group, suggesting that some patients in the late group could have benefited from NIV. On the contrary, we included a homogenous cohort of patients with pneumonia all treated in the ICU. Moreover, irrespective of the initial effect of HFNC, patients who deteriorated were intubated when they met clinical intubation criteria (14). This may explain why our median time to intubation was one day, somewhat shorter than other reports. Finally, in our study, other variables that have been associated with HFNC failure were well balanced between groups.

So how can the ROX be applied to help in the decision process of need for mechanical ventilation during high flow oxygen therapy? Because of the risk of excess mortality when delaying intubation in case of failure has been clearly demonstrated with NIV and

HFNC(8,28), we wanted the earliest possible predictor. This choice is associated with a higher proportion of misclassified patients (that of patients intubated but that might have evaded intubation had we waited longer be greater than with a later time point (i.e., at 18 or 24 h). On the other hand, a later, more accurate statistically speaking, time point is associated with a smaller number of misclassified patients, but exposed to a greater risk (that of a delayed intubation with its inherent risk of excess mortality). Because some patients are intubated after 24-48h of HFNC, it also possible to repeat the ROX index after 12 h, so as assess changes in ROX index. Clinical judgement must also be taken into account, and the importance of setting predefined intubation criteria is an important aspect to quality of care.

Some limitations should be noted. First, all our patients had pneumonia-related ARF and our results may not necessarily be generalizable to patients with ARF from other etiologies. However, pneumonia is by far the leading etiology of ARF treated with HFNC (7), so our index would apply for a majority of patients treated with HFNC. In addition, pneumonia is probably one of the ARF etiologies that takes the longer to reverse (by comparison with cardiogenic pulmonary edema or acute asthma for example) so having an index validated in this population makes sense. Another important issue is that ROX index is measured after 12 hours of HFNC treatment and HFNC failure may occur earlier. Nevertheless, the number of HFNC failure in the first 12 hours is limited (less than 10%) and 12 hours is shorter than the median duration of HFNC treatment reported in other series that included patients with ARF (3, 5, 6, 8, 16). Thus, most patients may be assessed with the ROX index. Second, it should be also noted that 28.6% of the patients included had a previous history of chronic respiratory disease and this variable was associated with HFNC success. However, it was recorded as comorbidity and not as the cause of respiratory failure and, therefore might not be a

limitation to generalize our results. Third, we used SpO_2 and not PaO_2 to create the index. Although it can be considered as a limitation, most of non-intubated ARF patients are currently managed with noninvasive monitoring. Interestingly, SpO_2/F_IO_2 correlates with PaO_2/F_IO_2 ratio(27) and it has been demonstrated that patients with ARDS diagnosed by the SpO_2/F_IO_2 ratio have very similar characteristics and outcomes compared with those patients diagnosed by PaO_2/F_IO_2 ratio(33). Moreover, ROX index can be rapidly measured at bedside. Finally, the unanswered question is when to intubate when a ROX index is below 4.88? Should one wait until all the intubation criteria are met, or act before? Obviously, further studies are warranted to confirm the validity of the present index and determine the optimal intubation time in a prospective study.

In conclusion, we present a feasible and easy-to-use index that is a determinant of HFNC success in patients with pneumonia.

