

Comparison of outcomes of high-flow nasal cannula and noninvasive positive-pressure ventilation in patients with hypoxemia and various APACHE II scores after extubation

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Abstract

Aims: The study aimed to compare and analyze the outcomes of high-flow nasal cannula (HFNC) and noninvasive positive-pressure ventilation (NPPV) in the treatment of patients with acute hypoxemic respiratory failure (AHRF) who had extubation after weaning from mechanical ventilation.

Methods: A total 120 patients with AHRF were enrolled into this study. These patients underwent tracheal intubation and mechanical ventilation. They were organized into two groups according to the score of Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II); group A: APACHE II score <12; group B: $12 \leq$ APACHE II score <24. Group A had 72 patients and patients given HFNC were randomly assigned to subgroup I while patients given NPPV were assigned to subgroup II (36 patients in each subgroup). Group B had 48 patients and patients given HFNC were randomly assigned to subgroup I while patients given NPPV were assigned to subgroup II (24 patients in each subgroup). General information, respiratory parameters, endpoint event, and comorbidities of adverse effect were compared and analyzed between the two subgroups.

Results: The incidence of abdominal distension was significantly higher in patients treated with NPPV than in those treated with HFNC in group A (19.44% versus 0, $p=0.005$) and group B (25% versus 0, $p=0.009$). There was no significant difference between the HFNC- and NPPV-treated patients in blood pH, oxygenation index, partial pressure of carbon dioxide, respiratory rate, and blood lactic acid concentration in either group ($p>0.05$). Occurrence rate of re-intubation within 72 h of extubation was slightly, but not significantly, higher in NPPV-treated patients ($p>0.05$).

Conclusion: There was no significant difference between HFNC and NPPV in preventing respiratory failure in patients with AHRF with an APACHE II score <24 after extubation. However, HFNC was superior to NPPV with less incidence of abdominal distension.

The reviews of this paper are available via the supplemental material section.

Keywords: acute hypoxemic respiratory failure, Acute Physiologic Assessment and Chronic Health Evaluation II, high-flow nasal cannula, noninvasive positive-pressure ventilation

Received: 27 January 2021; revised manuscript accepted: 22 February 2021.

Introduction

Acute hypoxemic respiratory failure (AHRF) is common in patients with severe pneumonia, cardiogenic pulmonary edema, acute respiratory distress syndrome, and sepsis, and is the main cause of admission to the intensive care unit (ICU).¹

Oxygen therapy is an important aspect of supportive care to avoid re-intubation, and currently there are three different noninvasive ventilation options that could increase the oxygenation index (OI) in patients with AHRF, including routine oxygen inhalation, high-flow nasal cannula (HFNC), and

Ther Adv Respir Dis

2021, Vol. 15: 1–11

DOI: 10.1177/
17534666211004235

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noninvasive positive-pressure ventilation (NPPV).^{2,3} Conventionally, NPPV is often used as it can provide positive end-expiratory pressure (PEEP) and positive airway pressure, and can improve heart/lung function and OI. However, compared with HFNC, NPPV is associated with higher tidal volumes, which increase the risk of ventilator-induced lung injury. In addition, a patient's tolerance to NPPV is low and comorbidity of adverse effect with NPPV (such as abdominal distension, aspiration, and sputum accumulation) is high.

HFNC is a novel therapeutic method that has recently been used in patients with AHRF after weaning from mechanical ventilation, which delivers optimal oxygen through a nasal cannula and generates low-level positive pressure. The humidified gas can improve cilia movement on the mucosal surface of the airway and enhance lung compliance. In addition, studies have shown that the effectiveness of clearing the dead space in nasal cavities has a linear positive dependency with nasal high-flow treatment, and that high-flow pressure increases the elimination of dead space gas during expiration, which results in improving OI and carbon dioxide clearance.⁴⁻⁶ However, HFNC application for patients who have had extubation following weaning from mechanical ventilation and have a score of >12 on Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II), remains to be further evaluated.⁷ It has been reported that patients with >15 APACHE II score have a higher risk of nosocomial infection and death.⁸ The current study was, therefore, designed to compare and evaluate the effect of HFNC and NPPV in the treatment of respiratory failure after weaning from mechanical ventilation and extubation for patients with AHRF by grouping patients into two groups based on APACHE II score: group A: APACHE II score <12 ; group B: $12 \leq$ APACHE II score <24 .

