

Clinical outcomes of high-flow nasal cannula oxygen therapy in acute heart failure patients with hypoxemia

A retrospective cohort study

Xiao Tong, MD^a, Ningning Tong, MD^b, Feifei Yao, MD^c, Jing Yan, MD^d, Caizhe Ci, MD^{d,*} 

Abstract

Acute heart failure (AHF) is life-threatening medical condition requiring hospital admission and appropriate oxygen therapy. High flow nasal cannula oxygen therapy (HFNC) has gained its popularity in treatment of AHF, however, there were less studies have demonstrated the physiological efficacy of HFNC. Purpose of this study was to evaluate the physiological responses and clinical outcomes of HFNC by comparing with noninvasive positive pressure ventilation (NPPV) therapy. A retrospective cohort investigation was conducted at emergency intensive care unit (EICU) and cardiovascular center of our hospital from June 2019 to March 2022, AHF patients with hypoxemia were reviewed. According to the received oxygen therapy model, patients were divided into HFNC and NPPV groups. Demographic data, arterial blood gas (ABG) parameter, echocardiography findings, complications and other related variables were extracted and collected from the electronic medical records (EMRs) by well-trained investigators. Physiological responses and clinical outcomes within and between 2 groups were analyzed. Finally, 156 patients with a mean age of 69.3 ± 7.1 years were reviewed, there were 82 (52.6%) male and 74 (47.4%) female patients in the sample and 70 (44.9%) and 86 (55.1%) patients classified III and IV score were included in this study, 80 patients received HFNC and 76 underwent NPPV oxygen therapy. There were no significant differences of baseline characteristics for the 2 groups patients. Changes of left ventricular function parameters, ABG and clinical outcomes were all improved satisfactorily after 24 h medical interventions in both group, what's more, patients underwent HFNC therapy could acquire a better amelioration when compared with NPPV groups ($P < .05$). HFNC may be an ideal model for patients with AHF, particularly those with hypoxemia. HFNC therapy could significantly improve several objective parameters of physiological responses and clinical outcomes.

Abbreviations: ABG = arterial blood gas, AHF = acute heart failure, APACHE II = physiology and chronic health evaluation-II, FiO_2 = inspired oxygen concentration, HF = heart failure, HFNC = high flow nasal cannula, HR = heart rate, LVEDV = left ventricular end diastolic volume, LVEF = left ventricular ejection fraction, LVESD = left ventricular and systolic diameter, LVESV = left ventricular end systolic volume, NPPV = noninvasive positive pressure ventilation, NT-proBNP = N-terminal pro-B-type natriuretic peptide, PaO_2 = arterial partial pressure of oxygen, RR = respiratory rate, SpO_2 = blood oxygen saturation.

Keywords: acute heart failure, high flow nasal cannula, hypoxemia, noninvasive positive pressure ventilation, oxygen therapy

1. Introduction

Heart failure (HF), a chronic and progressive clinical syndrome induced by structural or functional cardiac abnormalities, is characterized by a constellation of pathophysiological changes and displaying either reduced or preserved left ventricular ejection fraction,^[1,2] and acute heart failure (AHF) is defined as new or worsening of symptoms and signs of HF. AHF can manifest

either acute onset or decompensation of chronic heart failure and acute left heart failure is the most common clinical type of AHF.

According to the published reports, prognosis of AHF is poor, in-hospital mortality rate for those patients is approximately 10%, rehospitalization rate of 6-month after discharge is about 50%, moreover, 5-year fatality rate is 50%,^[3] and AHF is the most frequent cause of unplanned hospital admission in patients of >65 years of age. AHF is life threatening medical condition that requiring

The authors have no funding and conflicts of interest to disclose.

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

This study was approved by the Institutional Review Board of The Third Hospital of Hebei Medical University and received written consent from all the study participants.

^a Hengshui central blood station, Hengshui, Hebei, P.R. China, ^b Department of Orthopedic Surgery, The Second Hospital of Tangshan, Tangshan, Hebei, P.R. China, ^c Department of Cerebrovascular Surgery, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, P.R. China, ^d Department of Cardiology, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei, P.R. China.

