Austin Journal of Pulmonary & Respiratory Medicine

Open Access

Austin Publishing Group

Research Article

Predictive Factors for High Flow Nasal Cannula Failure in Acute Hypoxemic Respiratory Failure in an Intensive Care Unit

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Received: June 10, 2020; **Accepted:** October 09, 2020; **Published:** October 16, 2020

Abstract

Background and Objective: High-Flow Nasal Cannula (HFNC), a relatively new technique in Acute Hypoxemic Respiratory Failure (AHRF), is gaining popularity in intensive care units. Our study aims to identify the predictive factors for failure of HFNC.

Method: This is a 5-year retrospective cohort study in patients with AHRF using HFNC in an ICU of a regional hospital in Hong Kong. The primary outcome is to identify the predictive factors for failure of HFNC which is defined as escalation of treatment to Non-Invasive Ventilation (NIV), Mechanical Ventilation (MV), extra-corporeal membrane oxygenation or death.

Results: Of the 124 ICU patients with AHRF, 69 (55.65%) failed in the use of HFNC. The patients failing HFNC had higher APACHE IV scores, lower GCS scores, lower platelet counts and serum sodium levels upon ICU admission and higher pH on day of HFNC commencement. They had higher respiratory rates before HFNC and higher heart rates before and 1 hour after HFNC. The Respiratory Rate-Oxygenation (ROX) index which is defined as ratio of SpO_2/FiO_2 to respiratory rate was significantly lower in the failure group 1 hour and 12 hours after HFNC. By multivariate binary logistic regression, failure of HFNC is associated with lower ROX index at 12 hours after HFNC.

Conclusion: Respiratory Rate-Oxygenation (ROX) index at 12 hour serves as a valuable tool to monitor the responsiveness to HFNC treatment. Close monitoring is required to identify patient failing using HFNC.

Keywords: Critical care medicine; Ventilation; Clinical respiratory medicine

Abbreviations

HFNC: High Flow Nasal Cannula; AHRF: Acute Hypoxemic Respiratory Failure; APACHE: Acute Physiology and Chronic Health Evaluation; ECMO: Extra-Corporeal Membrane Oxygenation

Introduction

High-Flow Nasal Cannula (HFNC), a relatively new technique to provide support in patients with respiratory distress, is gaining popularity in intensive care units. HFNC has several advantages: (I) the high flow of gas reduces the entrainment of room air and dilution of oxygen [1,2]. (II) it creates a positive pressure effect; [3] (III) it washes out carbon dioxide in the upper airway and reduces the anatomic dead space; [4,5] (IV) the heat and humidification improve mucociliary motion and sputum clearance; [6,7] and (V) it reduces upper airway resistance and work of breathing and improves thoraco-abdominal synchrony, [8-10] (VI) it is better tolerated compared with other devices like Non-Invasive Ventilation (NIV).

Researchers began to evaluate the role of HFNC in adult patients with Acute Hypoxemic Respiratory Failure (AHRF) [10]. The FLORALI trial, a multicenter randomized control trial comparing HFNC and other oxygenation strategies, found a lower ICU and 90-day mortality, and longer ventilator-free days in patients receiving HFNC [11]. The post-hoc analysis found a lower intubation rate in the patients receiving HFNC in the subgroup of patients with a P/F ratio <200.

Kang, in his retrospective cohort of 175 HFNC failure patients, found that late intubation (beyond 48hours after HFNC) had a higher ICU mortality, a lower success rate in ventilator weaning, and fewer ventilator-free days compared to early intubation (within 48 hours after HFNC) [12]. Therefore, it is ideal to know the accurate predictive factors for failure of HFNC, so that physicians can early identify patients failing HFNC and timely escalate the ventilatory support.

The predictive factors for HFNC failure are however not well investigated, with inconsistent results in different studies. We performed a retrospective cohort study to identify factors for HFNC failure in Intensive Care Unit patients.