Materials and methods

Patient enrollment

This study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University. Informed consent was obtained from all the study subjects before enrollment. The study was performed in accordance with the Helsinki II declaration. A patient was enrolled into the study if he/she was not re-intubated within 24 h of extubation

and met the following criteria: (a) patients were conscious with a Glasgow score ≥ 13 , cough reflex, and sputum excretion; (b) acute respiratory failure (severe acute hypoxemia with PaO₂/Fraction of inspiration O₂ (FIO₂) ratio <300 and a high respiratory drive reflected by clinical signs of respiratory distress); (c) hemoglobin >80 g/L; (d) no contraindication to the application of NPPV.

Criteria for exclusion included: patients with hypercapnia during the spontaneous breathing trial (SBT); inconsistent blood flow (systolic blood pressure <80 mmHg); insufficient blood flow as indicated by electrocardiogram (ECG) (flattened or inverted T wave, or ST segment depression); severe arrhythmia; severe cardiac failure [left ventricular ejection fraction (LVEF) $<25\%$]; unconsciousness; high risk for aspiration or no cough reflex; complicated with other organ function failure (e.g. shock, digestive tract perforation, severe bleeding, or brain diseases); non-treated pneumothorax or mediastinal emphysema; re-intubated within 24 h of extubation; sepsis.⁹

Patients and grouping

As shown in Figure 1, a total of 120 patients with AHRF treated with mechanical ventilation at the Department of Critical Care, Wuhan No. 1 Hospital, from December 2014 to November 2018, were enrolled into this study. Based on the APACHE II score, they were grouped as follows: group A: a low-risk group with APACHE II score <12 on the day of extubation; group B: a high-risk group with $12 \leq$ APACHE II score <24 on the day of extubation. Using a random-numbers table, patients in each group were randomly assigned into two subgroups: patients in subgroup I were treated with HFNC while patients in subgroup II were treated with NPPV. An informed and signed consent form was obtained from the patients or their legal guardians. The study protocol was registered (Registration #: 2014-P-07).

Weaning from mechanical ventilation

Hamilton Medical G5 and C2 ventilators (Bonaduz, Switzerland) were used in the current study. The weaning protocol included daily assessment of patients according to the following criteria. The mechanical ventilation was set at spontaneous breathing mode with FiO₂ ≤ 0.4 and PEEP <8 cm H₂O. If the patient's diaphragm movement was >10 mm and OI >150 without

