BMJ Open Respiratory Research

Effect of high-flow nasal cannula versus non-invasive ventilation after extubation on successful extubation in obese patients: a retrospective analysis of the MIMIC-IV database

Yun Ge,[1] Zhenxuan Li,[2] Ao Xia,[1] Jingyuan Liu,[1] Dongmin Zhou [1]

To cite: Ge Y, Li Z, Xia A, *et al*. Effect of high-flow nasal cannula versus non-invasive ventilation after extubation on successful extubation in obese patients: a retrospective analysis of the MIMIC-IV database. *BMJ Open Respir Res* 2023;**10**:e001737. doi:10.1136/bmjresp-2023-001737

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjresp-2023-001737).

Received 31 March 2023
Accepted 28 July 2023

[1]Department of Critical Care Medicine, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, Henan, China
[2]Department of Thoracic Surgery, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, Henan, China

Correspondence to
Dongmin Zhou;
13937120236@sohu.com

ABSTRACT

Background The pathophysiological characteristics of the respiratory system of obese patients differ from those of non-obese patients. Few studies have evaluated the effects of high-flow nasal cannula (HFNC) and non-invasive ventilation (NIV) on the prognosis of obese patients. We here compared the effects of these two techniques on the prevention of reintubation after extubation for obese patients.

Methods Data were extracted from the Medical Information Mart for Intensive Care database. Patients who underwent HFNC or NIV treatment after extubation were assigned to the HFNC or NIV group, respectively. The reintubation risk within 96 hours postextubation was compared between the two groups using a doubly robust estimation method. Propensity score matching was performed for both groups.

Results This study included 757 patients (HFNC group: n=282; NIV group: n=475). There was no significant difference in the risk of reintubation within 96 hours after extubation for the HFNC group compared with the NIV group (OR 1.50, p=0.127). Among patients with body mass index ≥40 kg/m^2, the HFNC group had a significantly lower risk of reintubation within 96 hours after extubation (OR 0.06, p=0.016). No significant differences were found in reintubation rates within 48 hours (15.6% vs 11.0%, p=0.314) and 72 hours (16.9% vs 13.0%, p=0.424), as well as in hospital mortality (3.2% vs 5.2%, p=0.571) and intensive care unit (ICU) mortality (1.3% vs 5.2%, p=0.108) between the two groups. However, the HFNC group had significantly longer hospital stays (14 days vs 9 days, p=0.005) and ICU (7 days vs 5 days, p=0.001) stays.

Conclusions This study suggests that HFNC therapy is not inferior to NIV in preventing reintubation in obese patients and appears to be advantageous in severely obese patients. However, HFNC is associated with significantly longer hospital stays and ICU stays.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Few studies have evaluated the impact of high-flow nasal cannula (HFNC) therapy and non-invasive ventilation (NIV) on the short-term prognosis of obese patients after extubation.

WHAT THIS STUDY ADDS

⇒ In an obese population, the effects of HFNC therapy on the prevention of reintubation after extubation were not inferior to those of NIV. HFNC therapy demonstrated a significant advantage for severely obese patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study suggests that HFNC therapy is an effective treatment to prevent reintubation in the obese population. It provides further information for clinicians in making decisions about oxygen therapy modalities.

INTRODUCTION

The main forms of non-invasive respiratory support after extubation include routine oxygen therapy, non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC) therapy. In HFNC therapy, oxygen is delivered through a nasal cannula. This therapeutic modality not only ensures a constant and adjustable concentration of inhaled oxygen delivered at high flow rates but also provides low-level continuous positive airway pressure,[1] increases end-expiratory lung volume[2] and decreases the work of breathing. Additionally, the high gas flow velocity has a flushing effect, reducing the nasopharyngeal dead space.[3] The inhaled gas is also humidified and heated, which increases the patient's comfort levels. This may attenuate the airway inflammatory response[4] and promote clearance of respiratory tract secretions.[5] Therefore, HFNC therapy may serve as an alternative to non-invasive positive-pressure ventilation.

Previous studies have shown that, compared with routine oxygen therapy, HFNC therapy effectively enhances

postextubation oxygenation, thereby reducing the incidence of respiratory failure recurrence and reintubation rates of critically ill patients and patients with low reintubation risk.[6] However, its use in patients with high reintubation risk, such as obese patients, remains unsupported.

The rate of obesity among patients in the intensive care unit (ICU) is as high as 20%.[7] The increased oxygen consumption and work of breathing in obese patients result in oxygenation reduction with a body weight increase. Under resting-state conditions, oxygen consumption is 1.5 times higher in obese than in non-obese individuals.[8]

Obese individuals are also prone to atelectasis, as the weight of the chest wall and a large amount of abdominal fat compress the lungs and reduce pulmonary compliance, thereby reducing functional residual capacity and arterial oxygenation. The supine position, which is usually adopted by patients during mechanical ventilation, also further aggravates atelectasis.

