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ORIGINAL ARTICLE

Predicting nasal high-flow therapy failure by pediatric respiratory rate-oxygenation index and pediatric respiratory rate-oxygenation index variation in children

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Abstract

The primary objective of this study was to evaluate whether pediatric respiratory rate-oxygenation index (p-ROXI) and variation in p-ROXI (p-ROXV) can serve as objective markers in children with high-flow nasal cannula (HFNC) failure. In this prospective, single-center observational study, all patients who received HFNC therapy in the general pediatrics ward, pediatric intensive care unit, and the pediatric emergency department were included. High-flow nasal cannula success was achieved for 116 (88.5%) patients. At 24 h, if both p-ROXI and p-ROXV values were above the cutoff point (≥ 66.7 and ≥ 24.0, respectively), HFNC failure was 1.9% and 40.6% if both were below their values ($p < 0.001$). At 48 h of HFNC initiation, if both p-ROXI and p-ROXV values were above the cutoff point (≥ 65.1 and ≥ 24.6, respectively), HFNC failure was 0.0%; if both were below these values, HFNC failure was 100% ($p < 0.001$).

Conclusion: We observed that these parameters can be used as good markers in pediatric clinics to predict the risk of HFNC failure in patients with acute respiratory failure.

What is Known:
- *Optimal timing for transitions between invasive and noninvasive ventilation strategies is of significant importance.*
- *The complexity of data requires an objective marker that can be evaluated quickly and easily at the patient's bedside for predicting HFNC failure in children with acute respiratory failure.*

What is New:
- *Our data showed that combining p-ROXI and p-ROXV can be successful in predicting HFNC failure at 24 and 48 h of therapy.*

Keywords High-flow nasal cannula · Children · Acute respiratory failure · P-ROXI · P-ROXV

Abbreviations

AUROC	Area under the ROC curve
HFNC	High-flow nasal cannula
IMV	Invasive mechanical ventilation
NIMV	Noninvasive mechanical ventilation
p-ROXI	Pediatric respiratory rate-oxygenation index
p-ROXV	Variation in pediatric respiratory rate-oxygenation index
SpO_2	Pulse oximetry

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Introduction

While high-flow nasal cannula (HFNC) therapy is most commonly applied for infants with respiratory failure due to bronchiolitis [1, 2], studies have demonstrated its effectiveness in various cases including respiratory diseases such as acute respiratory failure [3, 4], post-extubation [5], and cardiogenic pulmonary edema [6]. Recent studies evaluating the efficacy and safety of HFNC in reducing the need for invasive mechanical ventilation (IMV) in pediatric patients with acute respiratory failure are ongoing. Although these studies are growing in number, the increasing use of HFNC brings with it the risk of delay in cases where intubation is required [7]. A predictor that accurately identifies patients at high risk of HFNC failure may be helpful to consider escalation of the respiratory support at the right time.

In an observational study evaluating adult patients receiving HFNC therapy for severe pneumonia, Roca et al. described respiratory rate-oxygenation (ROX) index as the ratio of SpO_2/FiO_2 to respiratory rate [8]. The results indicated a ROX index (ROXI) ≥ 4.88 after 12 h of HFNC therapy to be associated with a lower need for IMV. The researchers then conducted a study to validate the diagnostic accuracy of the ROXI in which five centers participated [9]. These studies showed that ROXI could be used to predict HFNC outcomes in adult patients. Studies evaluating the factors associated with HFNC failure are increasing daily. While there are many parameters to be considered in predicting HFNC failure in pediatric patients, a marker that can be used has not been proven yet. Considering changes in respiratory rate based on age in children, we used respiratory rate z-score instead of respiratory rate in the calculation and defined as pediatric respiratory rate-oxygenation index (p-ROXI).

Accordingly, this study aimed to evaluate whether p-ROXI and variations in p-ROXI (p-ROXV) could be used as objective markers in children with HFNC failure.

Materials and methods

Study design

This research was a prospective, single-center, observational study that included 131 patients between 1 month and 18 years of age, who received HFNC therapy between March 2018 and December 2019. It was approved by the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee. The parents of the included patients were informed about the study and provided their informed consent for inclusion.