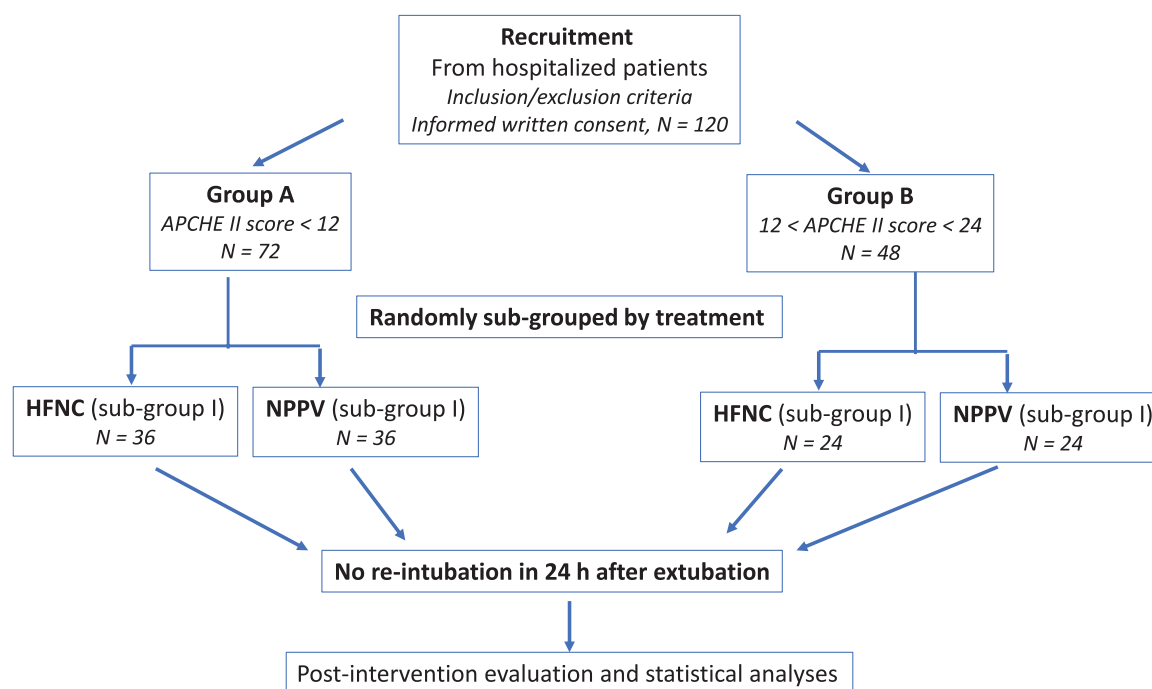


Figure 1. Schematic flowchart of patient enrollment and grouping. APACHE II, Acute Physiologic Assessment and Chronic Health Evaluation II; HFNC, high-flow nasal cannula; NPPV, noninvasive positive-pressure ventilation.

the following issues during a 120 min observation period,¹⁰ weaning was initiated: (a) respiratory rate (RR) >35 times/min or <8 times/min, which lasted for 5 min or longer; (b) altered level of consciousness; (c) ECG signs of myocardial ischemia; (d) acute arrhythmia; (e) two or more signs of respiratory distress including tachycardia (>130 beats/min), bradycardia (<60 beats/min), accessory muscle recruitment, paradoxical breathing, diaphoresis, and severe shortness of breath; (f) need for high doses of vasoactive drugs to maintain blood pressure.¹¹ Patients fulfilling these criteria underwent a SBT, either with a T-tube or 7 cm H₂O of pressure support for 30 min.

Patients who passed the SBT were randomized to receive either HFNC or NPPV.

Treatment option

Patients in the HFNC subgroup (subgroup I) were treated using a device from Fisher & Paykel (Guangzhou, China). Initial flow was 40 L/min, 37°C temperature, and adjustable FiO₂ to ensure >90% blood oxygen saturation. HFNC was given for 24 h followed by conventional oxygen inhalation if necessary.

Patients in the NPPV subgroup (subgroup II) were treated using V60 ventilator (Philips, Cambridge MA, USA), S/T mode, 10–12 cm H₂O inspiratory positive airway pressure, 4–6 expiratory positive airway pressure, 1.5–2.0 inspiration/expiration ratio, 0.5–1.0 s of pressure increase time, and adjustable FiO₂ to ensure >90% blood oxygen saturation. NPPV was given for 24 h followed by conventional oxygen inhalation if necessary.

Parameters and study termination criteria

The following general information was collected: age, gender, body mass index (BMI), smoking status, APACHE II score, cause of respiratory failure, heart rate (HR), mean blood pressure (MBP), RR, Oxygen saturation (SpO₂), body temperature, LVEF, arterial pH, blood lactate acid concentration, PaCO₂, and OI. Patients had insertion of a cannula needle into the radial artery in order to monitor artery pressure as well as to analyze artery blood gas. Blood pH, PaO₂, FiO₂, PaCO₂, blood lactic acid, and LVEF were recorded before the intervention as well as at 1 h and 6–12 h after the intervention. Re-intubation rate, abdominal distension, facial skin damage (facial skin turned red or broken), atelectasis,

28-day mortality, time of oxygen therapy, length of ICU stay, and in-ICU mortality were also recorded.

Abdominal distension was defined as patients feeling abdominal tension with an abdominal bulge that was higher than the chest, percussion revealed mid-tone or high-tone drum sound, and auscultation revealed bowel sounds decreased or disappeared.

The study was terminated if a patient had a second intubation within 72 h of extubation.

Statistics

SPSS 17.0 statistical software was used. Data were expressed as the mean \pm SD and statistical comparisons were performed using the Students *t*-test for the normal distributed data. The Wilcoxon rank-sum test was used for the non-normally distributed data analysis. The chi-squared test was used for the comparison of categorical variables.

Results

A total 120 patients with AHRF were enrolled into this study. Of these, 71 were men and 49 women, with average age of 67.11 ± 5.60 years. As shown in Table 1, there were no significant differences between the patients treated with NPPV or HFNC with regard to age, gender ratio, BMI, smoking status, cause of respiratory failure, HR, MBP, RR, SpO₂, body temperature, LVEF, arterial pH, blood lactate, PaCO₂, and OI ($p > 0.05$). Similarly, there were no significant differences in those parameters in group A ($p > 0.05$) (Table 2) or group B ($p > 0.05$) (Table 3) patients treated with either NPPV or HFNC.