*Correspondence: Caizhe Ci, Department of Cardiology, The Third Hospital of Hebei Medical University, Add: No. 139 Ziqiang Road, Shijiazhuang, 050051, Hebei Province, P.R. China (e-mail: CZ11339@126.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Tong X, Tong N, Yao F, Yan J, Ci C. Clinical outcomes of high-flow nasal cannula oxygen therapy in acute heart failure patients with hypoxemia: A retrospective cohort study. *Medicine* 2022;101:43(e31124).

Received: 24 June 2022 / Received in final form: 9 September 2022 / Accepted: 13 September 2022

<http://dx.doi.org/10.1097/MD.00000000000031124>

hospital admission and immediate and appropriate interventions, in which oxygen therapy is a very important measurement.

Noninvasive positive pressure ventilation (NPPV) can not only relieve the symptoms of AHF, but also correct pulmonary ventilation and oxygenation, which has great clinical value in improving the success rate of rescue. High flow nasal cannula oxygen therapy (HFNC) has gained its popularity and attracted much attention since it has the advantage of providing accurate oxygen concentration along with a satisfactory humidification effect, moreover, a certain positive airway pressure generated by high oxygen flow can promote alveolar recruitment and reduce the inspiratory effort. HFNC system can enhance the comfort and tolerability in patients by integrating additional functions for humidification and warming of high-flow oxygen, therefore, HFNC therapy was well tolerated and useful for early oxygenation during acute hypoxemic respiratory failure. In recent years, HFNC has been commonly used in therapy of acute pulmonary edema, acute or chronic respiratory failure, severe hypoxemia after cardiac surgery and other surgical disciplines and obstructive sleep apnea syndrome. However, currently there were less studies have demonstrated the physiological efficacy of HFNC, and few evidences about clinical outcomes of HFNC in patients with AHF were published. Therefore, we designed this retrospective cohort investigation with 2 purposes: I to analyze clinical effectiveness of oxygen therapy in patients with AHF focused on HFNC; II, to evaluated the physiological responses and clinical outcomes of HFNC by comparing with NPPV.

2. Materials and Methods

2.1. Patient selection

A retrospective cohort investigation was conducted at emergency intensive care unit (EICU) and cardiovascular center of our hospital from June 2019 to March 2022. AHF patients with hypoxemia and received oxygen therapy were recruited and reviewed, and Figure 1 demonstrated the patient recruitment in this study.

The diagnostic and inclusion criteria were: patients older than 18 years old; patients with previous comorbidity of heart disease or HF; arterial blood gas (ABG) analysis on admission showed arterial partial pressure of oxygen (PaO_2) less than 80 mm Hg and supplemental oxygen was needed to maintain a pulse blood oxygen saturation (SpO_2) more than 90%; evidence of pulmonary infiltrates was founded by the chest x-ray or computed tomography scan; moderate-to-severe cardiac insufficiency, namely, New York Heart association classified greater than grade 2 or left ventricular ejection fraction < 50%; B-natriuretic peptide > 100 pg/mL.

The exclusion criteria were: patients with weak spontaneous breathing or impaired consciousness and need emergency endotracheal intubation to maintain vital signs; patients with pneumothorax, malignant arrhythmia, hypotension shock or even sudden cardiac arrest or death; chronic kidney disease grade IV or above; patients with incomplete clinical data.

2.2. Preprocessing steps

After hospitalization, patients were given ambulatory ECG monitoring and received conventional anti-heart failure treatment, these measures including sitting upright posture, intravenous application of furosemide and other drugs for diuresis, cedilan and other digitalis drugs were used to maintain and strengthen cardiac systolic function, nitroglycerin or sodium nitroprusside was introduced to dilate blood vessels to reduce cardiac pre- and post-load, morphine was applied for pain relief and sedation, patients with infection and other initiating pathogenesis factors were given anti-infection or other primary intervening measures. According to the oxygen therapy methods, patients were divided into HFNC and NPPV groups.

2.3. HFNC protocol

The HFNC device (Sibairui®, Micomme, Hunan, China) could deliver 20 to 60L/min heated and humidified gas flow and between 0.21 and 1.0 fraction of the inspired oxygen concentration (FiO_2). The initial parameter of gas flow was setting as 30–40L/min, range of flow rate of 30 to 60L/min, FiO_2 of 40% to 100% and 37°C of airway humidification temperature were introduced and these values were timely adjusted to achieve the target goal of >90% SpO_2 .