Patients and definitions

All patients between 1 month and 18 years of age and treated in the general pediatrics ward, pediatric intensive care unit, and the pediatric emergency department and who received HFNC therapy were included in the study. Patients requiring urgent intubation within the first hour of HFNC and elective intubation for diagnostic or therapeutic reasons were excluded. HFNC failure was defined as follows: (1) the need for noninvasive mechanical ventilation (NIMV) or IMV support due to unstable condition and (2) providing HFNC support again within 24 h after HFNC termination. The patients with apnea, altered mental status, poor perfusion (cool extremities, capillary refill > 3 s), or bradycardia were considered unstable. The p-ROXI describes the ratio of SpO_2/FiO_2 to the respiratory rate z-score. The p-ROXV describes the percentage changes in p-ROXI for the first, second, fourth, sixth, 24th, and 48th hours of HFNC initiation.

Example of p-ROXI calculation:

$$SpO_2/FiO_2/\text{Respiratory rate z}-\text{score}$$

Example of p-ROXV calculation:

$$\text{First hour p}-\text{ROXV} = (\text{first hour p}-\text{ROXI}-0-\text{hour p}-\text{ROXI}) \times 100/0-\text{hour p}-\text{ROXI}$$

Device description and management

In the Çukurova University Faculty of Medicine, Department of Child Health and Diseases, HFNC therapy is carried out using two devices. The first is a Vapotherm Precision Flow, and the second is a Fisher and Paykel Airvo 2 Optiflow. The nasal cannula and set connected to the patient were the same brands as the device used and were adjusted based on the age of the patient.

Support for HFNC was provided to patients who could not maintain pulse oximetry (SpO_2) > 92%, despite a 15 L/min oxygen supplement with a non-rebreather mask, and whose respiratory rate was > 2 SD above the normal respiratory rate based on the age [10]. HFNC was initiated with a minimum flow rate of 1 L/kg/min and $FiO_2 = 0.6$. In the first hour, flow rate and FiO_2 were titrated to maintain pulse oximetry SpO_2 > 92%. If the respiratory rate or SpO_2 could not be maintained at the target values, the flow rate was gradually increased 0.5 L/kg/min every 15 min to the highest rate the patient could tolerate (maximum of 2.5 L/kg/min). FiO_2 was titrated by attending physician. FiO_2 was weaned at any time to provide the lowest possible oxygen percentage to maintain an oxygen saturation level of at least 92% and after 6 h of receiving an

Fio2 of 0.21, and HFNC therapy was stopped. There was no modification in the treatment modality according to patients' p-ROXI. Attending physicians were not informed about the p-ROXI.

Patients' sex, age, weight, the primary disease requiring HFNC, comorbidities, medical treatments, whether HFNC therapy had been successful, length of hospital stay, complications, and mortality during treatment were recorded. At the outset, the first, second, fourth, sixth, 24th, and 48th hours of HFNC initiation, respiratory rate and heart rate z-score [10], flow rate and FiO_2, blood gas parameters, SpO_2/FiO_2, p-ROXI, and p-ROXV values were recorded.

Statistical analysis

Categorical measurements were given as numbers and percentages, and numerical measurements were given as median (25th and 75th percentile) values. Chi-square or Fisher's exact test was used to compare categorical variables. In comparison with numerical measurements between groups, Student's *t* test or the Mann-Whitney *U* test was used, as appropriate. To assess the accuracy of different variables for correctly classifying patients who would succeed or failed HFNC, the receiver operating characteristic (ROC) curve was performed, and the area under the ROC curve (AUROC) was calculated. According to the ROC analysis, the best cutoff points were calculated using Youden's index. To compare the changes in numerical measurements over time for the same individual, one-way ANOVA or Friedman test was performed, as appropriate. The statistical significance level was taken as 0.05 in all tests. The IBM SPSS Statistics v. 20.0 software package was used to conduct statistical analysis of the data.

Results

General characteristics of the cohort

Our study included 131 patients who were treated with HFNC. The median age of patients was 23.0 (IQR, 9.0–92.0) months, and 65 of the patients were male (49.6%). Among the patients, 85.5% ($n = 112$) had an underlying chronic disease; the most common chronic disease was congenital heart disease (22.9%, $n = 30$), and 19 (14.5%) did not have any comorbidity. The most common reason for requiring HFNC therapy was pneumonia in 75 patients (57.3%) and bronchiolitis in 17 patients (12.9%). Sixty-seven of 75 (90%) patients with pneumonia had underlying disease. The median duration of HFNC therapy was 3.25 (IQR, 2.0–5.0) days. The general characteristics of the patients and the treatments are given in Table 1.