Materials and Methods

Study population

This retrospective cohort study was conducted in the Intensive Care Unit (ICU) of Pamela Youde Nethersole Eastern Hospital in Hong Kong. The hospital records of patients admitted to ICU between May 2012 to April 2017 were retrospectively evaluated, and patients

Citation: Lun C-T, Leung C-K, Shum H-P and So S-O. Predictive Factors for High Flow Nasal Cannula Failure in Acute Hypoxemic Respiratory Failure in an Intensive Care Unit. Austin J Pulm Respir Med 2020; 7(1): 1064.

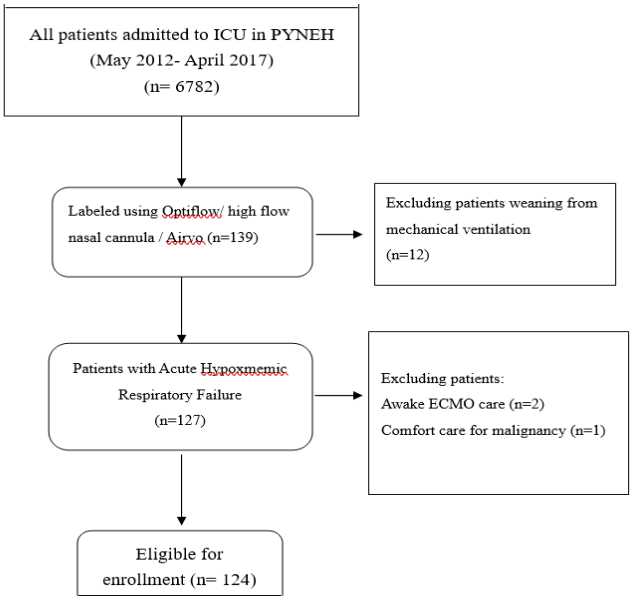

Figure 1: The enrolment of the study subjects.

were included if they had matched keywords of "Optiflow", "Airvo", or "high flow nasal cannula" as the oxygen device in the Clinical Information System (CIS, Philips Intellispace Critical Care and Anesthesia). Patients were excluded if they were (1) given High Flow Nasal Cannula (HFNC) as a tool to wean from mechanical ventilation, (2) given HFNC as a palliative management in malignancies, (3) considered not suitable for enrolment by the investigators.

The following clinical and laboratory data were collected: demographic data; diagnoses and the causes of respiratory failure; clinical parameters 1 hour before, 1 hour after and 12 hours after the use of HFNC; usage of vasopressor before commencement of HFNC; laboratory data including white blood cells, haemoglobin, platelets, prothrombin time, renal function tests, arterial blood gases upon ICU admission and on the day of HFNC use; details of oxygen therapy or mechanical ventilation before and after high flow nasal cannula; the settings of high flow nasal cannula including oxygen fraction and flow at commencement and 1 hour and 12 hours after; ; time of commencement and termination of HFNC; time of mechanical ventilation, non-invasive ventilation, extra-corporeal membrane oxygenation or death in that index admission; Acute physiology and Chronic Health Evaluation (APACHE IV) scores upon admission.

Outcomes

The primary outcome of the study is to identify the factors associated with failure of HFNC which is defined as treatment escalation to non-invasive ventilation, mechanical ventilation, extra-corporeal membrane oxygenation or death within 28 days from the commencement of high flow nasal cannula.

Statistical analyses

Statistical analysis was performed with Statistical Package for Social Science Version 19 (IBM SPSS). Baseline characteristics were expressed as mean (standard deviation) or median (interquartile range). Comparisons of continuous data for analysis were performed with Student's t-test or Mann-Whitney U test as appropriate. Fisher's exact test was used in small expected count. Comparisons of categorical data were made with Chi-square test. Discriminative power of predicting failure of HFNC was evaluated by the Receiver Operating Characteristics curve. P-values of <0.05 was considered statistically significant in univariate analysis and multivariate analysis.

This retrospective study was performed in compliance with ethical standard of the Helsinki declaration and approved by the research ethics committee of the Hospital Authority in Hong Kong, reference number HKECREC-2018-002. Written informed consent was waived.