2.4. NPPV protocol

noninvasive ventilator (BiPAP A40, Philips Respironics, Amsterdam, Netherlands) was applied for ventilation treatment and Bi-level positive pressure noninvasive ventilation mode was adopted. The oxygen concentration and respiratory rate were 5 to 10L and 15 to 20/min, inspiratory and expiratory pressure were set as 8 cmH_2O and 4 cmH_2O respectively. During the treatment period, oxygen flow, inspiratory and expiratory volume were adjusted according to the patient's specific conditions and tolerance, and these parameters were modulated once every 5 to 10 minutes and 2 to 4 cmH_2O each time.

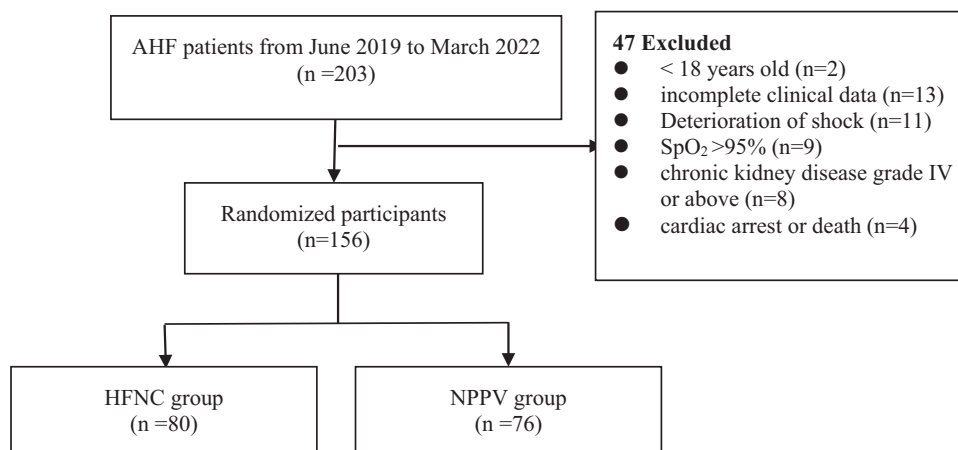


Figure 1. Follow diagram for patient recruitment in HFNC and NPPV group. HFNC = high flow nasal cannula, NPPV = noninvasive positive pressure ventilation.

2.5. Endpoint evaluation

Evaluation variables of therapeutic effectiveness of HFNC and NPPV in the AHF patients were included 2 aspects, namely physiological responses and clinical outcomes.

The primary outcomes were arterial blood gas (ABG) parameter such as partial pressure of carbon dioxide (PCO_2), PaO_2 , oxygenation index (PaO_2/FO_2) and PH value which recorded at the admission of hospitalization and 24 hours after clinical interventions. N-terminal pro-B-type natriuretic peptide (NT-proBNP) detected by Light initiated chemiluminescence assay (LiCA) was also extracted and analyzed. The left ventricular ejection fraction (LVEF), left ventricular and systolic diameter (LVESD), left ventricular end diastolic diameter, left ventricular end systolic volume (LVESV) and left ventricular end diastolic volume (LVEDV) were also determined to evaluate the functional status of left ventricle.

The secondary outcome was to examine heart rate (HR), respiratory rate (RR) between 2 groups. Degree of dyspnea was scored adopting 4 levels, which including supine position (4 score), nocturnal paroxysmal dyspnea (3 score), semi-recumbent position (2 score) and orthopnea (1 score). Dyspnea was diagnosed by 2 senior physicians in our center. Rate of intubation within 24 hours after emergency department admission was also introduced to analyze the difference of 2 types of oxygen therapy between HFNC and NPPV groups.

2.6. Statistical analysis

All statistical procedures were performed by SPSS 19.0 software package (SPSS Inc., Chicago, Illinois). Baseline characteristics were described as number or percentage, continuous variables were expressed as the mean \pm SD and categorical variables were expressed as frequencies or median. Whitney *U* test was carried

out for abnormally distributed continuous variables and chi-square tests or Fisher tests for categorical variables. A sensitivity analysis was performed to adjust between group differences at baseline. $P < .05$ was considered to represent statistically significant results.

