Original Article

High-flow nasal cannula oxygen therapy is equally effective to noninvasive ventilation for mild-moderate acute respiratory distress syndrome in patients with acute pancreatitis: A single-center, retrospective cohort study

Qingcheng Zhu[¶], Wenzhen Zhou[¶], Bingyu Ling, Huihui Wang, Dingyu Tan

Department of Emergency Medicine, Clinical Medical College, Yangzhou University (Northern Jiangsu People's Hospital), Yangzhou, China
[¶]These authors contributed equally to this work.

Abstract

Background: The use of high-flow nasal cannula (HFNC) oxygen therapy is gaining popularity for the treatment of acute hypoxic respiratory failure. However, limited evidence exists regarding the effectiveness of HFNC for acute respiratory distress syndrome (ARDS) in patients with acute pancreatitis (AP).

Methods: This retrospective analysis focused on AP patients with mild-moderate ARDS, who were treated with either HFNC or noninvasive ventilation (NIV) in the emergency medicine department, from January 2020 to December 2022. The primary endpoint was treatment failure, defined as either invasive ventilation or a switch to any other study treatment (NIV for patients in the NFNC group and vice versa).

Results: A total of 146 patients with AP (68 in the HFNC group and 78 in the NIV group) were included in this study. The treatment failure rate in the HFNC group was 17.6% and 19.2% in the NIV group – a risk difference of -1.6% (95% CI, -11.3 to 14.0%; $P = 0.806$). The most common causes of failure in the HFNC group were aggravation of respiratory distress and hypoxemia. However, in the NIV group, the most common reasons for failure were treatment intolerance and exacerbation of respiratory distress. Treatment intolerance in the HFNC group was significantly lower than that in the NIV group (16.7% vs 60.0%, 95% CI -66.8 to -6.2; $P = 0.023$). Multivariate logistic regression analysis showed that body mass index (≥28), acute physiology and chronic health evaluation II score (≥15), partial arterial oxygen tension/fraction of inspired oxygen (≤200), and respiratory rate (≥32/min) at 1 hour were independent predictors of HFNC failure.

Conclusion: In AP patients with mild-moderate ARDS, the usage of HFNC did not lead to a higher rate of treatment failure when compared to NIV. HFNC is an ideal choice of respiratory support for patients with NIV intolerance, but clinical application should pay attention to the influencing factors of its treatment failure.

Keywords: Acute respiratory distress syndrome, high-flow nasal cannula oxygen, noninvasive ventilation, pancreatitis

Address for correspondence: Dr. Dingyu Tan, Department of Emergency Medicine, Northern Jiangsu People's Hospital Affiliated with Yangzhou University, Yangzhou 225001, China.
E-mail: tdyhope@163.com

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INTRODUCTION

Acute pancreatitis (AP), characterized by rapid progression, multiple organ failure, and high mortality, is a common inflammatory disease of pancreas worldwide.[1] Most cases of AP are mild with a global incidence of 8 to 50/100,000 per year;[2] however, nearly 15% to 35% of patients will suffer a severe episode with high mortality up to 52%.[3] The incidence of AP is increasing globally without a significant change in mortality rates. The development of organ failure is a key factor contributing to mortality in AP patients.[4]

Acute respiratory distress syndrome (ARDS) is a prevalent form of organ failure in patients with AP, accounting for 45% of intensive care unit (ICU) admissions.[5] ARDS is not a primary disease in itself but rather a consequence of various direct and indirect respiratory insults. Direct causes of ARDS include pneumonia, inhalation injury, and aspiration, while sepsis, major burn injury, and pancreatitis are among the major indirect causes.[6] Despite variable management strategies for AP, incidence and mortality of AP-associated ARDS remained the same over a period of time. According to standard guidelines, noninvasive ventilation (NIV) is recommended as the first-line therapy for ARDS patients.[7] However, NIV may not be well tolerated, resulting in 25% failure of NIV treatment,[8] which has no ideal solution. While NIV can decrease the work of breathing and improve gas exchange, the failure of NIV is associated with increased mortality.[9]