Results

Patient characteristics

During the study period, 6782 patients admitted to the Intensive Care Unit were screened. One hundred and thirty-nine patients had the keywords of "Optiflow", "Airvo" or "high flow nasal cannula" matched in the Clinical Information System. Twelve patients received HFNC for weaning of mechanical ventilation; 1 patient for palliative care in terminal malignancy (n=1), and 2 patients for awake Extra-Corporeal Membrane Oxygenation (ECMO) care were all excluded (Figure 1). The baseline characteristics of the 124 eligible patients were summarized in (Table 1). The majority (77.4%) suffered from pneumonia as the primary cause of respiratory failure, followed by fluid overload/congestive heart failure (9.7%) and interstitial lung disease (4.8%). Before commencement of HFNC, 72 patients (58.1%), 35 patients (28.2%), 14 patients (11.3%) and 1 patient (0.8%) received

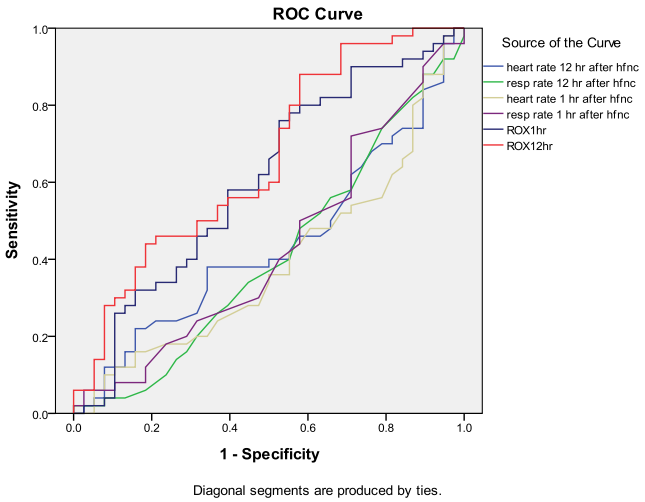

Figure 2: ROC curves predicting HFNC success.
The sensitivity and specificity would be 0.88 and 0.41 if cut-off value for ROX 12 hours would be 5.626.

	Area under curve
ROX at 12 hour after HFNC	0.659
ROX at 1 hour after HFNC	0.605
Heart rate 1 hour after HFNC	0.393
Respiratory rate 1 hour after HFNC	0.429
Heart rate 12 hour after HFNC	0.440
Respiratory rate 12 hour after HFNC	0.411

Table 1: Baseline characteristics of patients (n=124).

Age	65 (55-78)
Body weight (kg)	54.2 (44.28-59.95)
Height (cm)¥	157.86 (10.03)
Physical parameters upon ICU admission	
O_2 flow (LPM)	8 (6-15)
Respiratory rate	26 (22-32)
SpO_2	94 (91-97)
Temp (°C)	37.6 (36.93-38.3)
Heart rate ¥	107.54 (23.13)
MAP (mmHg)	85 (71.25-97.75)
Physical parameters before HFNC	
FiO_2 1 hour before HFNC	8 (6-11) LPM
Respiratory rate before HFNC	28 (23.75-32)
SpO_2 before HFNC	92 (90-94)
GCS before HFNC	15 (15-15)
Flow of HFNC at commencement (LPM)	40 (40-40)
Physical parameters 1 hour after HFNC	
Flow rate (LPM)	40 (40-40)
FiO_2	0.5 (0.45-0.6)
GCS	15 (14-15)
Heart rate	104.28 (21.61)
Respiratory rate	26 (23-32)
SpO_2	92 (90-94)
Physical parameters 12 hours after HFNC	
Heart rate ¥	96.2 (21.4)
Respiratory rate	27.25 (23-31)
ROX index	
ROX 1 hour	6.45 (4.95-8.24)
ROX 12 hours	7.14 (5.61-9.20)
Blood parameters on day of HFNC	
pH	7.46 (7.42-7.49)
$PaCO_2$ (kPa)	4.37 (3.86-5.18)
PaO_2 (kPa)	9.93 (8.66-11.6)
HCO_3 (mmol/L)	22.4 (19.8-26.0)
Hemoglobin (g/dL)	10.2 (9.1-11.9)
White cell count $x10^9$/L	12.2 (8.31-17.64)
Platelet $x10^9$/L	209 (108-288)
Sodium (mmol/L)	137 (133-140)
Potassium (mmol/L)	3.8 (3.5-4.1)
Urea (mmol/L)	6.9 (4.8-11)
Creatinine (μmol/L)	69 (55-127)
Bilirubin (mmol/L)	14 (9.23-22)
ICU stay days	6.6 (3.99-14.88)
APACHE IV score	68.5 (56.25-89.75)
Time from admission to HFNC (hours)	21.36 (5.04-54.72) hours
HFNC duration (hours)	27.41 (11.61-64.48) hours

Categorical baseline characteristics.