High-flow nasal cannula success and failure

Successful HFNC was achieved in 116 (88.5%) patients. There was no difference between HFNC success and failure patients in terms of primary disease, comorbidity, and the site of HFNC therapy. There was no difference between success and failure groups in terms of vital signs and blood gas parameters at HFNC initiation (Table 1). In all of the patients with HFNC failure, tachypnea continued after the initiation of HFNC; in 14 patients (93.3%), the need for FiO2 did not decrease, and in one patient (6.6%), respiratory acidosis was observed in the blood gas analysis.

In the entire cohort, one (0.7%) patient failed within the first 2 h, and eight (6.1%) patients failed within the first 48 h. Among HFNC failure patients, the maximum duration of HFNC therapy was 5 days. There was a significant difference between HFNC success and failure patients in terms of the duration of HFNC therapy (3.4 and 0.8 days, respectively, $p < 0.001$). Eight of HFNC failure patients were transferred to another hospital after the initiation of advanced respiratory support. Thirteen (86.7%) of HFNC failure patients received IMV and two (13.3%) received NIMV. Four patients with IMV and one with NIMV died during these treatments. The mortality rate of the entire cohort was 3.8%. No deaths occurred among patients where HFNC had been a success ($p < 0.001$). The length of hospitalization was 15.0 days for successful treatments. Statistical analysis did not carry out due to the deaths and the transfers in patients with HFNC failure.

Comparisons of flow rate and FiO2 provided by HFNC, respiratory rate z-score, and SpO2/FiO2 for successful and failed therapies are given in Online Resource 1. While there was no significant difference between the two groups at the initiation of therapy regarding SpO2/FiO2 ($p = 0.072$), SpO2/FiO2 significantly improved in patients where HFNC therapy had been successful as the treatment progressed ($p < 0.001$). While there was no flow rate difference between the groups at the initiation of HFNC ($p = 0.143$), the need for flow support in successful HFNC therapies was significantly lower at the 24th hour after HFNC initiation ($p = 0.014$). There was no improvement in respiratory rate z-score among patients for whom HFNC therapy failed, despite the presence of high-flow support ($p = 0.223$).

Pediatric respiratory rate-oxygenation index and rate-oxygenation variation

While the increase in p-ROXI was significant for patients with HFNC success ($p = 0.001$), there was no significant change in p-ROXI for patients with HFNC failure ($p = 0.471$). During HFNC therapy, the increase in percentage change in p-ROXI (p-ROXV) was also associated with success ($p < 0.001$), while there was no significant change in p-ROXV for patients where

Table 1 Characteristics of high-flow nasal cannula success and failure patients

	Cohort ($n = 131$) Median (25p-75p)	HFNC success ($n = 116$) Median (25p-75p)	HFNC failure ($n = 15$) Median (25p-75p)	p
Sex (male) *n* (%)	65 (49.6)	59 (50.8)	6 (40)	0.428
Age (months)	23.0 (9.0–92.0)	24.0 (11.0–95.0)	15.0 (5.0–26.0)	0.136
Primer diagnosis *n* (%)				0.294
Pneumonia	75 (57.3)	66 (56.9)	9 (60.0)	
Bronchiolitis	18 (13.7)	18 (15.5)	–	
Bronchopneumonia	9 (6.9)	8 (6.9)	1 (6.7)	
Post-extubation	9 (6.9)	9 (7.8)	–	
Heart failure	6 (4.6)	5 (4.3)	1 (6.7)	
Fluid overload	5 (3.8)	4 (3.4)	1 (6.7)	
Sepsis	5 (3.8)	3 (2.6)	2 (13.3)	
Asthma	1 (0.8)	1 (0.9)	–	
Others	3 (2.3)	2 (1.7)	1 (6.7)	
Comorbidities *n* (%)				*
Cardiac	30 (22.9)	25 (21.6)	5 (33.3)	
Renal-metabolic	26 (19.8)	22 (18.9)	4 (26.7)	
Neurologic	22 (16.8)	17 (14.7)	5 (33.3)	
Hematologic-oncologic	16 (12.2)	14 (12.1)	2 (13.3)	
Pulmonary	11 (8.4)	11 ((9.5)	–	
Immunocompromised	9 (6.9)	7 (6.0)	2 (13.3)	
Others	3 (2.3)	3 (2.6)	–	
None	19 (14.5)	19 (16.4)	–	
Site of HFNC therapy *n* (%)				0.401
General ward	80 (61.1)	69 (59.5)	11 (73.3)	
Emergency department	41 (31.3)	37 (31.9)	4 (26.7)	
PICU	10 (7.6)	10 (8.6)	0 (0)	
Heart rate (bpm)	144 (126–160)	142 (124–160)	151 (138–160)	0.450
Heart rate (z-score)	0.8 (0.3–1.5)	0.8 (0.3–1.5)	0.8 (0.0–1.3)	0.888
Systolic blood pressure (mmHg)	100 (90–100)	100 (90–102)	92 (90–100)	0.451
Diastolic blood pressure (mmHg)	60 (50–60)	60 (50–60)	60 (50–60)	0.747
pH	7.37 (7.32–7.44)	7.37 (7.32–7.44)	7.38 (7.33–7.44)	0.997
$PaCO_2$ (mmHg)	39 (34–47)	39 (34–48)	40 (35–47)	0.842
Lactate** (mmol/L)	1.8 (0.9–2.8)	1.7 (0.9–2.8)	2.6 (1.3–3.2)	0.452
Duration of HFNC therapy (days)	3.3 (2.0–5.0)	3.4 (2.3–5.2)	0.8 (0.3–2.6)	< 0.001