High-flow nasal cannula (HFNC) oxygen therapy is recommended as an optimized respiratory support method in different settings to reduce the incidence of hypoxia, especially for patients with hypoxemic respiratory failure.[10] It delivers heated and humidified gas with up to 100% oxygen at a rate of up to 60 L/min.[11] The flow level is high enough to generate positive end-expiratory pressure (PEEP), which reduces anatomical dead space and provides support to decrease the work of breathing.[12] There are many studies comparing the effects of HFNC to NIV in various conditions, such as severe pneumonia, postoperative cardiothoracic surgery, and chronic obstructive pulmonary disease.[13,14] However, there is no study report that directly compares the use of HFNC and NIV in the treatment of AP-associated ARDS.

We hypothesized that HFNC and NIV had similar therapeutic effects on mild-moderate ARDS secondary to AP. This retrospective analysis was conducted to compare the effectiveness of HFNC and NIV for these patients.

PATIENTS AND METHODS

Study design and eligibility

This was a retrospective study conducted in an 89-bed emergency medicine department (ED) of a tertiary teaching hospital in Jiangsu Province, China. It was performed in accordance with the ethical principles of the amended Declaration of Helsinki. The study was approved by the Institutional Ethics Committee of Northern Jiangsu People's Hospital (No. 2020021), and written informed consent was waived due to the retrospective study design.

Patients with a diagnosis of AP who developed mild or moderate ARDS between January 1, 2020 and December 31, 2022 were included in this study. The diagnosis of AP was established if at least two of three criteria were presented: abdominal pain, elevated amylase, or lipase greater than three times of the upper limit of normal or abdominal imaging consistent with AP, according to the 2012 revised Atlanta criteria.[15] The severity of ARDS was classified using the Berlin Definition.[16] Mild ARDS was defined as 200 mm Hg < partial arterial oxygen tension (PaO_2)/fraction of inspired oxygen (FiO_2) ≤300 mm Hg, and moderate ARDS was defined as 100 mm Hg < PaO_2/FiO_2 ≤200 mm Hg. Exclusion criteria were age less than 18 years, requiring immediate tracheal intubation (severe hypoxia, respiratory frequency ≥40 times/min, or Glasgow score <8), contraindications to NIV (poor sputum excretion ability, oral or facial trauma, hemodynamic instability), poor short-term prognosis (very high risk of death within seven days), or tracheotomy.

Treatment procedures

The patients were divided into two groups based on the time from admission to the ED and the initiation of first-line ventilatory support, which included HFNC or NIV. All patients received initial comprehensive treatment, including intravenous fluids, parenteral feeding, analgesia, prophylactic antibiotics, and supportive management. Those patients who were treated with HFNC within the first 2 hours from admission were assigned in the HFNC group, if they received more than 2 hours of HFNC within the first 24 hours. Those in whom NIV was started within the first 2 hours from admission were included in the NIV group, if they received at least 2 hours of NIV within the first 24 hours. A patient's group classification would remain the same even if they were to receive a different ventilatory support device or invasive mechanical ventilation later during their hospital stay.

In HFNC group (AIRVO™ 2, Fisher and Paykel Healthcare, Auckland, New Zealand), the initial airflow was set at 50 L/min, the temperature was set to 37°C, and FiO_2

was adjusted to maintain a pulse oxygen saturation (SpO_2) of 90–94%. The airflow was adjusted according to patient tolerance. If patients in HFNC group tolerated well, the treatment was continued, or it was applied intermittently. If the patient had no obvious respiratory distress and PaO_2 became stable, the airflow was gradually reduced. HFNC was discontinued when the airflow was reduced to 15 L/min and would be reused if needed.

In NIV group, settings were as follows: the initial expiratory pressure airway pressure was set to 4 cmH_2O, and the inspiratory airway pressure was initially set to 8 cmH_2O and gradually increased with acceptable tolerance in S/T mode. The pressure level and the FiO_2 were adjusted to maintain a 6–8 ml/kg ideal body weight tidal volume, an SpO_2 of 90–94%. The initial use of NIV was targeted to last at least 2 hours and then continued as needed. NIV was discontinued when the total daily treatment duration was less than 4 hours and would be reused if needed.