A case–control study of obese and non-obese patients receiving mechanical ventilation revealed that obese patients were at higher risk for difficult tracheal intubation (15% (obese) vs 6% (non-obese)) and stridor after extubation (15% (obese) vs 3% (non-obese)).[9]

The main challenge faced by clinicians after extubation of mechanically ventilated obese patients is the optimisation of postextubation oxygen therapy regimens, based on the pathophysiological characteristics of the respiratory system of obese patients, in order to reduce the risk of reintubation and improve patient outcomes. In recent years, HFNC therapy has received widespread attention due to its higher level of comfort than that of NIV.[10] Some studies have found no significant differences in effectiveness between HFNC therapy and NIV.[11] However, the effectiveness of HFNC therapy compared with NIV in obese patients remains unclear.

Therefore, we here compared the effects of HFNC therapy and NIV in preventing the need for reintubation after extubation in obese patients.

METHODS

Study population and data extraction

Data were obtained from the Medical Information Mart for Intensive Care (MIMIC-IV) database,[12] which is a critical care database developed and maintained by the Massachusetts Institute of Technology Laboratory for Computational Physiology. MIMIC-IV is a large, freely accessible single-centre critical care database containing comprehensive and high-quality data of patients hospitalised at the ICUs of Beth Israel Deaconess Medical Center between 2008 and 2019. One of the researchers was allowed to access and download data from the database after completing the Protecting Human Research Participants training. Data were extracted from the MIMIC-IV 1.0 database using PostgreSQL.

Study design

The data of patients who received invasive mechanical ventilation and for whom extubation had been planned were extracted and screened from the downloaded data. The inclusion criteria were as follows: obese patients (body mass index (BMI) ≥30 kg/m^2 or patients diagnosed with obesity in accordance with the 9th and 10th revisions of the International Classification of Diseases (ICD-9, ICD-10)); aged ≥18 years; who underwent HFNC therapy or NIV within 6 hours after extubation. Given that clinicians always used to give conventional oxygen therapy first after extubation, and then switch to HFNC or NIV immediately after finding that it was not applicable. If only these patients were recruited, a large portion of the population would be missed. Therefore, for the real-world data, we set relatively broad inclusion criteria and chose to include patients who received HFNC or NIV within 6 hours rather than just immediately after extubation. For patients with multiple ICU stays, only the data of the first hospital admission and first ICU stay were included. For patients with multiple extubations, only the data related to the first extubation were included. We excluded patients with a length of ICU stay <24 hours; tracheotomy and death occurred within 1 hour after extubation without reintubation (ie, patients in whom treatment had been abandoned).

Patients were grouped as follows: The HFNC group included patients who received postextubation continuous or intermittent HFNC therapy until improvement or deterioration (following which conversion to NIV or reintubation was performed) occurred. The NIV group included patients who underwent continuous or intermittent NIV postextubation until improvement or deterioration (following which reintubation was performed) of the patient's condition.

Baseline data

The following baseline patient data were collected: demographic data, anthropometric data, comorbidities, Simplified Acute Physiology Score (SAPS) II on ICU admission and diagnostic information. Other data collected include vital signs, inhaled oxygen concentration setting of the ventilator, tidal volume and arterial blood gases prior to removal of the tracheal catheter. The arterial oxygen tension/fractional inspired oxygen (FiO_2) ratio was calculated. The use of vasopressors, such as epinephrine, norepinephrine, phenylephrine, vasopressin and dopamine, prior to extubation, was also recorded.

Outcomes

The primary outcome was reintubation within 96 hours after extubation. Secondary outcomes were reintubation within 48 hours, reintubation within 72 hours, in-hospital reintubation, length of stay in ICU, length of hospitalisation, in-ICU mortality and in-hospital mortality. Other outcomes included the time from extubation to reintubation, the number of patients in the HFNC group

converted to NIV after deterioration and the number of HFNC patients subsequently reintubated.

Statistical analysis

Non-inferiority analyses were performed in this study. According to previous studies, the reintubation rate was about 10%–15% in obese patients treated with NIV after extubation,[13 14] and about 10%–20% treated with HFNC.[11 15 16] We hypothesised that the preset non-inferiority margin for the HFNC group was 10% based on considerations of clinical relevance and previous studies.[6 17] The sample size of 757 patients was determined sufficient to support the unilateral 95% CI analysis with a statistical power of 80%, and a maximum tolerated patient loss rate of 15%.

Statistical analysis was performed using R Studio (R V.4.2.1). Categorical data were expressed as number and percentage (no (%)), normally distributed measurement data were expressed as mean±SD, and non-normally distributed data were expressed as median (Q1, Q3). Multiple interpolation was used to fill in the missing values. Intergroup comparisons were performed using the t-test, χ^2 test or Mann-Whitney U test, as appropriate. Two-tailed tests were adopted, with differences considered statistically significant when p<0.05.