3. Results

Finally, 156 patients with a mean age of 69.3 ± 7.1 years were reviewed, there were 82 (52.6%) male and 74 (47.4%) female patients in the sample and 70 (44.9%) and 86 (55.1%) patients classified III and IV score were included in this study. Eighty patients received HFNC and 76 underwent NPPV oxygen therapy. Baseline characteristics of the 2 groups were showed in Table 1. Mean age, BMI for HFNC and NPPV group were 69.8 ± 7.4 versus 69.1 ± 6.9 years and 21.9 ± 3.4 versus 22.2 ± 3.9 kg/m² respectively. As for comorbidity, hypertension (49 vs 44), diabetes mellitus (30 vs 31), COPD (21 vs 21), HF (40 vs 36) and hyperlipaemia (9 vs 7) were the most common ones for HFNC and NPPV protocol patients. Statistics results shows that there was no significant difference in demographic data, comorbidity and concomitant medication between 2 groups ($P > .05$), these data demonstrated that the 2 group patients have homogeneity, and influence of BMI and other indicators on the prognosis outcome of AHF were eliminated.

Sequential organ failure assessment and APACHE II were used to assess the patients' basic physical condition, disease severity and prognosis, the results showed initial sequential organ failure assessment and APACHE II score were 4 and 4, 18.9 ± 4.4 and 18.9 ± 4.6 respectively for HFNC and NPPV group. HR (HFNC, 110 ± 29 ; NPPV, 109 ± 26) and RR (HFNC, 28 ± 7 ; NPPV, 28 ± 6) for the 2 groups were both higher than the value under normal physiological statue, and there were no significant differences for all the variables which mentioned above.

Table 1
Baseline characteristics between HFNC and NPPV group.

Variables	HFNC group (n = 80)	NPPV group (n = 76)	P value
Age (yr)	69.8 ± 7.4	69.1 ± 6.9	.420
Male/Female	33/29	29/25	.863
BMI (kg/m ²)	21.9 ± 3.4	22.2 ± 3.9	.307
Comorbidity			
Hypertension	49	44	.669
Diabetes mellitus	30	31	.674
COPD	21	21	.846
HF	40	36	.742
Hyperlipaemia	9	7	.675
SOFA score	4 [3–5]	4 [3–5]	.238
†APACHE II	18.9 ± 4.4	18.9 ± 4.6	.306
Degree of dyspnea (1–4)	3.60 ± 0.5	3.6 ± 0.5	.811
HR (beats/min)	110 ± 29	109 ± 26	.592
RR (breath/min)	28 ± 7	28 ± 6	.704
LVEF (%)	41.8 ± 5.0	40.9 ± 4.8	.511
LVESD (mm)	32.9 ± 3.6	32.6 ± 3.3	.875
LVEDD (mm)	56.6 ± 5.3	57.0 ± 5.5	.104
LVESV (mL)	79.8 ± 7.5	80.2 ± 7.7	.710
LVEDV (mL)	135.5 ± 11.8	136.0 ± 11.4	.826
PCO_2 (mm Hg)	53.1 ± 20.2	52.8 ± 19.9	.723
PO_2 (mm Hg)	49.4 ± 10.7	49.6 ± 11.2	.769
PaO_2/FO_2	144 [111–160]	148 [120–159]	.220
Ph	7.1 ± 0.1	7.1 ± 0.1	.755
NT-proBNP (pg/mL)	5913.2 ± 480.6	5866.7 ± 469.8	.263
Concomitant medication			
Digoxin	61	57	.856
Hydragogue	49	41	.356
Angiotensin blocker	75	70	.688
Beta-blocker	76	72	.941

†APACHE = physiology and chronic health evaluation-II, BMI = body mass index, COPD = chronic obstructive pulmonary disease, HFNC = high flow nasal cannula, NPPV = noninvasive positive pressure ventilation, SOFA = sequential organ failure assessment.

Cardiac function relevant parameter such as LVEF (41.8 ± 5.0 vs $40.9\% \pm 4.8\%$), LVESV (79.8 ± 7.5 vs 80.2 ± 7.7 mL) and LVEDV (135.5 ± 11.8 vs 136.0 ± 11.4 mL) between patients in HFNC and NPPV group were also underlying pathological condition and similarly, no obvious differences were found in echocardiography findings of left ventricle dimension, left ventricle ejection fraction and other parameters ($P > .05$). Regarding to the pulmonary function and arterial blood gas analysis, PCO_2 , PO_2 , PaO_2/FO_2 and PH value for these 2 groups were 53.1 ± 20.2 and 52.8 ± 19.9 mm Hg, 49.4 ± 10.7 and 49.6 ± 11.2 mm Hg, 144 and 148, 7.1 ± 0.1 and 7.1 ± 0.1 respectively, moreover, NT-proBNP (5913.2 ± 480.6 vs 5866.7 ± 469.8 pg/mL) was also higher than normal level. Results of arterial blood gas, physiological responses of patients in the 2 groups were similar at hospital admission, and all the baseline characteristics indicated a good comparability between HFNC and NPPV group ($P > .05$).