The indications for intubation and invasive mechanical ventilation in our unit were: no improvement in arterial blood gas parameters within 1 hour, severe hypoxia defined as a PaO_2 <50 mmHg despite full oxygenation, or respiratory or cardiac arrest.

Data collection

Physiological characteristics, demographic characteristics, comorbidities, disease severity, and organ failure were recorded at study entry. Disease severity was assessed with the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, and the Ranson score. Treatments for AP, including parenteral nutrition, antibiotics, and somatostatin analogs, and infections were also recorded.

Our study collected data on various aspects of respiratory support for patients, including daily respiratory support time, details of respiratory support switches (such as changes from HFNC to NIV or from NIV to HFNC or a change to invasive ventilation), and the specific time and reasons for these changes. We also recorded vital signs [heart rate (HR), blood pressure, respiratory rate (RR), and SpO_2], arterial blood gas analysis at different times after initial respiratory support, daily nursing airway care interventions (such as correcting unplanned device displacement, assisting in spitting, and eating), nasal facial skin breakdown, and total hospital and ICU length of stay.

Outcomes

The primary outcome was treatment failure, which was defined as either requiring invasive ventilation or a switch in respiratory support. The secondary outcomes were vital signs (RR, HR, and blood pressure), arterial blood gas analysis (pH、PaO_2, and oxygenation index), duration of device application, 28-day mortality, the number of nursing airway care interventions within the first 24 hours, comfort score, the incidence of adverse effects, and total ICU and hospital length of stay.

In addition, we further analyzed the causes of treatment failure, which included treatment intolerance, aggravation of respiratory distress, aggravation of hypoxemia, and aggravation of acidosis. Treatment intolerance is a relatively subjective indicator that patients self-report. Intolerances may be caused by factors such as claustrophobia, breathlessness, airflow or pressure that is too strong, coughing, and headaches. The aggravation of respiratory distress is subjectively determined by clinicians, with parameters including a RR ≥32 beats/min 1 hour post respiratory support treatment, or if the physician perceives a worsening of the patient's dyspnea. Hypoxemia is defined as PaO_2 <50 mmHg despite adequate oxygen therapy. Additionally, we considered lower pH and higher lactic acid levels as indicators of worsening acidosis in patients who received comprehensive treatment, including intravenous fluids, analgesia, prophylactic antibiotics, and supportive management.

Statistical analysis

All data analyses were conducted using SPSS 26.0 (IBM Corporation, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to test the normal distribution for measurement data. Normally distributed data were expressed as means ± standard deviation, and the skewed distributed data were reported as medians (quartiles). The two groups were compared using t tests or Mann–Whitney U tests. Categorical data were expressed as a percentage using χ 2 or Fisher's exact probability tests. Kaplan–Meier curves were used to assess the treatment failure. In a stepwise backward elimination method, variables with *P*- values less than 0.05 were included in the logistic regression model to identify independent risk factors associated with HFNC failure. A *P*- value <0.05 means significant statistical difference.

RESULTS

Patient characteristics

Among 181 AP patients who met the inclusion criteria during the study period, 35 were excluded (18 patients had invasive ventilation, 12 patients had contraindications to NIV or HFNC, 2 patients had advanced tumors, 2 patients had other organ failures, 1 patient had tracheostomies). One