The doubly robust estimation model was used to explore the relationships between exposure and the primary outcome variable. Doubly robust estimation combines the inverse probability of treatment weighting (IPTW) model targeted towards exposure and a regression model targeted towards outcomes to analyse causal effects. When the two models are used singly, the results are unbiased only when statistical models are correctly specified. However, the doubly robust estimation model only requires one of the two models to be correct for the generation of unbiased results. A series of sensitivity analyses were performed to assess the robustness of the findings. We also tested the interaction between treatment and the degree of obesity of the patient and so on.

Propensity scores were calculated using the multivariate logistic regression model, with a matching ratio of 1:1 and a calliper of 0.01. The IPTW model was constructed using weights based on the propensity scores and was used for further multivariate logistic regression analysis of the weighted cohort. Covariates included in the model were variables with residual imbalance after IPTW. Standardised mean differences were calculated to evaluate the validity of IPTW. Propensity score matching (PSM) was also adopted to balance baseline characteristics between the two groups.

RESULTS

Baseline characteristics

A total of 23 337 planned extubation records from the MIMIC-IV database were screened. Based on the inclusion and exclusion criteria stated above, 757 cases were ultimately included in this study (figure 1). The included patients had a median age of 65 (57, 73) years. Overall, 34.4% of the patients were women, and the median BMI of the patients was 36.8 (33.2, 43.2) kg/m^2. There were 282 patients in the HFNC group and 475 in the NIV group. The median SAPS II at ICU admission was 39 (32, 47) points. A total of 97 people were eventually reintubated, 52 in the HFNC group and 45 in the NIV group.

Table 1 shows the baseline characteristics of the two groups of patients. There were statistically significant differences in BMI, certain comorbidities (hypertension, coronary heart disease, chronic obstructive pulmonary disease (COPD), diabetes, cancer) and SpO_2, tidal volume, arterial blood gases and PO_2/FiO_2 ratio prior to extubation. After propensity score-based IPTW.[18 19] The majority of covariates were balanced between the two groups, but age remained significantly different (table 2). Figure 2 shows the comparison of covariate differences before and after adjustment using IPTW.

Primary outcome

Outcome regression was combined with IPTW using the doubly robust estimation method[20] for the construction of a regression model. Doubly robust estimation indicated that the risk of reintubation within 96 hours after extubation did not differ significantly between the HFNC and NIV groups (table 3) (OR 1.50, 95% CI 0.88 to 2.55, p=0.127 after adjustment for unbalanced covariates; OR 1.45, 95% CI 0.84 to 2.50, p=0.180 after adjustment for all covariates). To ensure the robustness of results, we performed a logistic regression analysis of multiple models, including post-PSM logistic regression analysis as well as logistic regression of the original cohort. The same conclusion was obtained with all models: compared with the NIV group, the HFNC group did not have a significantly elevated risk of reintubation within 96 hours after extubation (table 3). After PSM, the difference in rates of reintubation within 96 hours after extubation of the HFNC and NIV groups was not statistically significant (17.5% vs 14.3%, p=0.533; table 4).

Secondary outcomes and other outcomes

The outcomes of the two groups were compared after PSM had been performed, which yielded 154 matched patient pairs. The baseline characteristics of the two groups after PSM were shown in online supplemental table S1. The rates of reintubation within the various time frames after extubation did not differ significantly between the matched HFNC and NIV groups. Rates of reintubation within 48 hours after extubation were 15.6% vs 11.0% (p=0.314), that within 72 hours after extubation were 16.9% vs 13.0% (p=0.424), while rates of in-hospital reintubation were 20.1% vs 15.6% (p=0.372). The time from extubation to reintubation of the HFNC group was longer than that of the NIV group (13.7 hours vs 9.4 hours, p=0.002). The length of hospital stay and length of ICU stay were significantly longer in the HFNC than in the NIV group. The lengths of hospital stay and ICU stay were