Sex ¶	Male	82 (66.7%)
Cause of respiratory failure ¶	Pneumonia	96 (77.4%)
	Cancer or carcinomatosis	4 (3.2%)
	Interstitial lung disease	6 (4.8%)
	Fluid overload/CHF	12 (9.7%)
	ARDS	2 (1.6%)
	Hemoptysis	1 (0.8%)
	Pulmonary embolism	1 (0.8%)
	Pleural effusion	1 (0.8%)
	Atelectasis	1 (0.8%)
Cause of pneumonia ¶	Non-specific, bacterial	85 (88.5%)
	Influenza	3 (3.1%)
	CMV	1 (1%)
	Aspiration	3 (3.1%)
	PCP	1 (1%)
	Adenovirus	1 (1%)
	Other viruses	2 (2.1%)
Modality of O_2 delivery before HFNC ¶	Nasal cannula	35 (28.2%)
	Non-rebreathing mask	72 (58.1%)
	Hudson mask	1 (0.8%)
	Optiflow	2 (1.6%)
	NIV	14 (11.3%)
Choice of vasopressor 1 hr before HFNC ¶	None	109 (87.9%)
	Noradrenaline	14 (11.3%)
	Dopamine	1 (0.8%)
Choice of vasopressor 12 hrs after HFNC ¶	None	112 (90.3%)
	Noradrenaline	12 (9.7%)
	Dopamine	0 (0%)
Modality of O_2 delivery after HFNC ¶	Nasal cannula	48 (38.7%)
	NRM	5 (4%)
	Noninvasive ventilation	21 (16.9%)
	Mechanical ventilation	43 (34.7%)
	Death	2 (1.6%)
	ECMO	1 (0.8%)
	Direct high flow nasal cannula to general ward	4 (3.2%)
Success ¶	55	44.35%
Failure ¶		69 (55.6%)
	Direct to mechanical ventilation	43 (34.7%)
	Direct to NIV (in which 6 patients later escalate to mechanical ventilation)	21 (16.9%)
	Direct to ECMO	1 (0.8%)
	Death during HFNC	2 (1.6%)
	HFNC to Nasal cannula or NRM to mechanical ventilation	2 (0.8%)
Mortality ¶	31	25%

Results shown as median (inter-quartile range) unless otherwise specified
¶ number (%) ¥ mean +/- SD
FiO_2: Fraction of Inspired Oxygen; SpO_2: Peripheral Capillary Oxygen Saturation; MAP: Mean Arterial Pressure; HFNC: High Flow Nasal Cannula; GCS: Glasgow Coma Scale; CHF: Congestive Heart Failure; ROX: Ratio of Pulse Oximetry/ Fraction of Inspired Oxygen to Respiratory Rate; APACHE: Acute Physiology and Chronic Health Evaluation; AKI: Acute Kidney Injury; ARDS: Acute Respiratory Distress Syndrome; CMV: Cytomegalovirus; PCP: Pneumocystis Pneumonia; NRM: Non-Rebreathing Mask; NIV: Non-Invasive Ventilation; ECMO: Extracorporeal Membrane Oxygenation

non-rebreathing mask, nasal cannula, non-invasive ventilation, and Hudson mask respectively. There were two patients receiving HFNC since admission in ICU. The median flow rate was 8 (IQR 6-11) litres per minute one hour before commencement of HFNC. The median respiratory rate and the mean heart rate were 28 (IQR 23.75-32) and 102.7 (SD 20.43) per minute respectively one hour before HFNC. One hundred and nine patients (87.9%), 14 patients (11.3%) and 1 patient (0.8%) were receiving no vasopressor, nor-adrenaline and dopamine respectively. Among those receiving nor-adrenaline, the median dosage was 0.098 (IQR 0.057-0.244) mcg/kg/min. The median APACHE IV score upon ICU admission was 68.5 (IQR 56.25-89.75). At commencement of HFNC, the median flow of HFNC was 40 (IQR 40-40) litres per minute and the median FiO_2 was 0.5 (IQR 0.45-0.6).