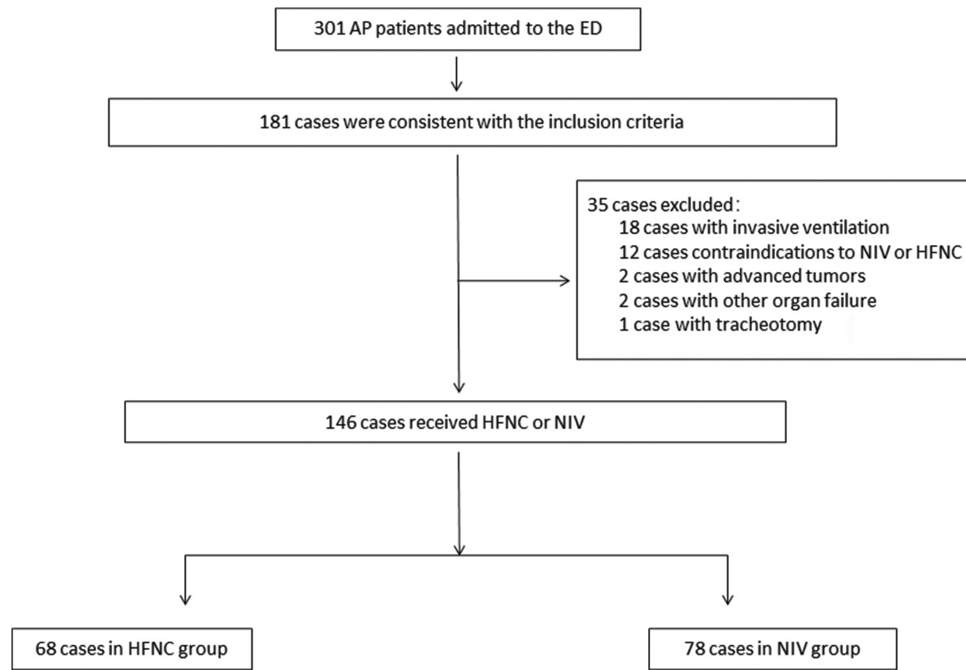

Figure 1: Flow chart of patient enrolment. ED, emergency medicine department; HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation

hundred and forty six patients were finally selected, including 68 in the HFNC group and 78 in the NIV group [Figure 1].

In the two groups, sex, age, body mass index (BMI), etiology, and relevant comorbidities were similar ($P > 0.05$, Table 1). The APACHE II score, SOFA score, and Ranson score were also not significantly different ($P > 0.05$). In the HFNC group, 42 cases (61.8%) were related to respiratory failure, followed by 11 cases (16.2%) related to circulatory failure and 2 cases (2.9%) related to persistent renal organ failure. Additionally, there were 13 cases (19.1%) of multiple organ failure. In NIV group, there were 51 cases (65.4%) of respiratory failure, 13 cases (16.7%) of circulatory failure, and 2 cases (2.6%) of renal failure with 12 cases (15.4%) of multiple organ failure. The rate of ICU admission was 66.2% (45/68) in the HFNC group and 65.4% (51/78) in the NIV group, respectively ($P > 0.05$). Patients from both groups received similar parenteral nutrition, antibiotics, and somatostatin analogs. No differences were found in pancreatic necrosis, pulmonary infection, and other infections between the two groups. Meanwhile, the length of hospital stays between the two groups were similar. On admission to ED, there was no significant difference between the two groups based on vital signs (HR, RR, and mean arterial pressure) or blood gas analysis (pH, PaO_2, and oxygenation index) ($P > 0.05$, Table 1).

Primary outcome and cause analysis

The treatment failure rate of HFNC group was 17.6%, which was noninferior to that of NIV group (19.2%) ($P > 0.05$). Kaplan–Meier curve analysis showed no significant difference between the two groups (log rank test 0.078, $P = 0.781$, Figure 2). Among treatment failure patients, the intubation rate in the HFNC group was 10.3% (95% CI, -10.1 to 10.7), which was similar to that in the NIV group. The treatment switch rate in the HFNC group was 7.3% (95% CI, -8.2 to 11.0), which was lower than that in the NIV group. However, there were no significant differences between the two groups in intubation or treatment switch rate [Table 2].

Analysis of treatment failure in the HFNC group showed that the most common reasons for failure were aggravation of respiratory distress and hypoxemia, accounting for 41.7% and 25.0%, respectively. However, in the NIV group, the most common reasons for failure were treatment intolerance and exacerbation of respiratory distress, accounting for 60% and 20%, respectively. Furthermore, the intolerance rate of HFNC was significantly lower than that of NIV (16.7%, 95% CI, -66.8 to -6.2; $P = 0.023$).