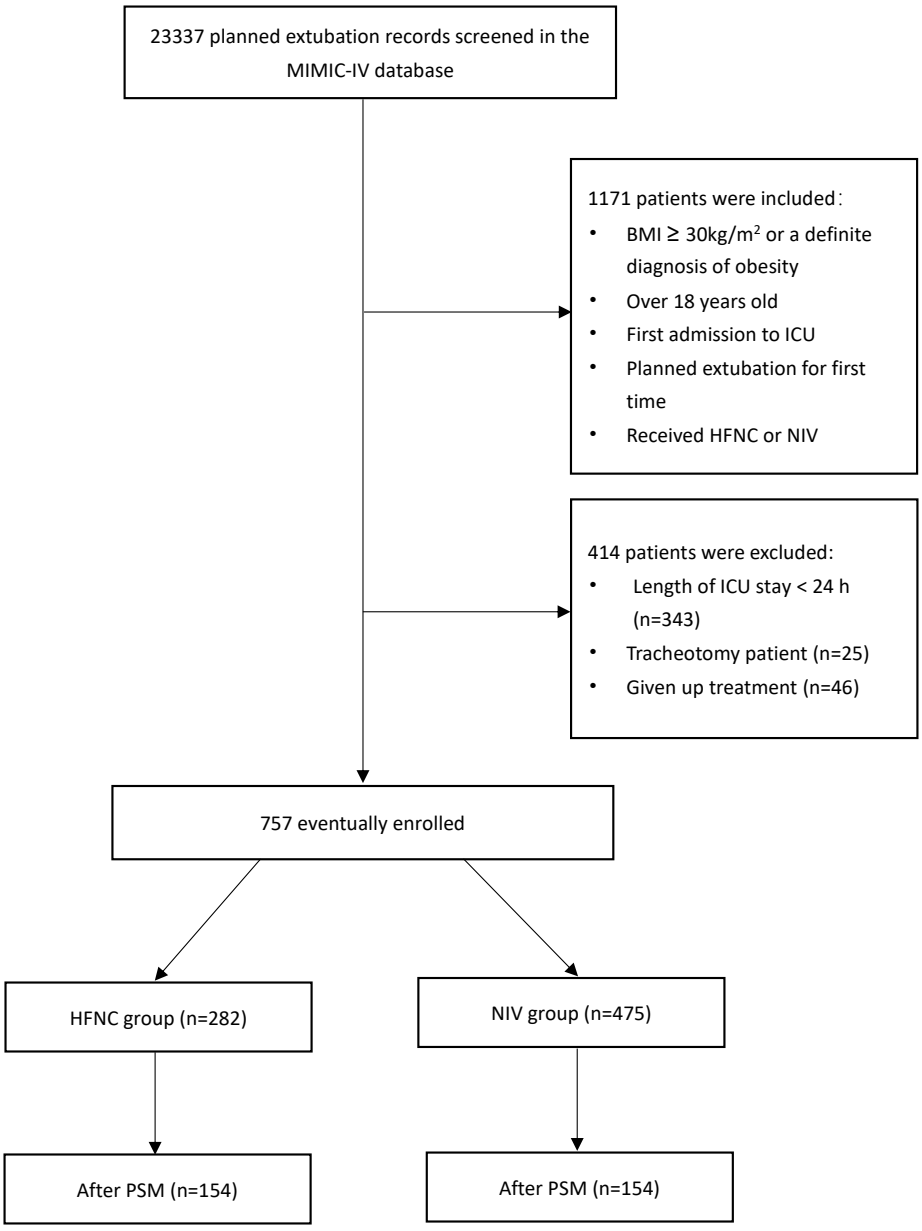

Figure 1 Study flow chart. BMI, body mass index; HFNC, high-flow nasal cannula oxygen; NIV, non-invasive ventilation; PSM, propensity score matching.

14 days vs 9 days (p=0.005), and 7 days vs 5 days (p=0.001), respectively. However, in-hospital mortality (3.2% vs 5.2%, p=0.571) and ICU mortality (1.3% vs 5.2%, p=0.108) did not differ significantly between the two groups (table 4). Forty-two patients of the HFNC group of the original cohort were converted to NIV. Among these patients, 10 were reintubated, resulting in an in-hospital reintubation rate of 23.8%.

Subgroup analysis

Figure 3 shows that the presence or absence of COPD (p for interaction=0.218) and patient age (p for interaction=0.233) did not interact significantly with the primary outcome in either group. However, significant interactions were found between BMI and the primary outcome (p for interaction=0.009). Patients with more severe obesity tended to benefit more from postextubation HFNC therapy and had a lower rate of reintubation within 96 hours after extubation. For patients with BMI ≥40 kg/m^2, the risk of reintubation within 96 hours after extubation was significantly lower in the HFNC group than in the NIV group (OR 0.06, 95% CI 0 to 0.39, p=0.016).

DISCUSSION

Critically ill patients usually have complex and varying health conditions that necessitate the consideration of many factors during treatment. The same diagnostic and