In the treatment process, digoxin (76.3% vs 75.0%), hydralazine (61.3% vs 53.9%), angiotensin blocker (93.8% vs 92.1%), beta-blocker (95.0% vs 94.7%) were applied to improve the status and functionality of heart and circulatory system. In terms of proportion drug use, there was no significant difference between patients among HFNC and NPPV group ($P > .05$).

Table 2 summarized the changes of left ventricular function parameters for HFNC and NPPV patients at admission and 24 hours after hospitalization. At the admission of hospital, parameters such as LVEF, LVEDD, LVESV, LVESD, and LVEDV between HFNC and NPPV group were similarly and no significant difference were founded ($P > .05$). The results demonstrated that LVEF (52.9 ± 3.1 vs $51.1\% \pm 2.8\%$), LVEDD (50.9 ± 3.7 vs 52.8 ± 4.0 mm), LVESV (54.6 ± 4.1 vs 58.8 ± 5.3 mL), LVESD (26.1 ± 1.9 vs 28.5 ± 2.2 mm) and LVEDV (110.6 ± 9.4 vs 115.7 ± 11.8 mL) were all improved satisfactorily after 24 hours medical interventions in patients underwent HFNC and NPPV therapy, what's more, patients underwent HFNC treatment could acquire a better amelioration when compared with NPPV groups ($P < .05$). Obviously, there is no doubt that under the premise of basic medication and other adjuvant therapy, patients received HFNC and NPPV oxygen model can achieve a better improvement of cardiac function.

Data of physiological responses and clinical outcomes at 24 hours for 2 groups patients were shown in Table 3. PCO_2 and PaO_2/FO_2 decreased to a relatively normal values (HFNC, 36.8 ± 4.2 mm Hg, 110; NPPV, 41.5 ± 4.9 mm Hg, 129), and PO_2 increased to 88.7 ± 7.4 and 83.0 ± 6.5 mm Hg. As for basic vital signs, HR and RR were also decreased to 80.1 ± 10.5 , 18.2 ± 2.9 and 88.2 ± 12.0 , 20.6 ± 3.8 . The changes of these indexes indicated that patient's lung oxygenation ability was improved and the oxygen carrying capacity of blood was improved, correspondingly the cardiac contractility enhanced. In-hospital outcomes showed that hospital stay (8 vs 9 day), intubation rate

(12.5% vs 19.7%) and cardiac death rate (5.0% vs 5.3%) were lower of HFNC group than NPPV patients, however, there were no significant difference between these variables, and a higher trend of vasopressor use rate (25% vs 40.8%) was founded in patients received NPPV treatment. Data showed in Tables 2 and 3 demonstrated that the improving the state of the circulatory system, maintaining the effective blood pumping function and alleviating pulmonary edema are complementary to efficient oxygen support in patients with acute heart failure, owing to the advantages of HFNC protocol, it can help human body live through the pathophysiological stage of hypoxemia as soon as possible, and thus avoid or reduce the risk of damage to other organs.