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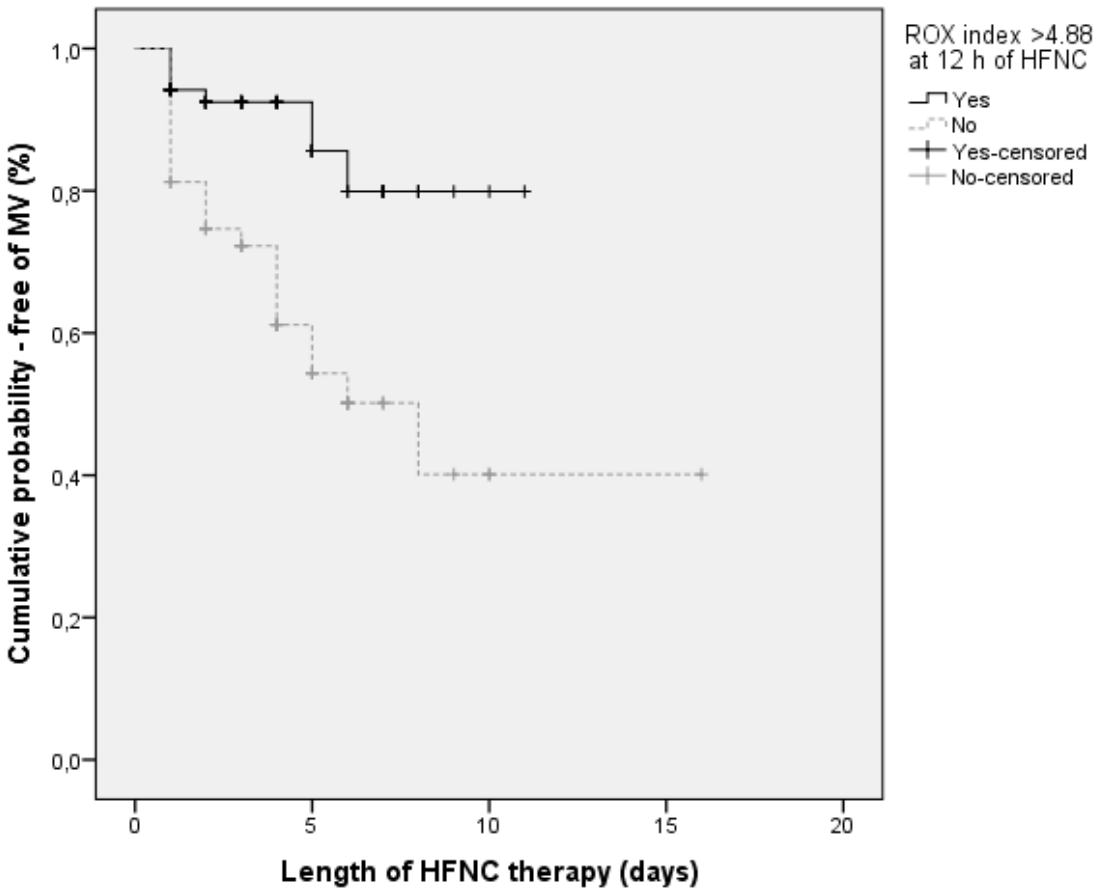
FIGURE LEGENDS.

Figure 1. Kaplan-Meier plot showing the cumulative probability of remaining free of intubation and mechanical ventilation in patients with pneumonia treated with HFNC therapy.



TABLES

Table 1. Baseline characteristics of the study population at ICU admission.

	HFNC Success (113)	**HFNC Failure (44)**	***p* value***
Gender (male)	74 (65.5%)	21 (50%)	0.079
Age	52 (40-66)	53 (37-66)	0.977
Comorbidities			
Immunosuppression	38 (33.6%)	16 (36.4%)	0.852
Chronic heart failure	11 (9.7%)	5 (11.4%)	0.773
Chronic liver disease	6 (5.4%)	3 (6.8%)	0.714
Chronic respiratory disease	38 (33.6%)	7 (15.9%)	0.031
Chronic renal failure	6 (5.4%)	2 (4.5%)	1.000
Type of pneumonia			0.042
Bacterial			
Community acquired	93 (82.3%)	29 (65.9%)	
Health care related	13 (11.5%)	7 (15.9%)	
Viral pneumonitis	7 (6.2%)	8 (18.2%)	
Pneumonia Severity Index	107 (82-137)	118 (81-144)	0.254
APACHE II of 24h ICU admission	13 (10-17)	16 (10-20)	0.252
SOFA ICU admission	4 (3-6)	6 (3-7)	0.014
Number of affected quadrants on Chest X-ray	2 (2-4)	3 (3-4)	0.020

HFNC= High flow nasal cannula; APACHE II= Acute Physiology and Chronical Health Evaluation; SOFA= Sequential Organ Failure Assessment; ICU= Intensive Care Unit.

Table 2. Respiratory variables during HFNC treatment.