Table 1 Baseline characteristics of the original cohort

Variables	HFNC group (n=282)	NIV group (n=475)	P value
Age, median (Q1, Q3), years	66 (58, 73)	65 (54, 75)	0.464
Female, no (%)	174 (36.6)	87 (31.0)	0.132
Ethnicity, no (%)			0.234
Black	31 (6.5)	11 (3.9)	
White	334 (70.3)	196 (69.8)	
Other	110 (23.2)	74 (26.3)	
BMI, median (Q1, Q3), kg/m^2	37.9 (34.3, 44.2)	34.7 (32.1, 38.0)	<0.001
Charlson Comorbidity Index, median (Q1, Q3)	5 (4, 7)	5 (4, 7)	0.462
Comorbidities, no (%)			
Hypertention	402 (84.6)	220 (78.3)	0.035
Coronary heart disease	152 (32.0)	58 (20.6)	0.001
Congestive heart failure	166 (34.9)	101 (35.9)	0.843
COPD	204 (42.9)	98 (34.9)	0.035
Diabetes	219 (46.1)	108 (38.4)	0.048
Liver disease	37 (7.8)	28 (10.0)	0.370
Renal disease	94 (19.8)	46 (16.4)	0.283
Cancer	21 (4.4)	24 (8.5)	0.031
SAPS II, median (Q1, Q3)	39 (31, 46)	39 (32, 46)	0.549
Use of the vasoactive drug, no (%)			0.135
Not used	371 (78.1)	231 (82.2)	
Use of a single class	89 (18.7)	47 (16.7)	
Concomitant use of two or more	15 (3.2)	3 (1.1)	
Vital signs before extubation			
MAP, median (Q1, Q3), mm Hg	78 (71, 86)	78 (71, 87)	0.829
Heart rate, median (Q1, Q3), times/min	83 (75, 94)	84 (72, 94)	0.975
Respiratory rate, median (Q1, Q3), times/min	20 (17, 23)	20.00 (18, 24)	0.100
SpO_2, median (Q1, Q3), %	98 (96, 99)	96 (94, 98)	<0.001
Tidal volume before extubation, mean±SD, mL	480±109	482±112	0.805
Length of mechanical ventilation before extubation, median (Q1, Q3), hour	18 (6, 53)	37 (15, 90)	<0.001
Arterial blood gas results before extubation			
pH, median (Q1, Q3)	7.38 (7.34, 7.42)	7.41 (7.37, 7.45)	<0.001
PO_2, median (Q1, Q3), mm Hg	101 (85, 123)	86 (74, 104)	<0.001
PCO_2, median (Q1, Q3), mm Hg	43 (39, 48)	41 (36, 45)	<0.001
PaO_2/FiO_2 ratio before extubation, median (Q1, Q3), mm Hg	232.5 (190.1, 285.0)	175.2 (148.3, 240.1)	<0.001

BMI, body mass index; COPD, chronic obstructive pulmonary disease; FiO_2, fraction of inspired oxygen; HFNC, high-flow nasal cannula oxygen; MAP, mean arterial pressure; NIV, non-invasive ventilation; PaO_2, arterial oxygen tension; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; SAPS, Simplified Acute Physiology Score; SpO_2, pulse oximetry.

treatment techniques may not apply equally in different populations.[21] For instance, diagnostic and treatment techniques that bring benefit to the general population may not be equally beneficial in specific populations, such as those with obesity. In this comparison between the effects of HFNC therapy and those of NIV on the need for reintubation of obese patients after weaning from invasive mechanical intubation, the doubly robust analysis found no significant differences in the need for reintubation within 96 hours postextubation between the two groups. However, among patients with BMI ≥40 kg/m^2, those who received HFNC therapy had a significantly lower risk of reintubation within 96 hours postextubation than those who received NIV.

We defined reintubation within 96 hours after extubation as treatment failure because of the following reasons: if the observation time is excessively short, then extubation failure is affected to a greater extent by factors such

Table 2 Baseline characteristics of the cohort after IPTW based on propensity scores*

Variables	HFNC group (n=751)	NIV group (n=738)	P value
Age, median (Q1, Q3), year	63 (53, 73)	66 (58, 74)	0.034
Gender, F, %	37.0	37.3	0.952
Ethnicity, %			0.574
Black	3.8	5.7	
White	69.3	69.2	
Other	26.9	25.0	
BMI, median (Q1, Q3), kg/m^2	36.0 (32.9, 42.4)	36.6 (33.5, 42.6)	0.389
Charlson Comorbidity Index, median (Q1, Q3)	5 (4, 7)	5 (4, 7)	0.198
Comorbidities, %			
Hypertention	78.7	81.5	0.484
Coronary heart disease	24.4	27.0	0.525
Congestive heart failure	38.4	33.6	0.287
COPD	41.2	42.2	0.834
Diabetes	42.7	44.9	0.639
Liver disease	10.3	8.8	0.618
Renal disease	13.4	18.7	0.085
Cancer	6.2	5.8	0.824
SAPSII, median (Q1, Q3)	38 (32, 45)	39 (32, 46)	0.381
Use of vasoactive drug, %			0.630
Not used	81.9	80.6	
Use of a single class	16.7	16.7	
Concomitant use of two or more	1.4	2.7	
Vital signs before extubation			
MAP, median (Q1, Q3), mm Hg	77 (70, 88)	78 (71, 87)	0.763
Heart rate, median (Q1, Q3), times/min	84 (72, 93)	83 (75, 95)	0.567
Respiratory rate, median (Q1, Q3), times/min	20 (18, 23)	20 (17, 23)	0.468
SpO_2, median (Q1, Q3), %	97 (95, 98)	97 (95, 99)	0.217
Tidal volume before extubation, mean±SD, mL	470±106	478±107	0.439
Length of mechanical ventilation before extubation, median (Q1, Q3), hour	23(8, 70)	21 (7, 72)	0.322
Arterial blood gas results before extubation			
pH, median (Q1, Q3)	7.39 (7.35, 7.43)	7.39 (7.35, 7.43)	0.647
PO_2, median (Q1, Q3), mm Hg	92(78, 112)	95.0 (78, 118)	0.683
PCO_2, median (Q1, Q3), mm Hg	42(38, 48)	42 (39, 47)	0.945
PaO_2/FiO_2 ratio before extubation, median (Q1, Q3), mm Hg	204.8 (160.0, 276.3)	214.5 (168.0, 270.0)	0.652