Forty-eight patients (38.7%), 5 patients (4%), 21 patients (16.9%), 43 patients (34.7%) and 1 patient (0.8%) received nasal cannula, non-rebreathing mask, non-invasive ventilation, mechanical ventilation and extracorporeal membrane oxygenation respectively after HFNC. Two patients (1.6%) died and 4 patients (3.2%) were transferred to general wards while receiving HFNC. The median HFNC duration was 27 (IQR 11.61-64.48) hours and the median time from admission to HFNC commencement was 21.36 (IQR 5.04-54.72) hours. 69 patients (55.6%) were defined as failure which was defined as any escalation to non-invasive ventilation, mechanical ventilation, Extra-Corporeal Membrane Oxygenation (ECMO) or death within 28 days after commencement of HFNC.

Primary endpoints

Compared to the 55 patients who succeeded with the use of HFNC, the 69 patients with HFNC failure had higher APACHE IV Scores and lower GCS scores upon ICU admission. (p=0.002, 0.024) They had higher respiratory rates 1 hour before HFNC (p= 0.032) and heart rates 1hour before and 1hour after HFNC (p=0.011, p<0.001). They had lower platelet counts (p=0.012) and serum sodium levels (p=0.011) upon ICU admission and a higher pH on the day of HFNC (p=0.029).

The Respiratory Rate-Oxygenation (ROX) index which is defined as a ratio of SpO_2/ FiO_2 to respiratory rate was significantly lower in the failure group at 1 hour and 12 hours after HFNC. (p=0.014, 0.014)

There was no statistically significant association between HFNC failure and different causes of respiratory failure (p=0.629) or modalities of oxygen therapy before high flow nasal cannula (p=0.646) or the time from admission to HFNC initiation (p=0.422).

Multivariate analysis

By multivariate binary logistic regression, HFNC failure is only associated with lower ROX index at 12 hours after HFNC commencement (p=0.012 OR 0.802) (Tables 2,3).

Table 2: Predictive factors for success of HFNC.

	success	failure	P value
Heart rate before HFNC ¥	97.53 (SD 19.20)	106.96 (SD 20.56)	0.011*
Heart rate 1 hour after HFNC ¥	96.76 (SD 19.07)	110.34 (SD 21.76)	<0.001*
Heart rate 12 hour after HFNC ¥	94.06 (20.76)	99.10 (22.12)	0.268
Respiratory rate before HFNC	27 (23-30)	30 (25-33)	0.032*
Respiratory rate 1 hour after HFNC	25 (22-30)	28 (23-35)	0.079
Respiratory rate 12 hr after HFNC	26.5 (22.25-30.75)	28 (23-34)	0.164
GCS upon ICU	15 (14-15)	15 (10-15)	0.024*
GCS 12 hours after HFNC	15 (15-15)	15 (13.75-15)	0.027*
pH on day of HFNC	7.44 (7.41-7.48)	7.47 (7.43-7.5)	0.029*
PCO_2 on day of HFNC	4.43 (4.04-5.19)	4.28 (3.72-4.98)	0.284
HCO_3 on day of HFNC	22.8 (19.8-25.7)	22.25 (19.88-26.38)	0.925
Platelet upon ICU	238 (152-299)	163 (100.5-251)	0.012*
Na upon ICU	137 (133-139)	134 (130.5-137)	0.011*
Bili on day of HFNC	11.5 (9-19)	16.5 (10-24.85)	0.051
APACHE IV score	62 (49-82)	75 (60.05-106.5)	0.002*
APACHE IV risk	0.18 (0.09-0.31)	0.26 (0.14-0.62)	0.003*
ROX 1 hour	7.13 (5.98-9.47)	6.93 (4.59-7.66)	0.014*
ROX 12 hours	7.39 (6.42-9.90)	6.10 (4.73-8.06)	0.014*
Time from adm to HFNC	1.01 (0.35-2.02)	0.68 (0.17-0.68)	0.422
HFNC duration (hrs)	47 (25.47-72)	18 (5.18-42.69)	<0.001*
ICU stay (days)	4.99 (3.40-7.06)	10.97 (5.33-23.04)	<0.001*
28-day mortality	0	31 (44.9%)	<0.001*
Cause of respiratory failure §			0.629
Oxygen modality before HFNC			0.646
Time from admission to HFNC	24.28 (8.32-48.43)	16.3 (4.09-59.61)	0.422

