Clinical usefulness of SpO_2/FiO_2 ratio in children with high flow nasal cannula

Ga Eun Kim

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Myung Hyun Sohn

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This certifies that the Master's Thesis of
Ga Eun Kim is approved.

Thesis Supervisor : Myung Hyun Sohn

Thesis Committee Member#1 : Kyung Won Kim

Thesis Committee Member#2 : Ji Ye Jung

The Graduate School
Yonsei University

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ABSTRACT

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Ga Eun Kim

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The Graduate School, Yonsei University

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Objectives: The high-flow nasal cannula (HFNC) is a useful treatment modality for acute hypoxemic respiratory failure (AHRF) in children. We compared the ability of the oxygen saturation to fraction of inspired oxygen ratio (S/F) and the arterial oxygen partial pressure to fraction of inspired oxygen ratio (P/F) to predict HFNC outcomes in children with AHRF.

Methods: This study included children treated with HFNC due to AHRF between April 2013 and March 2019 at the Severance Children's Hospital. HFNC failure was defined as the need for mechanical ventilation. We analyzed the trends of S/F and P/F during HFNC. To predict HFNC outcome, a nomogram was constructed based on predictive factors.

Results: A total of 139 patients with arterial blood gas data were included in the S/F and P/F analysis. The S/F <230 at initiation showed high prediction accuracy for HFNC failure (area under the receiver operating characteristic curve: 0.751). Univariate analyses identified S/F<230 at HFNC initiation and <200 at 2h (Odds Ratio (OR) 12.83, 95% CI 5.06–35.84), and hemato-oncologic disease (OR 3.79, 95% CI 1.12–12.78) as significant predictive factors of HFNC failure. The constructed nomogram had a highly

predictive performance, with a concordance index of 0.765 and 0.831 for the exploratory and validation groups, respectively.

Conclusions: S/F may be used as a predictor of HFNC outcomes. Our nomogram with S/F for HFNC failure within 2h may prevent delayed intubation in children with AHRF.

Key Words : acute hypoxemic respiratory failure, high flow nasal cannula, SpO_2/FiO_2

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I. INTRODUCTION

High flow nasal cannula (HFNC) treatment has been described as a safe and useful technique to deliver heated and humidified oxygen to patients with acute hypoxemic respiratory failure (AHRF).[1] Its reported beneficial effects include decrease in physiological dead space, improved oxygenation, and reduction in dyspnea by supplying oxygen at a high flow rate. As such, it may be used as a next-step respiratory support after nasal prongs or an oxygen mask in patients with respiratory failure.[2,3] It has been reported that the administration of HFNC is associated with a reduction in the rate of intubation with mechanical ventilation (MV) in patients with AHRF.[2] However, if the patients' respiratory symptoms, signs, or laboratory findings, including blood gas, do not improve after implementation of HFNC, a more aggressive ventilation technique, such as invasive MV, may be considered. Identifying which patients may respond to HFNC and who may need MV can be a challenging decision.[3] The decision to start MV is a critical one as delayed intubation has proven to be a concern during HFNC treatment.[3] Therefore, predicting the outcome of HFNC at an optimal time is crucial.

To date, improvements in gas exchange and respiratory rates (RR) have

reportedly remained a predictor of successful HFNC outcome.[4,5] In contrast, clinical parameters that warrant a subsequent need for intubation are absence of oxygenation improvement, absence of significant decrease in RR, presence of additional organ failure, or persistence of thoraco-abdominal asynchrony.[5,6] The ratio of arterial oxygen partial pressure and fraction of inspired oxygen (PaO_2/FiO_2; P/F) has been suggested as an outcome predictor for noninvasive ventilation in patients with AHRF.[7] However, P/F requires arterial blood gas sampling; a procedure that is invasive and not readily available in clinical practice, especially for children.[8] The oxygen saturation (SpO_2)/FiO_2 (S/F) ratio is a noninvasive, easily detectable, and readily available parameter that may be used as a surrogate marker for P/F in children.[8-10] Furthermore, low S/F has been reported in cases of severe AHRF.[11]

The prediction of HFNC outcomes may help clinicians make a timely and optimal decision to intubate children with AHRF. Given that P/F may predict HFNC outcomes, we sought to identify whether S/F could predict HFNC outcomes as well. We also aimed to construct a nomogram as a shortcut prediction tool for HFNC outcome.