*Using the estimated propensity scores as weights, the IPTW model was used to generate the weighted cohort.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; FiO_2, fraction of inspired oxygen; HFNC, high-flow nasal cannula oxygen; IPTW, inverse probability of treatment weighting; MAP, mean arterial pressure; NIV, non-invasive ventilation; PaO_2, arterial oxygen tension; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; SAPS, Simplified Acute Physiology Score; SpO_2, pulse oximetry.

as erroneous indications for extubation and associated to a lesser extent with the selection of oxygen therapy measures after extubation, and more than 80% of reintubations occur within 96 hours after extubation.[16 22 23] A multicentre study conducted in the USA showed that the choice of a time cut-off of 96 hours consistently caught about 90% of reintubation events in the ICU over a 12-year period, indicating that it was a stable indicator, and the researchers recommended that the 96 hours time cut-off be used as the criteria for reporting reintubation rates.[22]

Previous research data have shown that the rate of reintubation in ICU patients after weaning from mechanical ventilation is approximately 10%,[22] while the reintubation rates of patients with a low risk of extubation failure are within the range of 5%–13%.[24 25] Certain studies have

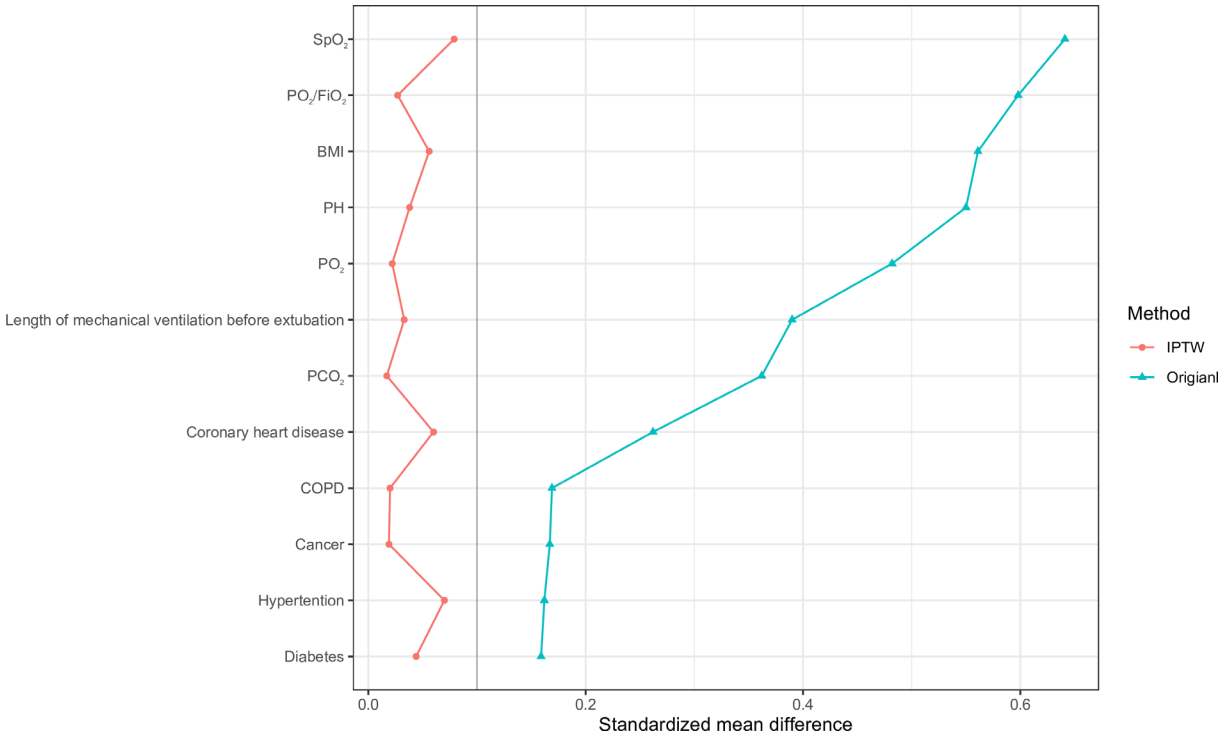

Figure 2 Standardised mean difference before and after IPTW. IPTW represents the variables of the cohort weighted by the inverse probability. Original represents variables of the original cohort. BMI, body mass index; COPD, chronic obstructive pulmonary disease; FiO_2, fractional inspired oxygen; IPTW, inverse probability of treatment weighting; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen.

reported that patients with a high risk of reintubation, who receive routine oxygen therapy, have reintubation rates of up to 22%–24%.[17 26] Our results indicated that the overall in-hospital reintubation rate and reintubation rate within 96 hours after extubation in patients in the HFNC and NIV groups were 12.8% and 11.6%, respectively, in agreement with previous studies.