Secondary outcomes

Vital signs and blood gas analyses

The HR and RR rate in both groups were significantly decreased at 1 hour, 12 hours, and 48 hours after respiratory treatment ($P < 0.05$). The mean differences for HR reduction from baseline to 1 hour, 12 hours, and 48 hours were -13.0 (±16.9), -14.3 (±16.2), and -15.6 (±15.8) in the HFNC group and -7.3 (±17.4), -13.5 (±15.5), -15.0 (±17.5) respectively, in the NIV group. Similarly, the mean

difference for RR reduction from baseline to the same time points were -3.3 (±8.3), -5.8 (±8.0), and -7.0 (±8.3) respectively, in the HFNC group and -3.7 (±7.5), -5.7 (±8.0), and -8.8 (±8.6) respectively, in the NIV group. The HR 1 h after HFNC had decreased and was lower than the HR in the NIV group ($P < 0.05$). However, there was no significant difference in HR between the two groups at 12 hours and 48 hours. The mean arterial pressures at different times after respiratory treatment in the two groups were not significantly different from baseline levels [Table 3]. Arterial blood gas analyses showed that the pH value and PaO_2/FiO_2 in both groups were higher than their baseline levels ($P < 0.05$), while there were no significant differences in pH value and PaO_2/FiO_2 between the two groups at different times (all $P > 0.05$, Table 3).

Table 1: Baseline characteristics of selected patients

Characteristics	HFNC (*n*=68)	NIV (*n*=78)	*P*
Male, *n* (%)	38 (55.9)	44 (56.4)	0.949
Age, years	42 (21-63)	40 (20-68)	0.241
Body mass index, kg/m²	23.1±4.5	23.8±4.1	0.125
Etiology, *n* (%)			
Smoking	25 (36.8)	30 (38.5)	0.833
Alcoholic	26 (38.3)	38 (48.7)	0.203
Biliary	50 (73.5)	51 (65.4)	0.288
Hyperlipidemia	15 (22.1)	19 (24.1)	0.743
Comorbidities, *n* (%)			
Diabetes mellitus	8 (11.8)	11 (14.1)	0.675
Coronary artery disease	7 (10.3)	13 (16.7)	0.264
Chronic liver disease	5 (7.4)	8 (10.3)	0.539
Chronic kidney disease	6 (8.8)	8 (10.3)	0.769
Malignancy	2 (2.9)	2 (2.6)	0.889
Severity of acute pancreatitis			
APACHE II score	8.81±3.12	9.11±3.24	0.685
SOFA score	2.15±0.12	2.21±0.13	0.953
Ranson score	4.05±1.21	4.17±1.03	0.765
Single persistent organ failure, *n* (%)			
Respiratory	42 (61.8)	51 (65.4)	0.650
Circulatory	11 (16.2)	13 (16.7)	0.936
Renal	2 (2.9)	2 (2.6)	0.889
Multiple organ failure, *n* (%)	13 (19.1)	12 (15.4)	0.550
ICU admission, *n* (%)	45 (66.2)	51 (65.4)	0.994
Treatment, *n* (%)			
Parenteral nutrition	45 (66.2)	52 (66.7)	0.950
Antibiotics	68 (100)	78 (100)	1.0
Somatostatin analogs	68 (100)	78 (100)	1.0
Infection, *n* (%)			
Infected pancreatic necrosis	8 (11.8)	10 (12.8)	0.847
Pulmonary infection	32 (47.1)	39 (50)	0.723
Other infections	28 (41.2)	29 (37.2)	0.621
Length of hospital stay, days	14.2±4.5	13.8±3.9	0.879
On admission			
Heart rate, beats/min	100.3±12.2	99.4±16.5	0.365
Respiratory rate,/min	28.5±9.8	29.2±10.1	0.238
Mean arterial pressure, mm Hg	88.5±8.8	85.1±6.6	0.438
Arterial pH	7.38±0.12	7.34±0.03	0.347
PaO_2, mm Hg	60.3±12.4	59.9±10.9	0.262
PaO_2/FiO_2, mm Hg	190.8±42.1	188.5±39.4	0.582

HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit; PaO_2, arterial oxygen partial pressure; FiO_2, fraction of inspired oxygen