II. MATERIALS AND METHODS

1. Study population and data sources

A retrospective chart review of children treated with HFNC due to AHRF was conducted at the Severance Children's Hospital, a single tertiary center, between April 2013 and March 2019. All patients who received HFNC treatment for AHRF were included in the study. Exclusion criteria were age >18 years, indication for endotracheal intubation within 1 h of HFNC initiation, post-extubation state, and congenital heart disease.[12,13] Patients were divided into two groups: HFNC success and HFNC failure. HFNC failure was defined as the need for invasive MV due to progressive respiratory failure; the intubation decisions were based on the following criteria: a clinical deterioration

such as tachypnea, chest retraction in respiratory status, a lack of improvement in signs of high respiratory muscle workload, or deterioration of the blood gas analysis, hemodynamic instability, and deterioration of neurological status. HFNC success was defined as an improvement of respiratory distress with HFNC. A total of 419 children were treated using HFNC during the aforementioned period. Among these, 165 patients were excluded for the following reasons: 47 patients needed endotracheal intubation within 1 h of HFNC initiation, 52 patients were in the post-extubation state, 60 patients had congenital heart disease, and 6 patients were treated with noninvasive ventilation (NIV) due to progressive respiratory failure. Among the remaining 254 children, 139 who had available arterial blood gas data during the HFNC treatment were assigned to the exploratory group, and 114 without arterial blood gas data were included in the validation group. This study was approved by the Institutional Review Board of Severance Hospital (Seoul, Korea, Institutional Review Board 4-2020-0036).

2. Variable measurement and definition

Demographic data such as age, sex, weight, underlying condition, and etiology of respiratory failure were recorded. Physiologic clinical variables such as the SpO_2, FiO_2, RR, heart rate (HR), and the flow rate of gas delivered (L/min) were also obtained at HFNC initiation. The P/F was obtained from the arterial blood gas analysis at the time of HFNC initiation.

To estimate oxygenation, we calculated the S/F as a noninvasive alternative to the P/F.[9] The SpO_2 and FiO_2 were recorded at 1, 2, 4, and 12 h after HFNC initiation, and the corresponding series of S/F were calculated. HFNC initiation was defined as the point of the when HFNC treatment was started.

We evaluated the S/F as either a continuous or categorical variable, based on whether the patients achieved the therapeutic goal of S/F >200.[14] The

continuous S/F variable was substituted for the new categorical form to construct a nomogram model.

3. Device description and management

HFNC was implemented using the Optiflow (Fisher & Paykel Healthcare, Auckland, New Zealand) device, which is composed of an air mixing device, a heated humidifier, a heated gas humidification chamber (MR290), a high-performance breathing circuit (900PT561), and a unique wide bore nasal cannula. The HFNC settings were determined by each attending physician.

4. Statistical analyses

The patients' characteristics are summarized using numbers and percentages for categorical variables, and medians (interquartile range) for continuous variables. For intergroup comparisons, the Mann-Whitney U test was used for continuous variables, and the Chi-squared test or Fisher's exact test was used for categorical variables.

Receiver operating characteristic (ROC) curve analyses were performed to assess the S/F and P/F cutoff for HFNC outcomes. The area under the ROC curve (AUC) was calculated as a measure of predictive capacity. The difference of AUC was determined using the Delong's method.[15]

Univariate logistic regression analysis was used to identify independent predictive risk factors for HFNC outcomes. Factors with *P* value <0.05 in the univariate analyses were included in the prediction model. The effect of each potential risk factor was denoted by the odds ratio (OR) and its 95% confidence interval (CI).

A nomogram was constructed based on selected predictive factors identified using the multivariate logistic regression model of the exploratory

group data. The goodness of fit for each nomogram was verified using the Hosmer–Lemshow test. The discrimination ability of the nomogram was analyzed using the AUC. The calibration curve was generated to assess the discriminative performance and predictive accuracy of the nomogram. The proposed prediction model was verified through external validation of the independent data. Statistical analyses were performed using Statistical Package for the Social Sciences version 25 and R (version 3.6.1, The R Foundation for Statistical Computing, Vienna, Austria). A two-sided *P* value <0.05 was considered statistically significant.

III. RESULTS

1. Baseline characteristic

A total of 139 children with AHRF were included in the exploratory cohort. Baseline characteristics of the study population are presented in Table 1. Fifty-nine (42.4%) patients who required intubation with MV were categorized as the HFNC failure group. The median time of HFNC treatment was 14.1 h (interquartile range, 4.5–17.9), and 50 (83%) patients were intubated within 24 h. The leading cause for AHRF was pneumonia, which accounted for 67% of the total cases. Other etiologies for AHRF were bronchiolitis, bronchospasm, and acute respiratory distress syndrome (ARDS). HFNC success was statistically significant in children with bronchiolitis (*P*= 0.041), and marginally significant in children with bronchospasm. However, HFNC treatment did not show any statistical significance in AHRF due to other etiologies. The most frequent underlying diseases associated with AHRF were neuromuscular disease (61.1%) and respiratory disease (12.2%); 17 children did not have any underlying disease. Patients with underlying hemato-oncologic diseases with AHRF frequently needed HFNC treatment (*P* = 0.021).