4. Discussion

When AHF occurred, atrial pressure, pulmonary artery and arterial static pressure will increase, and subsequently accompanied by an increased pulmonary microvascular pressure, and all these pathophysiological events accelerating the development of respiratory failure. Basic therapy such as drugs of cardiotoxic, diuretic and vasodilator can only reduce pre- and post-load of heart, and relieve pulmonary edema. Due to the limited airflow velocity and no humidifier, the traditional oxygen inhalation scheme will make it difficult for some patients to clear airway secretions, and proportion of the actual inhaled oxygen is significantly reduced. By contrast, NPPV can reduce venous return in overweight patients, improve respiratory function by improving gas exchange, and avoid multiple complications of invasive ventilation, which making it an available and cost-effective clinical measurement. As an ideal oxygen therapy method, HFNC has irreplaceable advantages in the treatment of hypoxemia caused by heart failure. However, to our knowledge, there are few clinical reports on the application of HFNC in relieving hypoxemia in AHF, moreover, currently, researches on the changes of pathophysiological indicators in AHF patients following HFNC are rare, thus, clinical role of HFNC worth exploring in depth. Considering the reality of present situation, we conducted the present study to demonstrated the beneficial effects of HFNC therapy in heart failure patients using objective parameters of RR, HR, echocardiography (LVEF), LVESD, left ventricular end diastolic diameter, LVESV and LVEDV), arterial blood gas (PCO_2 , PO_2 , PH and PaO_2/FO_2) and NT-proBNP. The quantitative scale was formulated to evaluate the patients' dyspnea before and after oxygen therapy, meanwhile, clinical outcomes variables such as hospital stay, intubation rate and cardiac death were also introduced to compare difference between HFNC and NPPV groups. Obviously, these parameters were clinically improved for all patients in the 2 groups when compared with baseline, and HFNC therapy improved several indexes more effective than the conventional NPPV oxygen therapy.

Due to the decrease of myocardial contractility and the aggravation of cardiac load, the cardiac output is sharply reduced and the ventricular filling pressure is rapidly increased, making AHF a common critical clinical disease^[2] and AHF would result in pulmonary congestion and acute pulmonary edema.^[4] Patients suffered from AHF often have limited ventilation deficiency and alveolar diffusion dysfunction, and always accompanied by hypoxemia and even respiratory failure.^[5,6] For relieving the symptom of hypoxemia caused by AHF, oxygen therapy through venturi mask or nasal catheter are commonly used in clinic practice, these 2 therapy methods are relatively comfortable for patients. However, conventional venturi mask or nasal catheter can only generate limited flow and concentration of oxygen, moreover, temperature and humidity of the inhaled oxygen are difficult to meet the ideal physiological criterion (37°C , 44mg/l), often causing dryness and discomfort to respiratory tract.^[7] Although, NVVP can provide positive airway pressure and positive end-expiratory pressure, prevent atelectasis, reduce

Table 2

Serial changes in left ventricular function parameters of 2 groups patients at admission and 24 h after hospitalization.

Variables	HFNC group (n = 80)		NPPV group (n = 76)		P value
	Admission	24h	Admission	24 h	
LVEF (%)	41.8 ± 5.0	$52.9 \pm 3.1^\dagger$	40.9 ± 4.8	$51.1 \pm 2.8^\dagger$.042‡
LVEDD (mm)	56.6 ± 5.3	$50.9 \pm 3.7^\dagger$	57.0 ± 5.5	$52.8 \pm 4.0^\dagger$.039‡
LVESV (mL)	79.8 ± 7.5	$54.6 \pm 4.1^\dagger$	80.2 ± 7.7	$58.8 \pm 5.3^\dagger$.020‡
LVESD (mm)	32.9 ± 3.6	$26.1 \pm 1.9^\dagger$	32.6 ± 3.3	$28.5 \pm 2.2^\dagger$.047‡
LVEDV (mL)	135.5 ± 11.8	$110.6 \pm 9.4^\dagger$	136.0 ± 11.4	$115.7 \pm 11.8^\dagger$.016‡

HFNC = high flow nasal cannula, NPPV = noninvasive positive pressure ventilation.

†Significant difference between admission and 24h hospitalization in each group.

‡Significant variables after 24h hospitalization between 2 groups.

Table 3
Physiological responses and clinical outcomes of patients in HFNC and NPPV group.

Variables	HFNC group (n = 80)		NPPV group (n = 76)		P value
	Admission	24h	Admission	24 h	
PCO ₂ (mm Hg)	53.1 ± 20.2	36.8 ± 4.2†	52.8 ± 19.9	41.5 ± 4.9†	.000‡
PO ₂ (mm Hg)	49.4 ± 10.7	88.7 ± 7.4†	49.6 ± 11.2	83.0 ± 6.5†	.000‡
PaO ₂ /FO ₂	144 [111–160]	110 [102–135]†	148 [120–159]	129 [113–158]†	.000‡
Ph	7.1 ± 0.1	7.3 ± 0.2†	7.1 ± 0.1	7.2 ± 0.1†	.501
NT-proBNP (pg/mL)	5913.2 ± 480.6	1776.4 ± 337.0†	5866.7 ± 469.8	1825 ± 360.4	.000‡
Degree of dyspnea (1–4)	3.60 ± 0.5	2.4 ± 0.2†	3.6 ± 0.5	2.6 ± 0.3†	.027‡
HR (beats/min)	110 ± 29	80.1 ± 10.5†	109 ± 26	88.2 ± 12.0†	.000‡
RR (breath/min)	28 ± 7	18.2 ± 2.9†	28 ± 6	20.6 ± 3.8†	.013‡
Hospital stay (days)		8 [6–15]		9 [7–17]	.247
Vasopressor use		20		31	.048‡
Requiring intubation		10		15	.295
Cardiac death		4		4	.7941