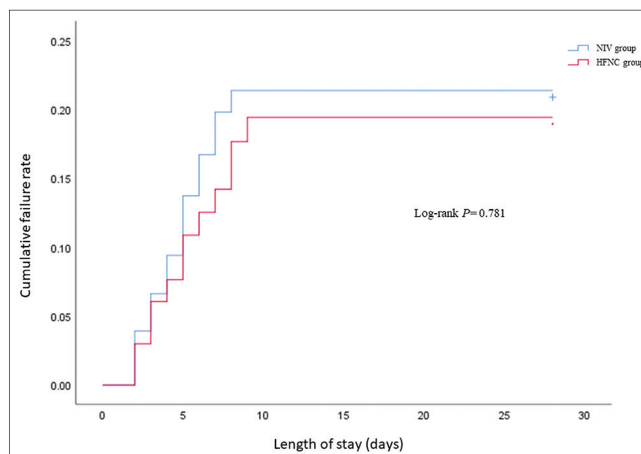

Figure 2: Kaplan–Meier curve analysis for cumulative failure rate. HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation

Other outcomes

There were no significant differences in the duration of respiratory support, dyspnea scores, ICU, or hospital total length of stay between the two groups (all $P > 0.05$, see Table 4). The number of daily airway care interventions was significantly lower in the HFNC group than in the NIV group [4 (2–7) vs 8 (4–13), $P = 0.011$]. The comfort score in the HFNC group was also significantly higher than that in the NIV group ($P = 0.009$), whereas the incidence of nasofacial skin breakdown was significantly lower in the HFNC group than in the NIV group ($P = 0.018$). The 28-day mortality in the HFNC group was 1.5%, which

Table 2: Primary outcome and cause analysis

	HFNC (*n*=68)	NIV (*n*=78)	Risk difference, % (95% CI)	*P*
Primary outcome, *n* (%)				
Treatment failure	12 (17.6)	15 (19.2)	-1.6 (-11.3-14.0)	0.806
Invasive ventilation	7 (10.3)	8 (10.3)	0.0 (-10.1-10.7)	0.945
Treatment switch	5 (7.3)	7 (8.9)	-1.6 (-8.2-11.0)	0.722
Analysis of treatment failure, *n* (%)				
Treatment intolerance	2/12 (16.7)	9/15 (60.0)	-43.3 (-66.8–6.2)	0.023
Aggravation of respiratory distress	5/12 (41.7)	3/15 (20.0)	21.7 (-12.0-51.1)	0.221
Aggravation of hypoxemia	3/12 (25.0)	2/15 (13.3)	11.7 (-17.7-41.5)	0.438
Aggravation of acidosis	2/12 (16.7)	1/15 (6.7)	10.0 (-16.1-38.7)	0.411

HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation

Table 3: Vital signs and arterial blood gas analysis

	HR (bpm)	MAP (mmHg)	RR (bpm)	pH	PaO_2/FiO_2 (mmHg)
HFNC (*n*=68)					
Baseline	99.2±11.8	90.5±6.8	28.6±6.4	7.31±0.04	190.8±43.2
1 h	86.2±12.1*	86.7±10.4	25.3±5.3*	7.34±0.11*	209.5±58.4*
12 h	84.9±11.1*	85.3±11.2	23.1±4.8*	7.36±0.05*	211.2±617*
48 h	83.6±10.5*	85.4±11.5	21.6±5.3*	7.41±0.03*	239.1±70.8*
NIV (*n*=78)					
Baseline	99.8±12.5	88.1±6.8	28.3±6.4	7.31±0.03	189.5±40.4
1 h	92.5±12.1#*	86.3±10.2	24.6±4.1*	7.35±0.11*	209.5±45.9*
12 h	86.3±13.7*	84.5±11.1	22.6±4.8*	7.36±0.03*	213.7±70.9*
48 h	84.8±12.2*	85.6±9.7	19.5±5.8*	7.39±0.05*	228.4±81.1*

Data are shown as means±standard deviation. HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation; HR, heart rate; MAP, mean arterial pressure; RR, respiratory rate; PaO_2, partial pressure of arterial oxygen; FiO_2, fraction of inspiration oxygen. *$P<0.05$, compared with the baseline in the same group; #$P<0.05$, compared with NIV at the same time point

was not significantly different from the 2.6% in the NIV group ($P = 0.642$, see Table 4).