Table 1. Subject characteristics in the exploratory group

Characteristics	HFNC success (n=80)	HFNC failure (n=59)	*P* value
Age, years	3.9 (1.2,9.3)	6.0 (1.69,13.7)	0.087
Male, n (%)	51 (63.7)	32 (53.3)	0.214
Cause of respiratory failure			
Pneumonia (n=94)	51 (63.7)	43 (72.9)	0.255
Bronchiolitis (n=16)	13 (16.3)	3 (5.1)	0.041
Bronchospasm (n=9)	8 (10.0)	1 (1.7)	0.078
ARDS (n=9)	3 (3.8)	6 (10.2)	0.169
Upper airway disease (n=3)	1 (1.3)	2 (3.4)	0.574
Underlying disease			
Neuromuscular disease (n=84)	48 (60.0)	36 (61.0)	0.904
Pulmonology (n=17)	12 (15.0)	5 (8.5)	0.246
Hemato-oncology (n=14)	4 (5)	10 (16.9)	0.021
Others (n=7)*	3 (3.8)	4 (6.8)	0.419

Data expressed as n (%) or median (interquartile range).
*Others include systemic lupus erythematosus (three patients), metabolic disorder (two patients), and chronic kidney disorder (two patients).
n, numbers; HFNC, high flow nasal cannula; ARDS, acute respiratory distress syndrome; FiO_2, fraction of inspired oxygen; SpO_2, pulse oximetry oxygen saturation; P/F, PaO_2/FiO_2

The validation cohort comprised 114 patients. No significant differences were found between the exploratory and validation groups. The results in the validation group were consistent with the exploratory group, and S/F was significantly lower in the HNFC failure group ($P < 0.001$). The patients with hemato-oncologic disease frequently needed MV in the validation group ($P = 0.039$) (Supplmentary Table 1)

Supplementary Table 1. Subject characteristics in the validation group

Characteristics	HFNC success (n=86)	HFNC failure (n=28)	*P* value
Age, years	1.7 (0.8, 5.6)	3.4 (1.3, 13.3).	0.042
Male, n (%)	53.0 (61.7)	18.0 (64.2)	0.064
RR	32.0 (25.0, 40.0)	32.5 (24.2, 46.0)	0.919
HR	147.0 (121.0, 163.0)	144.5 (134.2, 168.0)	0.206
S/F at initiation	250.0 (237.5, 326.6)	194.0 (184.0,246.9)	<0.001
Cause of respiratory failure			
Pneumonia (n=84)	59 (68.6)	25 (89.2)	0.031
Bronchiolitis (n=18)	17 (19.8)	1 (3.6)	0.041
Bronchospasm (n=7)	6 (6.9)	1 (3.6)	0.451
Upper airway disease (n=5)	4 (4.6)	1 (3.6)	0.642
Underlying disease			
Neuromuscular disease (n=56)	41 (47.4)	19 (67.8)	0.037
Pulmonology (n=22)	20 (23.2)	2 (7.1)	0.061
Hema-oncology (n=9)	4 (4.6)	5 (17.8)	0.039
Others (n=2)*	0 (0)	2 (7.1)	0.059

Data expressed as n (%) or median (interquartile range).
*Others include metabolic disorder (two patients)
n, numbers; HFNC, high flow nasal cannula; ARDS, acute respiratory distress syndrome; HR, heart rate; RR, respiratory rate

2. Respiratory variables and serial S/F monitoring during HFNC

Table 2 shows the respiratory variables at initiation and serial S/F monitoring between the HFNC success and failure groups during the HFNC treatment. The SpO_2 at HFNC initiation was significantly lower in the HFNC failure group than in the HFNC success group ($P < 0.001$). Patients in the HFNC failure group were treated with higher FiO_2 at initiation compared to the

patients in the HFNC success group (P = 0.001). Signs of respiratory distress such as RR and HR at HFNC initiation did not significantly differ between the two groups.

Table 2. Respiratory variables and serial S/F monitoring between HFNC success and failure groups during HFNC

	HFNC success (n=80)	**HFNC failure (n=59)**	***P* value**
Respiratory rate	35 (27.5,42.5)	29 (24.7,40.7)	0.424
Heart rate	152 (125.5,163.0)	153.0 (137,167.7)	0.077
HFNC setting at initiation			
FiO_2	0.4 (0.3,0.5)	0.45 (0.38,0.6)	0.001
Flow/weight	1.0 (0.8,1.3)	1.0 (0.6,1.4)	0.503
SpO_2 at initiation	97.0 (95.0,99.0)	89.0 (86.2,92.7)	<0.001
P/F at initiation	263.6 (213.4,340.0)	191.7 (143.5,286.5)	0.004
S/F			
Initiation (n=139)	242.5 (200.0,320.0)	202.5 (153.3,229.3)	<0.001
1 h (n=139)	243.7 (200.0,306.4)	214.1 (161.8,236.8)	<0.001
2 h (n=136)	247.5 (226.2,323.3)	196.0 (153.9,246.2)	<0.001
4 h (n=126)	250.0 (283.1,326.7)	221.1 (168.5,270.7)	<0.001
12 h (n=102)	250.0 (212.4,330.0)	212.4 (146.4,245.6)	<0.001