HFNC high-flow nasal cannula, *PICU* pediatric intensive care unit

*Statistical analysis did not carry out due to some patients with multiple comorbidities

**41 of HFNC success and 4 in HFNC failure group had lactate results were included in analysis

HFNC therapy failed ($p = 0.455$). p-ROXV was associated with HFNC success at the 24th and 48th hours (Table 2).

Predicting high-flow nasal cannula failure

The area under the ROC analysis was performed to evaluate the accuracy of p-ROXI and p-ROXV to predict HFNC failure at various time points during therapy (Table 3). At the 24th hour of HFNC therapy, the accuracy of p-ROXI and p-ROXV could successfully predict HFNC failure (AUROC, 0.79 and 0.72, respectively). The best predictive accuracy was observed at the 48th hour after HFNC initiation. The accuracy of p-ROXI and p-ROXV for predicting HFNC failure at the 48th hour after HFNC initiation had AUROC results of 0.88 and 0.88, respectively. In addition, the cutoff

Table 2 Pediatric respiratory rate-oxygenation index and pediatric respiratory rate-oxygenation index variation of high-flow nasal cannula therapy success and failure patients

	Time	HFNC Success	HFNC Failure	*p*
p-ROXI	0 h	68.0 (55.5–89.5)	63.5 (40.4–85.0)	0.191
	1 h	79.2 (62.9–102.2)	66.3 (44.4–80.7)	0.077
	2 h	79.9 (61.6–107.8)	66.4 (42.5–79.3)	0.055
	4 h	88.0 (67.0–125.4)	55.3 (37.1–124.6)	0.054
	6 h	94.1 (68.9–138.9)	66.7 (37.9–132.4)	0.103
	24 h	104.7 (74.6–178.4)	50.9 (44.3–66.4)	*0.008*
	48 h	130.0 (80.7–208.1)	52.9 (47.2–64.7)	*0.001*
p		*< 0.001*	0.471	
p-ROXV (%)	0 h	–	–	–
	1 h	8.9 (1.3–22.1)	3.5 (−0.6–14.1)	0.102
	2 h	10.0 (0.0–26.5)	0.0 (−3.7–14.1)	0.066
	4 h	16.9 (3.7–35.8)	0.6 (−2.6–32.1)	0.254
	6 h	27.1 (6.0–47.7)	17.0 (−1.8–39.4)	0.269
	24 h	37.2 (9.4–65.4)	14.4 (−12.5–23.6)	*0.035*
	48 h	47.9 (26.3–78.4)	11.3 (−35.2–17.6)	*0.001*
p		*< 0.001*	0.455	

p-ROXI pediatric respiratory rate-oxygenation index, *p-ROXV* pediatric respiratory rate-oxygenation index variation

points for sensitivity and specificity values above 90% at various time points are given in Online Resource 2.

When the best cutoff point for ROC curve was evaluated, p-ROXI ≤ 66.7 at the 24th of HFNC therapy predicted HFNC failure with 86% sensitivity and 79% specificity (Table 4). At the 48th hour of HFNC initiation, the best cutoff point for p-ROXI was 65.1, and its specificity had increased to 88%. The best cutoff points for p-ROXV at 24 and 48 h were 24.0 and 24.6, respectively.