Results shown as median (inter-quartile range) unless otherwise specified
¶ number (%) ¥ mean +/- SD
HFNC high flow nasal cannula; GCS Glasgow Coma Scale; ROX ratio of pulse oximetry/fraction of inspired oxygen to respiratory rate; APACHE Acute Physiology and Chronic Health Evaluation
** Clinical significance p<0.05*
§ categorical

Table 3: Multivariate analysis of the predictive factors for success of HFNC.

	Odds Ratio	P value
ROX at 12 hours	0.802	0.012

ROX respiratory-rate-oxygenation index
*Clinical significance p<0.05

The Receiver Operating Characteristics (ROC) curve has its largest area under curve if ROX index at 12 hours is used to predict the success of HFNC in our patients. (AUC=0.659) (Figure 2). The sensitivity and specificity would be 0.88 and 0.41 respectively if cut-off value for ROX 12 hours is set to be 5.626.

Discussion

Acute Hypoxemic Respiratory Failure (AHRF) is a fatal complication of many diseases and it contributes to 30% of ICU admissions [13,14]. It has been increasingly recognized that

mechanical ventilation is associated with various adverse events and the hospital mortality remained as high as 30% [15,16]. NIV is an established treatment to improve gas exchange and to decrease intubation rate and mortality in Chronic Obstructive Pulmonary Disease (COPD) and Congestive Heart Failure (CHF) [17,18]. However, the use of NIV in acute hypoxemic respiratory failure is debatable and is even shown to be detrimental in some studies.

High flow nasal cannula appears to be a good alternative to avoid mechanical ventilation in acute hypoxemic respiratory failure. Patients were found to have a higher PF ratio, and a lower respiratory rate, work of breathing and Thoraco-Abdominal Asynchrony (TAA), when they were receiving HFNC [10,19,20]. Sztrymf et al. reported a significant decrease in TAA at 1 hr in patients receiving HFNC (p=0.0007),10 and found that patients exhibiting higher percentage of TAA as early as 30 minutes after HFNC initiation were more likely to require endotracheal intubation.

Frat, in the FLORALI trial, [11] found lower ICU mortality and 90-day mortality rates, and longer ventilator-free days in the patients receiving HFNC, compared to patients receiving standard oxygen therapy or NIV. In the post hoc analysis of the subgroup of patients with P/F ratio <200, intubation rate was significantly lower in the patients receiving HFNC. Compared to standard oxygen therapy, HFNC was associated with significant reduction in the intubation rate (OR 0.52, 95% CI 0.34-0.79, P=0.002) in a meta-analysis by Zhao, [21] despite no difference in mortality (OR 1.01, 95% CI 0.67-1.53, P=0.96).

Heart rate, respiratory rate, SOFA score, APACHE II score, oxygenation, delirium, and thoraco-abdominal asynchrony have been inconsistently identified as predictive factors for HFNC failure in different studies [9,10,22-25].

In our study, the only factor associated with HFNC failure by multivariate analysis is the ROX index at 12 hours after HFNC commencement (OR 0.802, p= 0.012). The ROX index, a ratio of pulse oximetry (SpO_2)/fraction of inspired oxygen (FiO_2) to respiratory rate, was proposed by Roca to predict the HFNC failure [26]. In his 4-year observational cohort study, ROX index demonstrated the best prediction accuracy (AUROC, 0.74) at 12 hours after HFNC initiation, with the best cut-off value for the ROX index estimated to be 4.88. It was also better than other physiological parameters to predict failure when measured at 18 hours and 24 hours after HFNC initiation. Compared to other clinical parameters, our study showed the greatest Area under Receiver Operating Characteristics Curve (AUROC=0.659) if ROX at 12 hours with the sensitivity and specificity of 0.88 and 0.41 if cut-off value was set at 5.626. Our study shared similar findings with Roca's study that the ROX index at 12 hours was better than other physiological parameters to predict HFNC failure. ROX index appears to be a useful tool and can be easily incorporated in routine clinical monitoring in patients using HFNC. We would also like to point out that the ROX index at 1 hour after HFNC was significantly lower in patients with HFNC failure (p=0.014). Although the ROX index at 1 hour only has an AUROC of 0.605 only, it may be still worthy of calculating the ROX index as early as 1 hour after HFNC.