Data expressed as n (%) or median (interquartile range).
n, numbers; HFNC, high flow nasal cannula; FiO_2, fraction of inspired oxygen; SpO_2, pulse oximetry oxygen saturation; P/F, PaO_2/FiO_2; S/F, SpO_2/FiO_2

The P/F at initiation in the HFNC failure group was significantly lower than that in HFNC success group (P = 0.004). We confirmed that S/F was positively correlated with P/F, which showed a linear relationship using the regression equation (S/F at initiation = 135.199 + 0.375 × P/F at initiation, P < 0.001, Figure 1). Therefore, S/F was recorded as a respiratory oxygenation

variable through serial monitoring. The serial S/F displayed significant differences between the groups during HFNC treatment ($P < 0.001$).

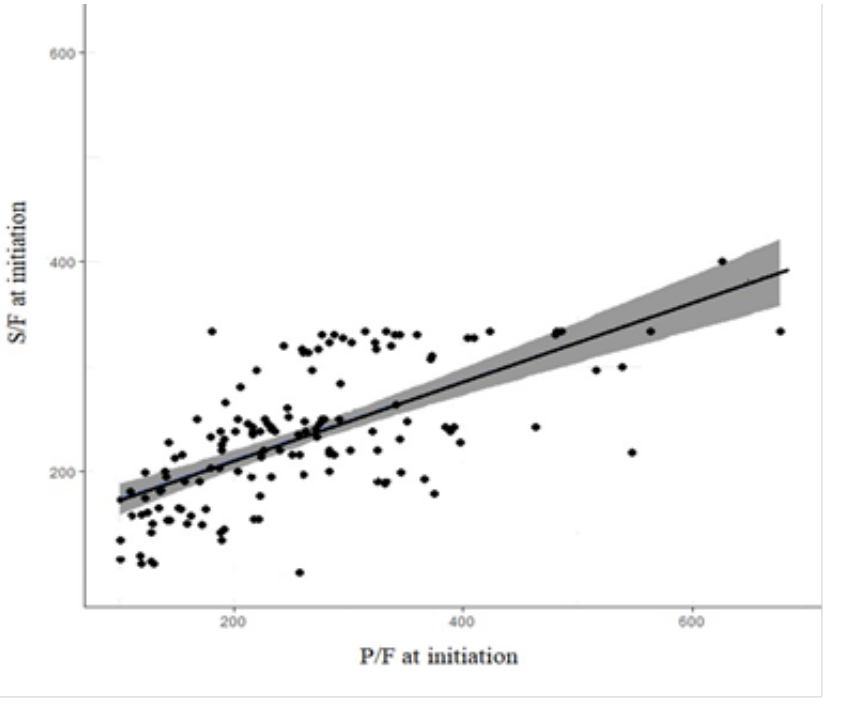

Figure 1 Scatterplot for S/F at initiation vs P/F at initiation.
The line represents the best-fit linear relationship; S/F at initiation=135.199+0.375xP/F at initiation ($P < 0.001$). (Correlation = 0.662, 95% Confidence Interval: 0.557–0.746, P <0.001

The mean S/F profile plot over time by linear mixed model is shown in Figure 2. The S/F of patients in the HFNC success group improved consistently during the initial 12 h after HFNC treatment. In the HFNC failure group, the S/F fluctuated within the first 4 h after HFNC initiation, with the lowest being 197.72 (185.4–209.9) at 2 h.