Multivariate logistic analysis of treatment failure in HFNC

Multivariate logistic regression analysis showed that BMI (≥28), APACHE II score (≥15), PaO_2/FiO_2 (≤200), and RR (≥32/min) at 1 hour were independent predictors of HFNC failure [Table 5].

DISCUSSION

Many studies have been conducted to compare the effects of HFNC and NIV in different conditions.[13,17] To the best of our knowledge, this is the first study that directly compares the efficacy of HFNC and NIV in the treatment of AP-associated ARDS. We found that HFNC and NIV had a similar treatment failure rate. However, HFNC was associated with better tolerance, less airway care interventions, and less incidence of skin breakdown compared to NIV, which means HFNC may be an ideal choice of respiratory support for AP patients, especially for those with NIV intolerance.

Acute respiratory failure (ARF) emerged as the predominant form of organ failure during both the early and late phases of AP.[1] In a retrospective study of 813,120 hospitalized patients with AP, Gajendran *et al.*[18] identified ARF in 21,415 cases (2.63%), with a corresponding mortality rate of 17%. Several studies had demonstrated that NIV could effectively alleviate respiratory distress, lower the rate of endotracheal intubation, and reduce mortality in patients with ARDS.[19,20] However, it is important to note that more than 15% of patients experience intolerance to NIV due to various reasons, which subsequently increases the risk of treatment failure and the need for reintubation.[8] In this particular study, HFNC therapy is explored as a novel approach to oxygen therapy, showing promising results in terms of patient tolerance. Nevertheless, there are limited data available on the use of HFNC in patients with AP-associated ARDS at present.

In recent years, HFNC has been increasingly recommended for patients with ARF. In a meta-analysis conducted by Zhao *et al.*,[21] it was found that HFNC was associated with a significant reduction in the intubation rate compared to conventional oxygen therapy. Theoretically, HFNC can provide high airflow, resulting in a small positive mean airway pressure.[22] This can help alleviate respiratory distress and reduce the work of breathing. However, compared to NIV, evidence for the efficacy and safety of HFNC is conflicting. Stephan *et al.*[23] reported that among cardiothoracic surgery patients with ARF, the use of HFNC did not result in a worse rate of treatment failure compared with NIV. But in the study by Frat, there was a significant

Table 4: Other outcomes in the HFNC and NIV groups

	HFNC (*n*=68)	NIV (*n*=78)	*P*
Duration of HFNC or NIV, hours	85 (59.5-98.5)	78 (51.8-91.8)	0.223
Airway care interventions, per day	4 (2-7)	8 (4-13)	0.011
Comfort score	8.8±3.6	5.2±1.8	0.009
Dyspnea score	2.8±2.6	2.6±1.9	0.512
Nasal facial skin breakdown, *n* (%)	2 (2.9)	11 (14.1)	0.018
Length of stay in ICU, days	8 (6-10)	9 (6-12)	0.215
Length of stay in hospital, days	12 (7-17)	11 (7-16)	0.312
28-day mortality, *n* (%)	1 (1.5)	2 (2.6)	0.642

Data are shown as means±standard deviation, number (%) patients, or median (interquartile range). HFNC, high-flow nasal cannula oxygen therapy; NIV, non-invasive ventilation; ICU, intensive care unit

Table 5: Multivariate logistic analysis of treatment failure in HFNC

	OR	95% CI	*P*
Age, years	2.018	0.892-4.651	0.156
Body mass index ≥28	2.146	1.211-6.875	0.002
APACHE II score ≥15	2.412	1.813-3.864	0.013
Initial pH ≤7.35	0.144	0.131-12.384	0.127
PaO2/FiO2 at 1 h of treatment ≤200	1.456	1.114-1.613	0.031
HR at 1 hour of treatment ≥120	0.855	0.759-1.415	0.114
RR at 1 hour of treatment ≥32	1.268	1.015-1.426	0.032