According to our study, heart rates before and 1 hour after HFNC were predictive of HFNC failure. Apart from being a haemodynamic parameter, patient heart rate also reflects the degree of stress and the dosage of vasopressors. Interestingly, Frat also found the heart rate one hour after HFNC commencement was the only factor associated with intubation in the post-hoc analysis of the FLORALI study [25].

We found that HFNC failure patients had significant higher APACHE IV Scores and lower GCS scores upon ICU admission (p=0.002, 0.024). Obviously, a higher APACHE score signifies higher illness severity, and it has been identified as a factor for failure in previous studies. Imai, in his retrospective cohort, found delirium as a predictor of failure in high flow nasal cannula in 106 patients with acute respiratory failure [22]. Impaired consciousness in ICU patients may lead to a lower threshold for endotracheal intubation, and on the other hand it may reflect the severity of underlying illnesses.

The failure rate of 55.65% in our study seems to be high when compared to the intubation rate of 38% in the FLORALI study [11]. However, the definition of failure of HFNC differed in the two studies. Apart from intubation, we also regard escalation to NIV and 28-day mortality as HFNC failure. After excluding these patients, 43 patients (34.7%) required mechanical ventilation and the intubation rate was comparable to that in the FLORALI study. Interestingly, among 21 patients with escalation to non-invasive ventilation, a majority of 15 patients (71.4%) did not need escalation to mechanical ventilation. The role of non-invasive ventilation as escalation of support after failure of HFNC has never been investigated and may warrant further studies.

In our study, patients with higher APACHE IV scores, more deranged physical parameters including high heart rates & respiratory rates and blood parameters of low platelet counts, sodium levels and higher pH were at higher risk of HFNC failure. Close monitoring of clinical response is deemed important in patients receiving HFNC. As early as 1 hour after HFNC initiation, the heart rate can provide additional information to predict treatment failure. ROX index at 12 hours has a valuable role in clinical monitoring. As supported by findings from Roca's cohort 26 and our study, escalation of treatment has to be considered if ROX index is lower than the cut-off value or patient condition deteriorates. Because HFNC has an advantage of improving patient comfort and patients probably may tolerate for long period of time, physicians should beware of delaying endotracheal intubation.

Our study had several limitations. Firstly, it is a retrospective study without predetermined protocol for the indication, initiation and cessation of HFNC. Secondly, patients' comfort, dyspnoea and TAA were not assessed as they were not routinely documented in the medical record. Thirdly, the ROX index at 12 hours, as a tool to predict failure, is unable to identify patients failing HFNC within 12 hours. Fourthly, our study has a small sample size and is prone to be under-powered. Finally, there is heterogeneity in the causes of acute hypoxemic respiratory failure, though no relationship was found in our study between HFNC failure and the etiology of the respiratory failure.

Conclusion

HFNC is an excellent modality of respiratory support with advantages of simplicity and excellent tolerance, with proven benefit in terms of patient physiological parameters and clinical outcome.

Close monitoring of the physical parameters is crucial. The ROX index has a predictive role in treatment failure and can be easily employed as a routine monitoring parameter for patients on HFNC. Physicians should beware of delayed intubation which was shown to have worse clinical outcome.

Authorship Statement

Dr. Chung-tat Lun designed, analysed the data and wrote the paper; Dr. Chi-kin Leung collected data and wrote the paper; Dr Hoi-ping Shum collected and analysed the data and Dr. Sheung-on So designed and supervised the writing.

Disclosure Statement

All the authors did not have any conflicts of interest. The study is not funded by any organization.

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