Incidence of abdominal distension, the primary outcome of this study, was significantly higher in the patients treated with NPPV (21.67%) than in patients treated with HFNC (0%) ($p < 0.001$) (Table 4). However, there were no significant differences in other parameters between patients treated with NPPV or HFNC (Table 4).

Comparison of the secondary outcomes between the patients treated with NPPV or HFNC in group A is shown in Table 5. It was found that re-intubation within 72 h of extubation occurred neither in

the NPPV nor HFNC treatment subgroups (Table 5). Incidence of abdominal distension, however, was significantly higher in the patients treated with NPPV than in those treated with HFNC (19.44% *versus* 0, $p = 0.005$). Facial skin damage occurred in one patient (2.78%) treated with NPPV, but not in patients treated with HFNC ($p > 0.05$) (Table 5). Time of oxygen therapy was not significantly different between the patients treated with NPPV or HFNC [107.72 ± 39.31 h (interquartile range, 87–110) in NPPV *versus* 118.69 ± 23.85 h (interquartile range, 102–132) in HFNC; 95% confidence interval (CI): -26.26 to 4.31 ; $p = 0.157$]. No significant differences were found in the length of ICU stay, in-ICU mortality, and 28-day mortality between the patients treated with NPPV or HFNC (Table 5). Comparison of other outcomes including HR, MBP, RR, body temperature, LVEF, arterial pH, blood lactate, PaO₂, PaCO₂, and OI between patients treated with NPPV or HFNC at 1 h and 6–12 h is also showed in Table 5. There were no significant differences in these parameters.

Comparison of the secondary outcomes between patients treated with NPPV or HFNC in group B is shown in Table 6. It was found that re-intubation within 72 h of extubation occurred in one patient (4.17%) in the NPPV group and none (0%) in the HFNC group ($p = 0.312$) (Table 6). Incidence of abdominal distension was significantly higher in the patients treated with NPPV than in those patients treated with HFNC (25% *versus* 0) ($p = 0.009$). Time of oxygen therapy was not significantly different between the two subgroups [133.88 ± 40.56 h (interquartile range, 108–164) in the patients treated with NPPV *versus* 122.38 ± 42.41 h (interquartile range, 95–123) in the patients treated with HFNC; 95% CI: -13.3 to 34.8 ; $p = 0.342$] (Table 6). Similarly, the length of ICU stays between the patients treated with NPPV (165.21 ± 41.08 h) or HFNC (172.56 ± 38.05 h) ($p = 0.523$) were not statistically different (Table 6). None of the patients in group B had facial skin damage or died within 28 days of extubation (28-day mortality) or during treatment in the ICU (in-ICU mortality). Comparison of other outcomes including HR, MBP, RR, body temperature, LVEF, arterial pH, blood lactate, PaO₂, PaCO₂, and OI between the patients treated with NPPV or HFNC at 1 h and 6–12 h are also showed in Table 6. There were no significant differences in these parameters.

Table 1. Baseline comparison of patients treated with NPPV or HFNC.

	NPPV (n = 60)	HFNC (n = 60)	p value
Age (years)	66.87 ± 6.92	67.35 ± 4.85	0.659
Gender (male/female)	39/21	32/28	0.194
Body mass index (kg/m ²)	22.49 ± 2.10	22.35 ± 1.69	0.677
Smoking (case)	30	31	0.855
Cause of respiratory failure			
Pulmonary infection (case)	38	35	0.575
Cardiogenic pulmonary edema (case)	11	14	0.500
Specific	3	1	0.309
Other identified causes (case)	7	8	0.782
Not identified causes (case)	1	2	0.559
Parameters at baseline			
Heart rate (beats/min)	93.12 ± 15.83	87.70 ± 16.92	0.073
Mean blood pressure (mmHg)	93.72 ± 13.29	92.50 ± 11.60	0.594
Respiratory rate (breaths/min)	23.67 ± 3.50	22.88 ± 3.49	0.222
Body temperature (°C)	37.02 ± 0.74	37.23 ± 0.79	0.138
Left ventricular ejection fraction	51.65 ± 5.56	53.81 ± 6.53	0.053
Arterial pH	7.36 ± 0.04	7.37 ± 0.04	0.135
Blood lactate (mmol/L)	2.23 ± 0.68	2.03 ± 0.80	0.143
PaO ₂ (mmHg)	51.75 ± 4.29	52.12 ± 5.60	0.688
PaCO ₂ (mmHg)	39.92 ± 4.87	40.30 ± 5.07	0.673
FiO ₂ (%)	0.45 ± 0.08	0.43 ± 0.06	0.111
Oxygenation index (mmHg)	118.87 ± 23.66	121.38 ± 20.70	0.536
Mechanical ventilation time (hours)	69.22 ± 12.53	70.83 ± 13.61	0.502
FiO ₂ , fraction of inspired oxygen; HFNC, high-flow nasal cannula; NPPV, noninvasive positive-pressure ventilation; PaCO ₂ , partial pressure of carbon dioxide; PaO ₂ , partial pressure of oxygen.			