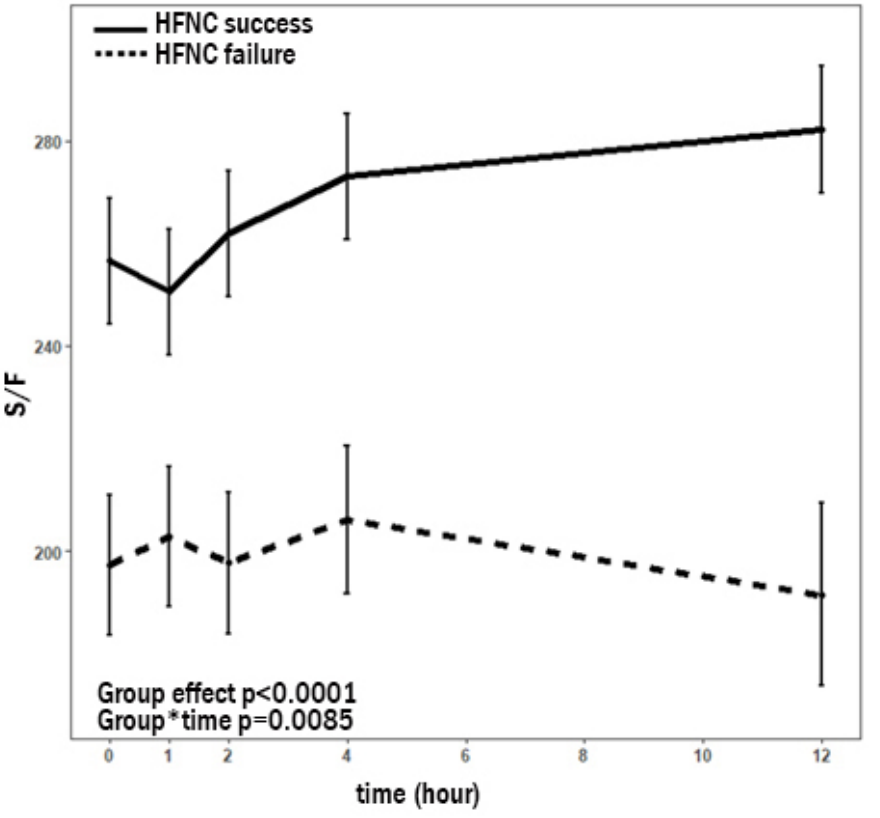

Figure 2. Serial mean S/F over time between success and failure groups during HFNC
The mean S/F values were derived from a linear mixed model, with 95% confidence intervals (error bars). The graph shows interaction effects between groups (p value <0.0001), and time *group (p value =0.0085)
S/F, ratio of oxygen saturation and fraction of inspired oxygen (SpO_2)/FiO_2; HFNC, high flow nasal cannula

The AUC of S/F at initiation for predicting HFNC failure was 0.759, and the optimal cutoff was 230 (Figure 3). The S/F <230 showed 78.0% sensitivity and 68.7% specificity. The AUC for P/F at HNFC initiation was 0.643, and the cutoff <195 showed 54.2% sensitivity and 81.2% specificity for predicting HFNC failure. The prediction power of S/F was observed to be better than that of P/F (P = 0.005)

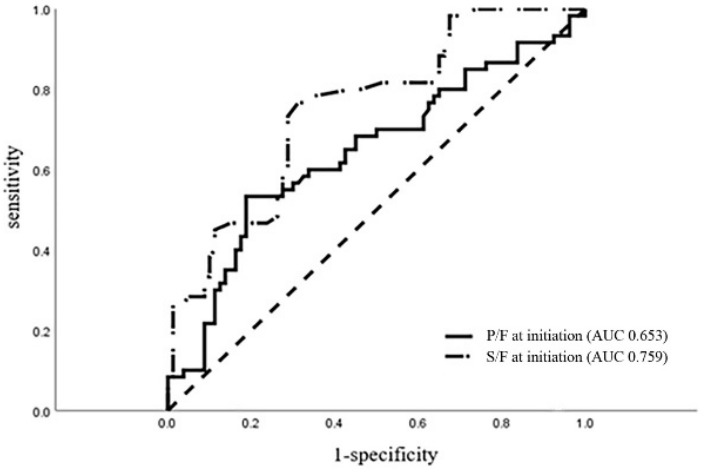

Figure 3. Comparison of receiver operating characteristic curve of P/F and S/F for predicting HFNC failure. AUC was 0.653 for P/F at initiation and 0.759 for S/F at initiation. The difference between the AUCs was statistically significant (P = 0.005 by Delong's method).
P/F, ratio of arterial oxygen partial pressure to fraction of inspired oxygen (PaO_2/FiO_2); S/F, ratio of oxygen saturation to fraction of inspired oxygen (SpO_2)/FiO_2; AUC, area under the curve; HFNC, high flow nasal cannula

Univariate logistic regression analysis of predictor of HFNC

Predictive potential risk factors for HFNC failure were identified using univariate logistic regression analyses in the exploratory group. The following variables were included in the analysis: RR, HR, flow/weight of HFNC setting at initiation, underlying disease, and newly categorized variables using an S/F <230 at HNFC initiation and <200 at 2 h (Table 3), which was identified based on the result of an analysis using various S/F cutoffs (Supplementary Table 1). A combination of S/F <230 at HNFC initiation and S/F <200 at 2 h (OR 13.067; 95% CI 5.06–35.84, P <0.001), and hemato-oncologic disease (OR 3.799; 95% CI 1.129–12.78, P = 0.031) were significantly associated with HFNC failure. Therefore, we chose these two variables (combination of S/F <230 at initiation and <200 at 2 h), and the presence of hemato-oncologic disease for multiple logistic regression analysis to construct a nomogram.