HFNC = high flow nasal cannula, NPPV = noninvasive positive pressure ventilation.

†Significant difference between admission and 24 h hospitalization in each group.

‡Significant variables after 24 h hospitalization between 2 groups.

pulmonary edema, and improve hypoxemia.^[8,9] However, NVVP always accompanied by complications such as expectoration difficulties, airway desiccation, and gastrointestinal flatulence. HFNC is a new respiration oxygen therapy mode, and currently HFNC has gained popularities. Some large randomized clinical trials have reported that HFNC was widely applied to critically ill patients with diverse underlying diseases.^[10,11] HFNC provides medical gases at higher flow and with more predictable FIO₂ than with other devices. Through HFNC is an open circuit, it can create positive end expiratory pressure (PEEP) and may increase end-expiratory lung volume.^[12]

Many clinical evidence supported the efficacy and safety of HFNC. Grieco^[13] and his colleague have conducted an observational study and compared the effectiveness of HFNC and helmet noninvasive ventilation in acute hypoxemic respiratory failure (AHRF), fifteen hypoxemic patients with PaO₂/FiO₂ < 200 mm Hg received helmet NIV (PEEP ≥ 10 cmH₂O, pressure support = 10–15 cmH₂O) and HFNC (50 L/min) in randomized cross-over order, and they found HFNC and NIV could both improves oxygenation, reduces dyspnea, inspiratory effort and simplified pressure-time product. What is more, HFNC therapy was also plays an important role in relieving symptoms of acute pulmonary edema in patients with HF. In a multi-center study, Ko DR^[3] et al prospective enrolled 67 adults patients diagnosed with HF within the previous year and pulmonary edema confirmed at admission. There were significant differences in the RR in the initial, 30 minutes, and 60 minutes measurements and in the SpO₂ at 30 and 60 minutes between the HFNC and conventional O₂ therapy groups. With regard to the ABGA parameters, there were significant between-group differences in the PaO₂ and SpO₂ at 30 and 60 minutes, and all parameters showed greater improvement with HFNC therapy than with conventional therapy.

On December 31, 2019, a new strain of coronavirus was isolated and named as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) by the International Committee on Taxonomy of Viruses (ICTV) and on March 11, 2020, the World Health Organization (WHO) announced that COVID-19 is a “public-health emergency of international concern.”^[14] Authors suggested that HFNC has positive role in the treatment of COVID-19, HFNC provides high concentrations of oxygen to the patients, who cannot reach with conventional devices. HFNC can reduce the requiring of intubation in patients with COVID-19, and it can decrease the length of intensive care unit stay, and complications related to mechanical ventilation.^[15] A literature review has analyzed the current evidence of HFNC in pediatric patients, the results confirmed that HFNC is a relatively safe, well-tolerated and feasible method for delivering

oxygen to infants and young children in a general pediatric ward.^[16] In surgical discipline, HFNC can maintain patients’ oxygenation in cardiac surgery.^[17]

There are some limitations of our study. First of all, the retrospective study design inevitably inherited some select bias. Secondly, the sample size of this study was relatively small. It has been demonstrated that low level of body mass index (BMI) was the important risk factor of death in patients with AHF and complicated by hyponatremia. Levels of plasma IL-6 (interleukin-6) and IL-10 (interleukin -10) were increased, and the ratio of IL-10/IL-6 was decreased, with the progression of CHF, the plasma BNP level was positively correlated with the levels of IL-6 and IL-10 and the levels of BNP and IL-6 were the independent risk factors in prognostic evaluation of AHF patients. Correlations between homocysteine (HCY) and HF was also confirmed and the serum HCY level may reflect the severity of CHF and increase with the severity degree of CHF. However, some important variables such as BMI, blood homocysteine levels, rehabilitation program, electrolyte, leukocyte count, type of cardiomyopathy, etc were not extracted and analyzed, however, these factors have certain association between oxygen therapy and physiological responses and clinical outcomes. Despite these limitations, our study demonstrated the effectiveness and safety of HFNC model in the treatment of AHF patients.