Our results demonstrated that in an obese population, the effect of HFNC therapy in preventing reintubation following extubation was not inferior to that of NIV. The prophylactic use of NIV after extubation in obese patients was generally considered beneficial because positive pressure ventilation can prevent alveolar collapse, improve lung inflation and reduce the inspiratory threshold load in obese patients.[13] However, poor patient tolerance has always been a major challenge in NIV treatment. A previous study found that 29% of NIV failures were due to treatment intolerance, which was significantly higher than the 4% rate of HFNC.[27] Patients often remove the mask or interrupt respiratory support due to claustrophobia, coughing up sputum, drinking or eating when treated by NIV.[28] However, HFNC can generally be used continuously for several days because of its comfort.[29] Compared with NIV, HFNC only creates a lower level of positive airway pressure through nasopharyngeal and airway resistance to high flow gases.[29 30] Nevertheless, it provides appropriate temperature and high humidity gas, which can promote mucociliary clearance, thus improving small airway function and decreasing airway resistance in obese patients.[31 32] Moreover, Corley *et al*[33] found that HFNC increased end-expiratory volume in subjects, especially in obese subjects. A post hoc analysis of a large trial showed that NIV was not superior to HFNC in obese patients after thoracic surgery (mean BMI of 34 kg/m^2), with 15% and 13% treatment failure in the NIV and HFNC groups, respectively.[32]

This study also suggests that HFNC therapy results in a lower risk of reintubation in severely obese patients compared with NIV. Previous studies on the application of high-flow oxygen therapy in severely obese patients were limited. A randomised controlled trial indicated

Table 3 Analysis using different models of the primary outcome

Methods	OR	95% CI	P value
Doubly robust with unbalanced covariates*	1.50	0.88 to 2.55	0.127
Doubly robust with all covariates	1.45	0.84 to 2.50	0.180
PSM†	1.27	0.69 to 2.35	0.436
Multivariate logistic regression	1.38	0.81 to 2.34	0.225

*Only variable that remained unbalanced after IPTW were included, of which only a single variable, age.
†The two groups were matched by propensity scores and a multivariate logistic regression analysis was performed.
IPTW, inverse probability of treatment weighting; PSM, propensity score matching.

Table 4 Secondary outcome analysis after PSM

Outcomes	HFNC group (n=154)	NIV group (n=154)	P vlaue
Reintubation			
Within 48 hours, no (%)	24 (15.6)	17 (11.0)	0.314
Within 72 hours, no (%)	26 (16.9)	20 (13.0)	0.424
Within 96 hours, no (%)	27 (17.5)	22 (14.3)	0.533
In-hospital, no (%)	31 (20.1)	24 (15.6)	0.372
Time from extubation to reintubation, median (Q1, Q3), hour	13.7 (7.8,21.5)	9.4 (6.4,15.3)	0.002
Length of stay, median (Q1, Q3), day			
Hospital	14 (8, 19)	9 (6, 15)	0.005
ICU	7 (4, 11)	5 (2, 8)	0.001
Mortality			
Hospital, no (%)	5 (3.2)	8 (5.2)	0.571
ICU, no (%)	2 (1.3)	8 (5.2)	0.108

HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, non-invasive ventilation; PSM, propensity score matching.

that HFNC improves the efficiency of apnea oxygenation in morbid obesity (BMI ≥40 kg/m^2),[34] in the case of apnea, the flow rate and the proximity of fresh gas to the airway epithelium both affect the efficiency of respiratory oxygenation.[35] In addition, we speculated that severe obesity might be associated with limited treatment adherence and a higher propensity for NIV intolerance based on clinical experience. In contrast, HFNC treatment provides a higher level of comfort. However, more studies are needed to support this idea.

Oxygen supplementation through HFNC or NIV may significantly improve the oxygen saturation of patients compared with conventional oxygen therapy, as a result, the time from extubation to reintubation will be prolonged compared with conventional oxygen therapy. HFNC, in particular, improves patient tolerance to respiratory failure due to its comfort. One study by Sztrymf *et al* has stated that patients who are not intubated tolerate HFNC for long periods.[36] A randomised controlled trial showed that the time from extubation to reintubation