Table 3. Univariate analysis of predictive factor for HFNC failure

	Odds ratio	95% CI	*P* value
Respiratory rate	0.988	0.959-1.018	0.424
Heart rate	1.013	0.998-1.026	0.055
Flow/weight of HFNC setting	1.055	0.597-1.862	0.8541
Achievement of therapeutic goal of S/F			
S/F at initiation ≥230 & S/F at 2 hr <200	1 [Ref]		
S/F at initiation <230 & S/F at 2 hr ≥200	3.967	1.286-8.136	0.002
S/F at initiation <230 & S/F at 2 hr <200	13.067	5.06-35.84	<0.001
Underlying disease			
Neuromuscular disease	1.072	0.540-2.130	0.841
Pulmonology	0.515	0.171-1.551	0.384
Hemato-oncology	3.799	1.129-12.78	0.031

Data expressed as odds ratios with 95% confidence intervals.
HFNC, high flow nasal cannula; S/F: SpO2/FiO2
*Therapeutic goals: S/F ≥ 200 after initiation of HFNC

Supplementary Table 2. Univariate analysis of predictive factor for HFNC failure

	Odds ratio	95% CI	*P* value
S/F at initiation			
S/F	0.985	0.978-0.991	<0.0001
S/F <200	2.80	1.364-5.787	<0.0001
S/F <230	7.00	3.29-14.89	<0.0001
Achievement of therapeutic goal of S/F			
S/F at 1 hr <200	3.032	1.449-6.346	0.003
S/F at 2 hr <200	7.250	3.124-16.824	<0.0001

HFNC, high flow nasal cannula; S/F: SpO2/FiO2

Nomogram construction and validation with HFNC

Figure 4A shows a nomogram that was constructed according to two independent predictors from the multiple logistic regression analysis. The Hosmer–Lemshow test showed that the fit for multiple logistic regression model was good *(P* >0.9999). In the exploratory group, the ROC curve according to the predicted probability of the multiple logistic regression analysis is shown in Figure 4B, and the AUC was 0.765 (95% CI, 0.687–0.844). The calibration curve showed that the model was close to ideal (Figure 4C). A higher score calculated in the nomogram was associated with a higher likelihood of HFNC failure. For example, a patient with a hemato-oncologic disease whose initial S/F was 190, and 210 at 2 h, would get a total score of 90, which corresponded to approximately 70% HFNC failure risk.

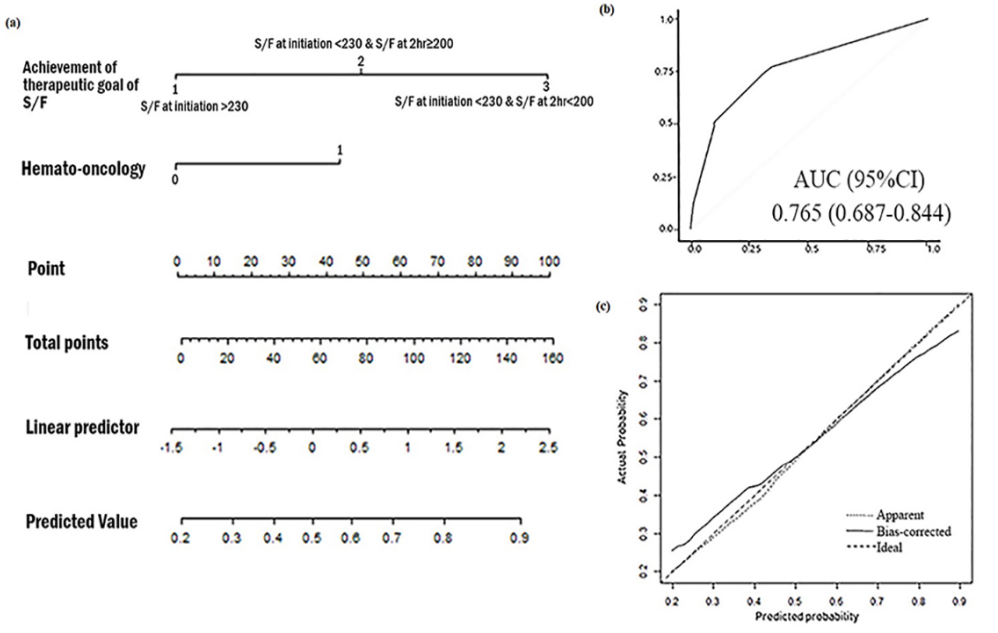

Figure 4. The constructed nomogram and performance of the model in training cohort for predicting HFNC outcomes. (A) The nomogram according to clinical indices for predicting HFNC outcomes. The nomogram is used by adding up points identified on the points scale for each variable. (B)The ROC curve of the nomogram in predicting HFNC failure in training cohort. AUC shows the ability of the nomogram. (C) Calibration curve of nomogram in the training cohort.. AUC, Area under the ROC