5. Conclusion

This study showed that HFNC may be an ideal model for patients with AHF, particularly those with hypoxemia and pulmonary edema. HFNC therapy could significantly improve several objective parameters over time such as RR, left ventricular function, and ABG reflection of oxygenation and ventilation after admission in AHF patients. HFNC oxygen therapy model could be a more effective device than NVVP for patients with severe hypoxemia. A well designed randomized controlled trial or real-world data are needed to demonstrate and confirm the results derived from this retrospective cohort study, and further study on the treatment of AHF by virtue of HFNC combined with other clinical interventions and relationship between demographic data, biochemical indicators, rehabilitation program and HF should also be investigated.

Authors’ contributions

Caizhe Ci designed the study, Ningning Tong and Jing Yan searched relevant studies, Xiao Tong analyzed and Feifei Yao

interpreted the data, Caizhe Ci and Ningning Tong wrote the manuscript, Caizhe Ci approved the final versions of the manuscript.

Data curation: Xiao Tong, Feifei Yao.

Formal analysis: Caizhe Ci.

Investigation: Ningning Tong, Jing Yan.

Methodology: Caizhe Ci.

Resources: Caizhe Ci.

Software: Feifei Yao.

Supervision: Caizhe Ci.

Writing – original draft: Ningning Tong.

Writing – review & editing: Caizhe Ci.

References

- [1] Arrigo M, Jessup M, Mullens W, et al. Acute heart failure. *Nat Rev Dis Primers*. 2020;6:1–15.
- [2] Kurmani S, Squire I. Acute heart failure: definition, classification and epidemiology. *Curr Heart Fail Rep*. 2017;14:385–92.
- [3] Ko DR, Beom J, Lee HS, et al. Benefits of high-flow nasal cannula therapy for acute pulmonary edema in patients with heart failure in the emergency department: a prospective multi-center randomized controlled trial. *J Clin Med*. 2020;9:1937.
- [4] Boersma EM, Ter Maaten JM, Damman K, et al. Congestion in heart failure: a contemporary look at physiology, diagnosis and treatment. *Nat Rev Cardiol*. 2020;17:641–55.
- [5] Gheorghide M, Pang PS. Acute heart failure syndromes. *J Am Coll Cardiol*. 2009;53:557–73.
- [6] Mentz RJ, O'connor CM. Pathophysiology and clinical evaluation of acute heart failure. *Nat Rev Cardiol*. 2016;13:28–35.
- [7] Nishimura M. High-flow nasal cannula oxygen therapy in adults: physiological benefits, indication, clinical benefits, and adverse effects. *Resp Care*. 2016;61:529–41.
- [8] Hannan LM, Dominelli GS, Chen Y-W, et al. Systematic review of non-invasive positive pressure ventilation for chronic respiratory failure. *Resp Med*. 2014;108:229–43.
- [9] Köhnlein T, Windisch W, Köhler D, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med*. 2014;2:698–705.
- [10] Frat J-P, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372:2185–96.
- [11] Stéphan F, Barrucand B, Petit P, et al. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA*. 2015;313:2331–9.
- [12] Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care*. 2013;58:1621–4.
- [13] Grieco DL, Menga LS, Raggi V, et al. Physiological comparison of high-flow nasal cannula and helmet noninvasive ventilation in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med*. 2020;201:303–12.
- [14] Li X, Wang W, Zhao X, et al. Transmission dynamics and evolutionary history of 2019-nCoV. *J Med Virol*. 2020;92:501–11.
- [15] Gürün Kaya A, Öz M, Erol S, Çiftçi F, et al. High flow nasal cannula in COVID-19: a literature review. *Tuberk Toraks*. 2020;68:168–74.
- [16] Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. *Scand J Trauma Resusc Emerg Med*. 2016;24:1–12.
- [17] Wang Y, Zhu J, Wang X, et al. Comparison of high-flow nasal cannula (HFNC) and conventional oxygen therapy in obese patients undergoing cardiac surgery: a systematic review and meta-analysis. *In Vivo*. 2021;35:2521–9.