Variable	Time	HFNC Success	HFNC Failure	*p* value
SpO_2/F_IO_2	2h	100 (98-125)	99 (95-124)	0.291
	6h	121 (99-160)	100 (96-140)	0.202
	12h	129 (115-162)	100 (96-126)	0.007
	18h	158 (115-165)	100 (95-133)	0.030
	24h	162 (125-205)	104 (95-124)	0.001
RR (bpm)	2h	25 (20-28)	26 (22-28)	0.223
	6h	24 (20-27)	24 (21-29)	0.480
	12h	22 (18-26)	26 (22-28)	0.059
	18h	22 (19-25)	28 (24-33)	0.001
	24h	21 (18-24)	25 (22-30)	0.121
$PaCO_2$ (mmHg)	2h	36.00 (32.75-40.18)	37.75 (31.78-45.53)	0.849
	6h	36.80 (34.00-43.23)	36.20 (32.28-43.50)	0.932
	12h	38.25 (33.75-42.53)	40.70 (35.00-49.40)	0.312
	18h	39.00 (34.75-43.60)	40.00 (31.80-51.50)	1.000
	24h	37.75 (33.75-42.40)	39.50 (30.00-46.10)	0.710
Flow (L/min)	2h	40 (40-60)	55 (40-60)	0.470
	6h	40 (40-60)	50 (40-60)	0.695
	12h	40 (40-60)	55 (40-60)	0.226
	18h	40 (40-60)	55 (40-60)	0.329
	24h	40 (40-60)	40 (40-60)	0.769
ROX index	2h	4.40 (3.53-5.62)	3.65 (3.17-5.41)	0.216
	6h	4.95 (4.13-7.34)	4.60 (3.73-5.71)	0.426
	12h	5.89 (4.58-7.85)	4.36 (3.55-5.31)	0.001
	18h	6.09 (5.05-8.17)	4.18 (3.14-5.41)	0.003
	24h	7.69 (5.33-10.00)	4.19 (3.61-5.22)	<0.001

HFNC: high flow nasal cannula; SpO_2/F_IO_2: pulse oxymetry; RR: respiratory rate; $PaCO_2$: carbon dioxide arterial pressure

Table 3. Diagnostic accuracy of different respiratory variables at different time points of need for MV in patients treated with HFNC.

	Variable	AUROC	95% CI	*p* value
12h	SpO_2/F_IO_2	0.71	0.61-0.82	<0.001
	RR (bpm)	0.64	0.54-0.75	0.018
	Flow (L/min)	0.58	0.46-0.69	0.213
	ROX index	0.74	0.64-0.84	<0.001
18h	SpO_2/F_IO_2	0.72	0.61-0.83	0.001
	RR (bpm)	0.77	0.67-0.88	<0.001
	Flow (L/min)	0.60	0.48-0.72	0.120
	ROX index	0.83	0.74-0.92	<0.001
24h	SpO_2/F_IO_2	0.82	0.73-0.92	<0.001
	RR (bpm)	0.73	0.61-0.84	0.003
	Flow (L/min)	0.59	0.47-0.72	0.136
	ROX index	0.87	0.77-0.96	<0.001

MV: mechanical ventilation; HFNC: high flow nasal cannula; SpO_2/F_IO_2: pulse oxymetry; RR: respiratory rate

Table 4. Cox's proportional hazards model (Cox regression) to analyze the effect of ROX index≥4.88 after 12 hours of HFNC therapy and potential covariates on the risk for MV.

	Hazard ratio	**95% confidence interval**	***p* value**
Unadjusted ROX ≥4.88	0.269	0.119-0.608	0.002
Adjusted by gender			
ROX ≥4.88	0.275	0.120-0.629	0.002
Gender (male)	0.412	0.187-0.909	0.028
Adjusted by chronic respiratory disease			
ROX ≥4.88	0.324	0.143-0.735	0.007
Chronic respiratory disease	0.196	0.046-0.841	0.028
Adjusted by SOFA			
ROX ≥4.88	0.291	0.128-0.660	0.003
SOFA	1.127	0.970-1.309	0.120
Adjusted by number of quadrants affected in chest X ray			
ROX ≥4.88	0.316	0.135-0.740	0.008
Number of quadrants affected in chest X ray	1.193	0.813-1.751	0.366
Adjusted by APACHE II			
ROX ≥4.88	0.292	0.129-0.664	0.003
APACHE II	0.994	0.942-1.050	0.838
Adjusted by PSI			
ROX ≥4.88	0.286	0.126-0.650	0.003
PSI	0.998	0.989-1.007	0.680
Adjusted by shock at HFNC onset			
ROX ≥4.88	0.259	0.115-0.588	0.001
Shock at HFNC onset	2.760	0.942-8.087	0.064
Adjusted by renal failure at HFNC onset			
ROX ≥4.88	0.264	0.117-0.600	0.001
Renal failure at HFNC onset	0.942	0.427-2.077	0.882

SOFA: sequential organ failure assessment; APACHE II: Acute Physiology and Chronical Health Evaluation; PSI: Pneumonia severity index.

HIGHLIGHTS

- We describe a feasible and easy-to-use index defined as the ratio of SpO_2/F_IO_2 to respiratory rate.
- When measured 12 hours after HFNC onset, a ROX index≥4.88 is a determinant of HFNC success in patients with pneumonia.
- Intubation after more than 48 hours of HFNC treatment was not associated with worse prognosis.