curve; ROC, receiver operating characteristic; HFNC, high flow nasal cannula

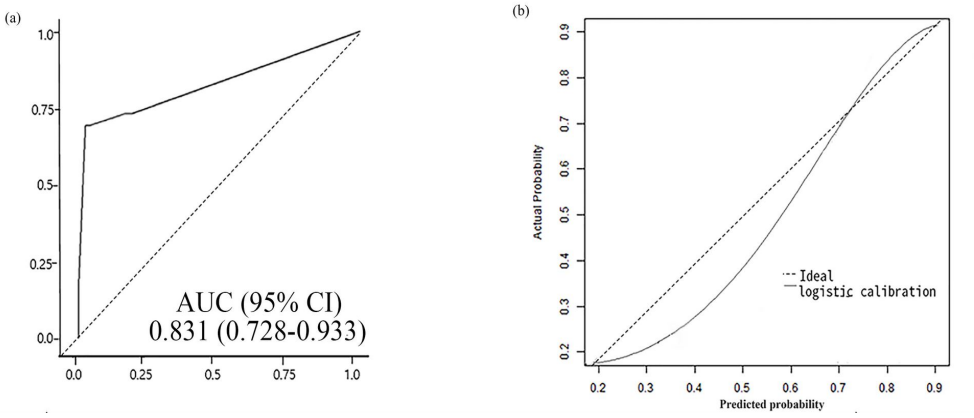

Figure 5. Validation of nomogram for predicting HFNC outcomes in patients with AHRF

(A) The ROC curve of the nomogram with 114 patients in the validation cohort. (B) Calibration plot of the nomogram in the validation cohort. The black line indicates logistic calibration of the validation cohort. The x-axis is the predicted probability from nomogram, and y-axis is the actual probability. The dashed line represents performance of ideal nomogram (predicted outcome perfectly corresponds with actual outcome).

ROC, receiver operating characteristic; HFNC, high flow nasal cannula; AHRF, acute hypoxemic respiratory failure

The nomogram also displayed its accuracy in the validation group, with an AUC = 0.831 (95% CI, 0.728–0.933) (Figure 5A). The calibration curve presented an optimal agreement between the predicted and actual probabilities in the validation group (Figure 5B).

IV. DISCUSSION

Our study showed that S/F, a noninvasive continuous monitoring variable, might be a good predictor for HFNC outcomes in children with AHRF. We created a nomogram for HFNC failure using S/F as a variable at initiation and 2 h after HFNC implementation, and the presence of hemato-oncologic disease, as a shortcut prediction tool.

Multiple studies have shown that S/F has a good correlation with P/F in patients with respiratory failure.[10,16] Our study showed similarly consistent

results with a good correlation between S/F and P/F. Furthermore, we showed that S/F had a better predictive power for HFNC failure than P/F. The best predictive S/F cutoff at initiation of HFNC was 230 in our study, which was higher than that in a previous study that reported S/F <195 during the first hour of treatment to be associated with HFNC failure.[17] The aforementioned study included patients with cardiac comorbidity, while we excluded children with congenital heart diseases because they have distinct S/F levels due to their underlying diseases. We acknowledge that our inclusion criteria might have led to different S/F cutoff levels for the prediction of HFNC failure. Fine-tuning of S/F cutoff is essential to achieve an excellent prediction power for HFNC failure. Accordingly, we used a previously reported therapeutic goal of S/F and combined it with our initial S/F cutoff to create a categorical variable.[14] Finally, an S/F cutoff of <230 at initiation and <200 at 2 h was observed to have a remarkable prediction power (OR, 13.067; 95% CI 5.06–35.84).

An emerging issue for HFNC implementation in patients with AHRF is the concern of delayed intubation, which might worsen the clinical deterioration.[18,19] Therefore, timely and appropriate identification of HFNC failure is crucial. Several indices such as P/F and S/F have been reported to be predictors for HFNC outcome.[14,20] Respiratory rate oxygenation (ROX) index, the ratio of SpO_2/FiO_2 to RR, has recently been proposed to be a better predictor for HFNC failure than S/F alone in adults.[3,21] However, the ROX index is difficult to apply in children with AHRF due to the variability of RR with age in children. Our categorical S/F variable may help clinicians decide whether endotracheal intubation should be performed within 2 h, which, in turn, would prevent delayed intubation.

Our study showed that the presence of an underlying hemato-oncologic disease was independently associated with HFNC failure, suggesting the deleterious effect of such a disease on HFNC outcome. Our findings support those of a previous study that reported that HFNC neither improved discomfort

nor decreased the need for intubation in patients with hemato-oncologic diseases.[22] In our study, 70% of patients with hemato-oncologic diseases in the HFNC failure group had a severe AHRF with a P/F of 150 mm Hg at HFNC initiation, and pneumonia was the cause of AHRF in all patients with hemato-oncologic diseases. This result parallels that of a previous study, which showed that the etiology of AHRF (pneumonia, OR 11.2) was a significant risk factor for HFNC failure.[23] HFNC failure in children with hemato-oncologic diseases might lead to various clinical conditions, complications and problems unrelated to AHRF.[24] Further, the conditions associated with the hemato-oncologic diseases might not be influenced by the mode of oxygen delivery.[25] Moreover, supporting evidence has shown that the time needed to improve oxygenation during AHRF might be longer in patients with hemato-oncologic diseases than in other patients.[26] These findings may explain why the presence of underlying hemato-oncologic disease was identified as an independent parameter for HFNC failure in our study data. As such, HFNC in patients with hemato-oncologic diseases and AHRF should be monitored with more caution.