Discussion

AHRF is characterized by severe acute hypoxemia (OI < 300) and causes a high respiratory drive reflected by clinical signs of respiratory distress.¹² Highly labored breathing usually results in hyperventilation and hypocapnia. For patients with impending respiratory muscle fatigue, hypercapnia may be induced. The therapeutic

approach for patients with AHRF is to treat etiological factors such as infection, cardiac insufficiency, or fluid overload as well as to provide supportive care while awaiting resolution. Oxygen therapy, including conventional oxygen therapy, HFNC, and NPPV, is an important aspect of supportive care.¹³ However, it is not clear which oxygen therapy is more appropriate

Table 2. General characteristics of the patients in group A.

	NPPV (n=36)	HFNC (n=36)	p value
Age (years)	66.25 ± 6.97	67.64 ± 5.07	0.337
Gender (male)	23	20	
Body mass index	22.24 ± 2.51	22.37 ± 1.70	0.806
Smoking	17	18	
Cause of respiratory failure			
Respiratory infection	22	20	0.633
Cardiogenic pulmonary edema	7	9	0.571
Specific	2	1	0.555
Other identified causes	4	6	0.496
Not identified causes	1	0	0.314
Parameters at baseline			
Heart rate (beats/min)	92.75 ± 10.95	87.73 ± 13.33	0.085
Mean blood pressure (mmHg)	92.83 ± 12.90	91.72 ± 9.92	0.683
Respiratory rate (breaths/min)	23.95 ± 3.29	22.67 ± 3.89	0.137
Body temperature (°C)	37.17 ± 0.83	37.28 ± 0.80	0.575
Left ventricular ejection fraction	52.00 ± 4.88	54.19 ± 4.77	0.058
Arterial pH	7.35 ± 0.05	7.37 ± 0.04	0.133
Blood lactate (mmol/L)	2.23 ± 0.69	2.02 ± 0.78	0.216
PaO ₂ (mmHg)	51.97 ± 3.85	51.06 ± 4.77	0.137
PaCO ₂ (mmHg)	40.11 ± 4.74	40.67 ± 4.96	0.628
FiO ₂ (%)	0.45 ± 0.09	0.43 ± 0.06	0.214
Oxygenation index (mmHg)	120.47 ± 26.37	118.11 ± 17.19	0.654
Mechanical ventilation time (hours)	68.57 ± 14.32	68.22 ± 11.53	0.909
FiO ₂ , fraction of inspired oxygen; HFNC, high-flow nasal cannula; NPPV, noninvasive positive-pressure ventilation; PaCO ₂ , partial pressure of carbon dioxide; PaO ₂ , partial pressure of oxygen.			

for patients at different risk who have undergone extubation.

Here, patients with AHRF were randomly assigned into two groups by APACHE II score, and outcomes of HFNC and NPPV in the treatment of patients with AHRF who had extubation after mechanical ventilation due to acute exacerbation,

were compared and analyzed. APACHE II is a severity-of-disease classification system, which is often used to predict risk of death for severely ill patients. APACHE II has also been used to predict prognosis of acute exacerbation of AHRF¹⁴ and especially, APACHE II score could be used for making decisions on the application of mechanical ventilation in acute exacerbation of AHRF.¹⁵ In

Table 3. General characteristics of the patients in group B.