Kaplan-Meier analysis was performed to compare HFNC failure according to high and low values from the best cutoff points determined for p-ROXI and p-ROXV. HFNC failure was found to be higher in patients who were below the cutoff points for p-ROXI and p-ROXV at 24 h of HFNC therapy ($p < 0.001$ and $p < 0.001$, respectively). In patients who were below the cutoff points, HFNC failure was also found to be higher for p-ROXI and p-ROXV at 48 h of HFNC therapy ($p = 0.016$ and $p < 0.001$, respectively). Kaplan-Meier analyses were also performed by combining cutoff points for p-ROXI and p-ROXV. At 24 h, if both p-ROXI and p-ROXV values were above the cutoff point (≥ 66.7 and ≥ 24.0, respectively), HFNC failure was 1.9% and 40.6% if both were below these values ($p < 0.001$). At 48 h after HFNC initiation, if both p-ROXI and p-ROXV values were above the cutoff point (≥ 65.1and ≥ 24.6, respectively), HFNC failure was 0.0%; and if both were below these values, HFNC failure was 100% ($p < 0.001$).

Table 3 AUROC analysis of pediatric respiratory rate-oxygenation index and pediatric respiratory rate-oxygenation index variation at different time points of high-flow nasal cannula therapy

	HFNC failure/success (*n*)	Variable	AUROC	95% CI	*p*
0 h	15/116	p-ROXI	0.64	0.40–0.88	0.223
		p-ROXV	–	–	–
1 h	15/116	p-ROXI	0.69	0.47–0.90	0.102
		p-ROXV	0.66	0.48–0.84	0.161
2 h	14/116	p-ROXI	0.67	0.43–0.91	0.132
		p-ROXV	0.62	0.42–0.82	0.294
4 h	13/116	p-ROXI	0.76	0.53–1.00	*0.021*
		p-ROXV	0.70	0.50–0.89	0.077
6 h	13/115	p-ROXI	0.69	0.41–0.96	0.099
		p-ROXV	0.59	0.35–0.82	0.451
24 h	7/105	p-ROXI	0.79	0.59–0.99	*0.010*
		p-ROXV	0.72	0.56–0.88	0.054
48 h	7/92	p-ROXI	0.88	0.78–0.98	*0.001*
		p-ROXV	0.88	0.80–0.96	*0.001*

AUROC area under the ROC curve, *CI* confidence interval, *HFNC* high-flow nasal cannula, *p-ROXI* pediatric respiratory rate-oxygenation index, *p-ROXV* pediatric respiratory rate-oxygenation index variation

Discussion

Optimal timing for transitions between invasive and noninvasive ventilation strategies is of significant importance. Accordingly, the decision to continue HFNC therapy or advanced respiratory support, which may affect mortality and morbidity in pediatric patients with acute respiratory failure, remains an important challenge for clinicians.

Although HFNC failure rate varies according to demographic and clinical features such as age, HFNC

Table 4 Predicting power of high-flow nasal cannula failure by the pediatric respiratory rate-oxygenation index and pediatric respiratory rate-oxygenation index variation at 24 and 48 h of high-flow nasal cannula therapy

		Cutoff	Sensibility	Specificity	PPV	NPV
p-ROXI	24 h	66.7	86	79	23.1	98.8
	48 h	65.1	86	88	35.3	98.8
p-ROXV	24 h	24.0	86	65	14.6	98.6
	48 h	24.6	100	77	25.0	100

HFNC high-flow nasal cannula, *NPV* negative predictive value, *PPV* positive predictive value, *p-ROXI* pediatric respiratory rate-oxygenation index, *p-ROXV* pediatric respiratory rate-oxygenation index variation

indication, and underlying disease, it was reported that this rate may reach up to 50% among children experiencing acute respiratory failure [11–14]. In retrospective studies conducted by Betters et al., the relationship between high FiO2, history of intubation, cardiac comorbidity, and HFNC failure was demonstrated [14]. The Pediatric Risk of Mortality score >4.5, $PaCO_2/PaO_2$ >0.64, and high PCO_2 were also found to be associated with HFNC failure [15, 16]. The complexity of data requires an objective marker that can be evaluated quickly and easily at the patient's bedside for predicting HFNC failure in children with acute respiratory failure. However, studies on this subject remain limited.

No study was found in the literature that evaluated the effectiveness of ROXI in pediatric patients. However, as is known, the respiratory physiology of adults and children differ in some respects, and the age and respiratory rate in children change inversely. Therefore, it will not be appropriate to simply establish a ROXI value for children of all ages. We modified ROXI and evaluated the relationship of p-ROXI with outcomes in children receiving HFNC therapy due to acute respiratory failure. We also calculated the percentage variation in the p-ROXI between the initiation and different therapy hours. We evaluated p-ROXI and p-ROXV individually and in combination.