Our study is the first to build a nomogram that predicts HFNC failure in children with AHRF. With the help of our nomogram, which was constructed using a combination of S/F and hemato-oncologic disease as predictors, clinicians may estimate the individual probability of HFNC outcome in a patient without the need for an invasive examination. This, in turn, may help clinicians make a timely decision for intubation. Furthermore, we included both internal and external validation procedures, which demonstrated strong discrimination and calibration. With the ability to estimate individual risk in an easy to use and straight forward manner, we believe that our nomogram has an advantage over simple predictors.

Our results should be interpreted with caution, as six patients who required escalation to other NIVs were not assessed. NIV was actively

implemented during the middle of the study period; consequently, those patients were excluded to maintain the homogeneity of the study. We also acknowledge the inclusion of measurements in the analysis that were performed with >97% SpO2, where the oxyhemoglobin dissociation curves might have been unchanged.[16] However, several children with AHRF who receive appropriate oxygen therapy have an SpO_2 >97%.[27] Real-world clinical evidence in children with AHRF is necessary, and it can reasonably include patients with >97% SpO_2 to reflect current practice. A good correlation between S/F and P/F using data with S/F >97% has been also demonstrated, which is consistent with our results.[28]

V. CONCLUSION

In conclusion, S/F may be an easy-to use predictor of HFNC outcomes in children with AHRF. We constructed a nomogram using S/F for HFNC failure within 2h, which may prevent delayed intubation in children with AHRF.

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ABSTRACT (IN KOREAN)

소아의 고유량 비강 캐뉼라 요법에서 산소포화도/흡입산소분율 비의 임상적 유용성

<지도교수 손 명 현 >

연세대학교 대학원 의학과

김 가 은

배경 : 고유량 비강 캐뉼라는 소아의 급성 저산소성 호흡곤란에 유용한 치료 방법이다. 고유량 비강 캐뉼라의 치료가 실패하는 경우 기관내 삽관 이 지연될 수 있기에, 기계환기의 필요성 여부에 대한 결정은 환자의 예후를 향상시키기 위해서 매우 중요하다. 이에 우리는 산소포화도/흡입산소분율 비와 동맥혈산소분압/흡입산소분율 비를 비교하여 급성 저산소성 호흡곤란을 가진 환아들의 고유량 비강 캐뉼라의 치료 결과를 예측하고자 하였다.

방법: 본 연구는 2013년 4월부터 2019년 3월까지 세브란스 어린이병원에 급성 저산소성 호흡곤란으로 고유량 비강 캐뉼라 치료를 받은 환아들을 대상으로 하였다. 고유량 비강 캐뉼라의 실패는 기관삽관 및 기계환기가 필요한 환아들로 정의하였다. 고유량 비강 캐뉼라의 적용 동안의 산소포화도/흡입산소분율 비와 동맥혈산소분압/흡입산소분율 비를 비교하였고, 고유량 비강 캐뉼라의 치료 결과를 예측하기

위한 로지스틱 회귀모형의 노모그램을 제시하고자 하였다.

결과 : 총 139명의 환자들의 동맥혈산소분압/흡입산소분율 비와 산소포화도/흡입산소분율 비가 연구에 포함되었다. 초기의 산소포화도/흡입산소분율 비 가 230미만이었고, 고유량 비강 캐뉼라의 실패에 대한 높은 예측도를 보였다. (area under the receiver operating characteristic curve: 0.751). 단변량 분석 결과 고유량 비강 캐뉼라 초기 적용 시점의 산소포화도/흡입산소분율 비가 230미만인 경우와 혈액종양학적 질병을 가지고 있는 환자들이 고유량 비강 캐뉼라 실패의 의미있는 위험요인으로 확인이 되었다. (odds ratio 3.79, 95% CI 1.12–12.78). 구축된 노모그램은 개발 코호트 그룹과 검증 코호트 그룹에서 각각 concordance index 0.765와 0.831로 높은 예측력을 보였다.

결론 : 산소포화도/흡입산소분율 비는 고유량 비강 캐뉼라의 결과를 예측 할 수 있는 좋은 지표로 사용될 수 있을 것으로 사료된다. 또한 고유량 비강 캐뉼라의 적용 후 2시간 후의 산소포화도/흡입산소분율 비를 기반으로 생성된 노모그램은 급성 저산소성 호흡곤란을 가진 환아들에게서 기계환기의 지연을 방지할 수 있는 좋은 도구가 될 것이다.

핵심되는 말 : 급성 저산소성 호흡곤란, 고유량 비강 캐뉼라