	NPPV (n = 24)	HFNC (n = 24)	p value
Age (years)	67.79 ± 6.89	66.92 ± 4.58	0.607
Gender (male)			
Body mass index	22.87 ± 1.20	22.32 ± 1.70	0.202
Smoking	13	13	1.000
Cause of respiratory failure			
Respiratory infection	16	15	0.763
Cardiogenic pulmonary edema	4	5	0.712
Specific	1	0	0.312
Other identified causes	3	2	0.637
Not identified causes	0	2	0.149
Parameters at baseline			
Heart rate (beats/min)	94.00 ± 13.26	87.42 ± 9.70	0.056
Mean blood pressure (mmHg)	95.04 ± 14.02	93.67 ± 13.89	0.734
Respiratory rate (breaths/min)	23.25 ± 3.84	23.21 ± 2.84	0.966
Body temperature (°C)	36.80 ± 0.53	37.16 ± 0.77	0.067
Left ventricular ejection fraction	50.67 ± 6.03	53.67 ± 4.23	0.052
Arterial pH	7.38 ± 0.04	7.38 ± 0.04	0.597
Blood lactate (mmol/L)	2.23 ± 0.67	2.03 ± 0.69	0.313
PaO ₂ (mmHg)	51.42 ± 4.94	53.71 ± 6.42	0.173
PaCO ₂ (mmHg)	39.63 ± 5.14	39.75 ± 5.29	0.934
FiO ₂ (%)	0.45 ± 0.04	0.43 ± 0.05	0.298
Oxygenation index (mmHg)	116.46 ± 19.16	126.29 ± 24.65	0.130
Mechanical ventilation time (hours)	70.17 ± 13.81	72.45 ± 14.21	0.576
FiO ₂ , fraction of inspired oxygen; HFNC, high-flow nasal cannula; NPPV, noninvasive positive-pressure ventilation; PaCO ₂ , partial pressure of carbon dioxide; PaO ₂ , partial pressure of oxygen.			

this study, patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) were assigned to group A: <12 APACHE II score and group B: 12 ≤ APACHE II score <24. We found that there were no differences in HR, MBP, RR, body temperature, LVEF, arterial pH, blood lactate, PaO₂, PaCO₂, and OI in patients treated

with HFNC or NPPV regardless of whether they were in group A or group B. However, incidences of abdominal distension and facial skin damage were higher in subgroup II (treated with NPPV) than in subgroup I (treated with HFNC), suggesting HFNC was superior to NPPV in patients with AHRF after weaning from mechanical ventilation.

Table 4. Comparison of parameters in all patients treated with NPPV or HFNC.

Parameters	1 h			6–12 h		
	NPPV (n = 60)	HFNC (n = 60)	p value	NPPV (n = 60)	HFNC (n = 60)	p value
Heart rate (beats/min)	82.40 ± 10.26	82.42 ± 8.20	0.992	78.60 ± 7.76	78.60 ± 7.71	1.000
Mean blood pressure (mmHg)	89.52 ± 11.04	87.70 ± 10.49	0.357	90.18 ± 12.88	86.00 ± 13.14	0.081
Respiratory rate (breaths/min)	20.95 ± 3.91	20.63 ± 3.31	0.633	18.00 ± 2.77	18.90 ± 2.56	0.067
FiO ₂ (%)	0.42 ± 0.07	0.43 ± 0.05	0.843	0.43 ± 0.07	0.42 ± 0.07	0.196
Body temperature (°C)	37.03 ± 0.61	37.26 ± 0.73	0.064	36.82 ± 0.56	36.61 ± 0.65	0.060
Left ventricular ejection fraction (%)	51.22 ± 5.48	53.10 ± 5.17	0.056	51.77 ± 6.20	53.85 ± 5.90	0.062
Arterial pH	7.38 ± 0.03	7.38 ± 0.03	0.860	7.38 ± 0.02	7.38 ± 0.02	0.434
Blood lactate (mmol/L)	2.32 ± 0.97	2.01 ± 0.86	0.060	1.69 ± 0.77	1.46 ± 0.49	0.053
PaO ₂ (mmHg)	65.75 ± 5.57	63.72 ± 6.26	0.066	73.76 ± 5.36	72.21 ± 6.39	0.153
PaCO ₂ (mmHg)	40.52 ± 3.12	40.17 ± 3.02	0.533	39.77 ± 2.13	39.70 ± 2.43	0.873
Oxygenation index (mmHg)	159.03 ± 29.54	152.25 ± 26.44	0.118	176.58 ± 31.33	169.72 ± 36.66	0.272
	NPPV (n = 60)		HFNC (n = 60)	p value		
Re-intubation rate (%)	1 (1.66)		0	0.315		
Abdominal distension (%)	13 (21.67)		0	0.000		
Facial skin damage (%)	1 (1.66)		0	0.315		
28-day mortality (%)	0		0	–		
Time of oxygen therapy (hours)*	118.15 ± 41.56		120.43 ± 32.13	0.737		
Length of ICU stay (hours)	150.57 ± 40.51		157.21 ± 26.13	0.288		
In-ICU mortality (%)	0		0	–		

*During HFNC or NPPV treatment.
 FiO₂, fraction of inspired oxygen; HFNC, high-flow nasal cannula; ICU, intensive care unit; NPPV, noninvasive positive-pressure ventilation; PaCO₂, partial pressure of carbon dioxide; PaO₂, partial pressure of oxygen.