In our study, we evaluated changes in p-ROXI and p-ROXV in patients from the initiation to the 48th hour of HFNC therapy. While the increase in p-ROXI and p-ROXV values was significant among HFNC success patients, we did not find any improvement in HFNC failure patients. With the improvement of the patients' clinical condition, a decrease in the flow rate they needed was observed by the 24th hour; this situation was not observed in HFNC failure group. Similar relationships existed in patients' FiO_2 requirements and SpO_2 values.

In the ROC analysis, the best cutoff points for p-ROXI and p-ROXV at 24th hour were 66.7 and 24.0, respectively. When both were evaluated in combination, if both values were above the cutoff points, HFNC failure was 1.9%, and it was 40.6% if both were below the cutoff points. In HFNC failure patients, 47% of patients still received HFNC support after 48 h, and the best predictive values for HFNC failure were denoted at the 48th hour. When p-ROXI and p-ROXV values were evaluated in combination, HFNC failure was 0.0% after 48 h of therapy if both values were above the cutoff points; all patients where both values presented under the cutoff points failed.

The findings of this study are promising for predicting early HFNC failure. According to these results, considering that approximately one in two patients whose values were below the cutoff points after 24 h failed, it is suggested that these patients be followed closely in terms of HFNC failure and that healthcare staff working together be informed in the event this occurs and to have the required materials ready for urgent intubation. Data at the 48th hour of HFNC initiation revealed that the combined use of p-ROXI and p-ROXV enabled predicting HFNC failure with high sensibility. Providing the necessary conditions can thus help to prevent delays in cases where intubation is needed and reduce the risk of intubation-related complications.

After Roca et al. suggested that ROXI could be used to predict HFNC failure [8], several clinicians published articles regarding their concerns about the reliability of ROXI and its clinical use. Karim and Esquinas suggested that ROXI will be more reliable when modified with PaO2/FiO2 and various hemoglobin concentrations, considering the oxyhemoglobin association–dissociation curve [17]. However, if the purpose was to establish a marker that could be employed easily and quickly at the patient's bedside, it will be more appropriate to consider SpO2 in the foreground because of the difficulty concerning blood sampling and the risk of an arterial puncture in children. Mauri et al. reinterpreted data from their existing prospective studies in which they demonstrated that flow rate affected oxygenation, respiratory rate, and ROXI [18, 19]. They suggested that the cutoff values of ROXI be determined according to diverse flow rates and that variations in ROXI would be more successful in terms of predicting outcomes. As in adults, there is no consensus regarding children in terms of how flow rate should be adjusted based on patient groups. In addition, since lung capacity varies greatly according to age, different opinions exist on the current rate that requires adjustment. Additional issues include whether the mouth is open or closed, effective humidification, cannula diameter/nostril diameter ratio, and how patient comfort may affect the physiological effectiveness of HFNC [20]. Considering the reasons noted here, it will be difficult to carry out strong randomized controlled studies evaluating the effectiveness of ROXI in children with HFNC. At this stage, we believe that ROXI and ROXV can be used as markers for identifying children who may be at the risk of HFNC failure, rather than using invasive ventilation approaches.

Our study includes some limitations. While evaluations within the research were generalized to children with acute respiratory failure, no additional analysis was conducted for etiological causes, due to an insufficient number of patients. As this was an observational study, FiO2 supports were adjusted by clinicians. The advanced respiratory support timing was decided by the

clinical care team. Despite of definitions, unstable condition criteria are prone for subjective interpretation.

Conclusions

In conclusion, this research represents the first pediatric study in which p-ROXI and p-ROXV were used in combination. Our data showed that combining p-ROXI and p-ROXV can be successful in predicting HFNC failure at 24 and 48 h of therapy. We believe that these parameters can be used as useful markers in pediatric clinics to help predict the risk of HFNC failure in patients experiencing acute respiratory failure. However, further research is needed in this regard.

Authors' contribution DY conceived and designed the study and critically reviewed the manuscript.

AY collected and analyzed the data and wrote the first draft of the manuscript.

GI collected the data and wrote a part of the first draft of the manuscript.

OOH acquired the data and critically reviewed the manuscript.

FE acquired the data and critically reviewed the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee.

Informed consent Informed consent was obtained from legal guardians.

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