HFNC, high-flow nasal cannula oxygen therapy; APACHE II, Acute Physiology and Chronic Health Evaluation II; PaO_2: partial arterial oxygen tension; FiO_2: fraction of inspired oxygen; HR, heart rate; RR, respiratory rate

difference in favor of HFNC in 90-day mortality in patients with nonhypercapnic ARF.[24] In our study, no significant differences were found for treatment failure or mortality in these two groups. The flow-dependent nature of PEEP and FiO_2 through nasal prongs often leads to unpredictable clinical outcomes. Due to the physiological effects of HFNC, it is extremely unlikely that its ventilation effect is better than that of NIV. Therefore, noninferiority studies should be used to compare HFNC with NIV.

Although NIV plays a crucial role in the treatment of ARDS, approximately 20% of patients may have contraindications to NIV or experience intolerance due to various reasons, including eye irritation, skin damage, or claustrophobia.[25] A recent meta-analysis conducted by Lewis *et al*.[17] examined the impact of HFNC compared to NIV on patients with respiratory failure. The study found uncertainty regarding the effect of HFNC on both short-term and long-term comfort. However, in the trial reported by Carratala, it was found that HFNC was more comfortable compared to NIV for elderly patients with respiratory failure.[26] In our previous randomized controlled study, we also found that HFNC had better tolerance and comfort than NIV in patients with hypercapnic respiratory failure.[27] This study showed that the comfort score in the HFNC group was significantly higher than that in the NIV group. The analysis of treatment failure also revealed that the tolerance of HFNC was significantly superior to NIV, and intolerance was identified as a crucial factor contributing to the failure of NIV. HFNC is well tolerated because it provides adequate heating and humidity, which helps maintain mucosal function, promote secretion clearance, prevent epithelial injury, and improve patient comfort.[28]

A previous study had shown that delayed intubation due to HFNC treatment failure could increase mortality.[9] Therefore, in this study, we performed a regression analysis on the predictors of HFNC treatment failure in AP-associated ARDS. Strict monitoring of high-risk patients and treatment by experienced staff can help prevent failure of HFNC therapy. According to Liu's study, BMI was not found to be an independent indicator for predicting AP-associated ARDS.[29] However, in our study, BMI ≥28 could predict HFNC failure. Obesity leads to changes in respiratory anatomy and physiology that complicate airway management. Patients with obesity have an increased susceptibility to lung collapse and therefore necessitate higher PEEP to prevent it.[30] In addition, we found that APACHE II score ≥15 could be a risk factor to predict HFNC failure. An APACHE II score ≥15 indicates that the overall condition of the patient is severe. Our study also found that PaO_2/FiO_2 (≤200) and RR ≥32 beats/min after 1 hour treatment are independent predictors of HFNC failure. The lower PaO_2/FiO_2 is an indicator of hypoxemic conditions, and a decreased PaO_2/FiO_2 may indicate a forewarning stage of ARDS development triggered by AP. Additionally, a treatment duration of at least 1 hour with a RR ≥32 beats/min may suggest that HFNC ineffectively reduces the risk of respiratory distress.

There are some limitations to this study. First, this study was a retrospective, single-center study, which means it may have been influenced by the limitations inherent in retrospective analysis. Second, the primary endpoint of this study was a composite of reintubation rate and switching to another treatment modality, which had potential limitations. But the composite end point of treatment failure rate reflects the actual application of HFNC and NIV in daily clinical practice. Third, in this study, the settings of HFNC were mainly based on patient tolerance, which was somewhat subjective, and objective indicators such as ultrasonic diaphragm movement could be explored later. Finally, this study initially explored the predictive factors of HFNC treatment failure but did not conduct clinical verification, nor did it form a process application standard.

In conclusion, AP patients with mild-moderate ARDS, the usage of HFNC did not lead to a higher rate of treatment failure when compared to NIV. HFNC is an ideal choice of respiratory support for patients with NIV intolerance, but clinical application should pay attention to the influencing factors of its treatment failure.

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Conflicts of interest

There are no conflicts of interest.

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