In this study, 13 of the NPPV-treated patients had abdominal distension, and 1 patient had respiratory failure after re-intubation. However, the patient with respiratory failure did not have abdominal distension, suggesting abdominal distension might not contribute to the development of respiratory failure.

AHRF, which is often caused by airway infection, results in lung inflation, increased RR, respiratory fatigue, and decreased blood oxygen.¹⁶ Sequential mechanical ventilation from invasive to noninvasive

is an effective method for the treatment of respiratory failure resulting from AHRF exacerbation.¹⁷ In this regard, NPPV is often used in the ICU for patients with AHRF after weaning from mechanical ventilation and extubation. However, a patient's tolerance to NPPV is low and thus, approximately 29% of patients switch to re-intubation due to intolerance to NPPV.¹⁸ In contrast, HFNC provides a warm and humidified gas-flow delivered *via* nasal prongs, which is more comfortable and easier for patients to accept. Compliance is an important determining factor in order for a patient to have

Table 5. Comparison of parameters after treatment in group A.

Parameters	1 h			6–12 h		
	NPPV (n=36)	HFNC (n=36)	p value	NPPV (n=24)	HFNC (n=24)	p value
Heart rate (beats/min)	81.06 ± 10.34	82.69 ± 8.53	0.466	75.31 ± 6.64	76.92 ± 6.85	0.314
Mean blood pressure (mmHg)	91.08 ± 9.40	87.39 ± 9.43	0.101	88.86 ± 8.94	85.36 ± 8.40	0.091
Respiratory rate (breaths/min)	19.36 ± 3.10	20.19 ± 4.06	0.331	17.53 ± 2.26	18.47 ± 2.82	0.122
FiO ₂ (%)	0.42 ± 0.08	0.43 ± 0.05	0.559	0.42 ± 0.07	0.44 ± 0.08	0.167
Body temperature (°C)	37.19 ± 0.59	37.35 ± 0.78	0.318	36.61 ± 0.32	36.66 ± 0.47	0.540
Left ventricular ejection fraction	51.39 ± 5.14	53.06 ± 4.55	0.150	52.17 ± 4.28	54.00 ± 3.84	0.060
Arterial pH	7.37 ± 0.03	7.38 ± 0.03	0.479	7.37 ± 0.02	7.38 ± 0.02	0.088
Blood lactate (mmol/L)	2.32 ± 0.70	2.03 ± 0.73	0.097	1.64 ± 0.54	1.41 ± 0.57	0.074
PaO ₂ (mmHg)	67.22 ± 4.38	65.11 ± 5.59	0.079	74.56 ± 4.81	72.39 ± 5.26	0.072
PaCO ₂ (mmHg)	40.78 ± 3.09	40.89 ± 2.39	0.865	40.11 ± 1.77	39.50 ± 2.77	0.269
Oxygenation index (mmHg)	164.47 ± 31.09	153.64 ± 25.25	0.109	183.17 ± 30.72	170.22 ± 32.86	0.089
	NPPV (n=36)		HFNC (n=36)		p value	
Re-intubation rate (%)	0		0		–	
Abdominal distension (%)	7 (19.44)		0		0.005	
Facial skin damage (%)	1 (2.78)		0		0.314	
28-day mortality (%)	0		0		–	
Time of oxygen therapy (hours)*	107.72 ± 39.31		118.69 ± 23.85		0.157	
Length of ICU stay (hours)	138.03 ± 42.65		140.86 ± 26.07		0.735	
In-ICU mortality (%)	0		0		–	
*During HFNC or NPPV treatment. FiO ₂ , fraction of inspired oxygen; HFNC, high-flow nasal cannula; ICU, intensive care unit; NPPV, noninvasive positive-pressure ventilation; PaCO ₂ , partial pressure of carbon dioxide; PaO ₂ , partial pressure of oxygen.						

effective oxygen therapy by maximizing tolerance to the therapy.¹⁹ In addition, HFNC preserves high FiO₂ and generates the PEEP counterbalances auto-PEEP due to a high flow of gas, which also provides washout of the upper airway dead space. Continuous positive airway pressure can also lead to inflation of the alveoli, supply of fresh oxygen, and enhanced gas exchange in the alveoli, which results in continuous elimination of CO₂.⁵

Re-intubation due to post-extubation respiratory failure (PERF) is associated with increased

duration of ICU stay, hospital stay, and mortality. Previous studies on the clinical effects of HFNC in post-extubation patients demonstrated that HFNC was superior to NPPV with lower length of stay in the ICU and lower rate of PERF with hypoxigen. However, for hypercapnic respiratory failure, there is limited and controversial evidence for the role of HFNC therapy in managing hypercapnia except for the mechanism of dead space washout. In this regard, Hernández *et al.* reported a higher rate of hypercapnia after extubation in the NPPV group than in the HFNC group (6.7% *versus* 3.8%). In

Table 6. Comparison of parameters after treatment in group B.

Parameters	1 h			6–12 h		
	NPPV (n = 24)	HFNC (n = 24)	p value	NPPV (n = 60)	HFNC (n = 60)	p value
Heart rate (beats/min)	84.42 ± 10.01	82.00 ± 7.83	0.356	83.54 ± 6.72	81.13 ± 8.36	0.275
Mean blood pressure (mmHg)	87.17 ± 12.99	88.17 ± 12.10	0.784	92.17 ± 8.60	87.83 ± 10.53	0.125
Respiratory rate (breaths/min)	23.33 ± 3.84	21.92 ± 1.69	0.105	19.42 ± 3.53	20.17 ± 3.31	0.451
FiO ₂ (%)	0.43 ± 0.04	0.42 ± 0.05	0.556	0.45 ± 0.05	0.44 ± 0.05	0.195
Body temperature (°C)	36.93 ± 0.72	37.24 ± 0.71	0.130	37.16 ± 0.68	37.00 ± 0.70	0.441
Left ventricular ejection fraction	50.67 ± 6.03	53.38 ± 3.62	0.066	51.08 ± 4.07	52.58 ± 3.11	0.158
Arterial pH	7.39 ± 0.03	7.38 ± 0.04	0.294	7.38 ± 0.03	7.38 ± 0.02	0.443
Blood lactate (mmol/L)	2.32 ± 0.58	1.98 ± 0.90	0.131	1.73 ± 0.62	1.49 ± 0.75	0.227
PaO ₂ (mmHg)	63.21 ± 5.63	60.75 ± 5.95	0.148	68.96 ± 5.42	71.63 ± 4.19	0.063
PaCO ₂ (mmHg)	40.13 ± 3.18	39.08 ± 3.55	0.290	39.25 ± 2.52	40.00 ± 1.81	0.244
Oxygenation index (mmHg)	139.88 ± 29.21	143.50 ± 30.19	0.674	154.33 ± 24.57	167.29 ± 25.48	0.079
	NPPV (n = 24)	HFNC (n = 24)	p value			
Re-intubation rate (%)	1 (4.17)	0	0.312			
Abdominal distension (%)	6 (25)	0	0.009			
Facial skin damage (%)	0	0	–			
28-day mortality (%)	0	0	–			
Time of oxygen therapy (hour)*	133.88 ± 40.56	122.38 ± 42.41	0.342			
Length of ICU stay (hours)	165.21 ± 41.08	172.56 ± 38.05	0.523			
In-ICU mortality (%)	0	0	–			

*During HFNC or NPPV treatment.
 FiO₂, fraction of inspired oxygen; HFNC, high-flow nasal cannula; ICU, intensive care unit; NPPV, noninvasive positive-pressure ventilation; PaCO₂, partial pressure of carbon dioxide; PaO₂, partial pressure of oxygen.

the current study, patients who developed hypercapnia during SBT were excluded.²⁰

A limitation of the current study was that it was a single-center study with a limited number of cases. With accumulation of case numbers, we plan next to further compare and analyze the outcomes of HFNC and NPPV on the comorbidities of lung infection, liver and kidney function alteration, and interval between extubation and re-intubation. In addition, without sample size power analysis and stratified blocked randomization, type II error (false negative)

in the outcomes of HFNC and NPPV treatment in the two groups, which remains to be addressed in the future study, might exist in this study.

Taken together, the current study indicated that HFNC seems to be superior to NPPV for the treatment of patients with AHRF after weaning from mechanical ventilation.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Funding

This study was supported by grants from the National Natural Science Foundation of China (No. 81873507, 82070348, and 81420108004).

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Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental material

The reviews of this paper are available via the supplemental material section.

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