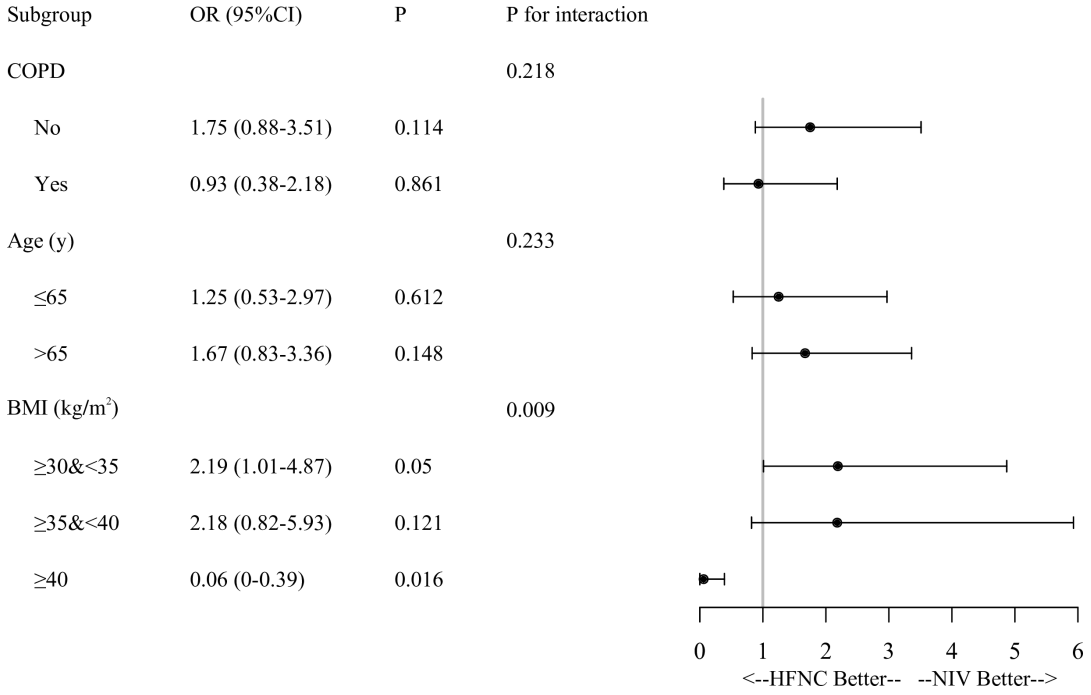

Figure 3 Logistic regression analysis of the primary outcome according to the predefined strata. BMI, body mass index; COPD, chronic obstructive pulmonary disease; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation.

was longer in patients receiving HFNC than in those receiving NIV,[15] which is consistent with our study.

The duration before reintubation of the HFNC group was significantly longer than that of the NIV group. This may be due to the higher level of comfort and improvement in blood gas indicators associated with HFNC therapy, which may have masked the deterioration in patient condition to a certain extent and thus led to a delay in reintubation. Previous studies have demonstrated that delayed intubation may increase the risk of adverse outcomes, including death,[37] but this was inconsistent with the results of this study.

The lengths of hospital stay and ICU stay of the HFNC group were significantly longer than those of the NIV group in this study. This may be partly attributed to delayed reintubation in the HFNC group. However, prolongation of hospital and ICU stay inevitably increases the costs of hospitalisation, which is an issue that requires consideration.

This study had certain limitations. The data used in this study were obtained from electronic health records. Although the majority of high-risk factors for reintubation have been included in our analysis, some factors were excluded due to missing or omitted data. Moreover, adjustments to the data based on the year of hospitalisation have not been made. Since the database spans a relatively long period, treatment methods may have evolved, but this was not taken into consideration. Furthermore, this was a single-centre retrospective study. Although biases have been reduced to a certain extent by doubly robust estimation, future multicentre, prospective studies with a large sample size are still required to validate our findings. Also noteworthy, we chose to include patients who received HFNC or NIV within 6 hours rather than just immediately after extubation, which means that a portion of patients might receive the two treatments because of developing respiratory distress after extubation, therefore, this study only examined the effects of HFNC and NIV on the prevention of extubation failure, but cannot represent the effects of the two treatments on the prevention of respiratory failure.

This retrospective observational study showed that, in an obese population, the effect of HFNC therapy in preventing reintubation after extubation was not inferior to that of NIV. Additionally, HFNC therapy demonstrated an advantage in severely obese patients. However, it is noteworthy that HFNC led to significantly longer hospital stay and ICU stay than NIV in obese subjects.

Acknowledgements The authors would like to thank Changpeng Liu from the Medical Records Office of Henan Cancer Hospital for advice on the statistical analysis of this study.

Contributors YG was responsible for the conception and design of the study, as well as data extraction and drafting and revision of the manuscript. AX and JL were responsible for the collection of the literature and its systematic analysis. ZL performed data processing and statistical analyses. DZ was involved in the conception and design of the study and critically revising important elements of the manuscript. All authors read and approved the final manuscript. YG is responsible for the overall content of the manuscript as the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The MIMIC-IV database is an anonymous public database that was created with the approval of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. The investigators were granted access to the original database and data acquisition. The study protocol was approved by the Ethics Committee of Henan Cancer Hospital (approval number: 2022-475-001).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. The datasets analysed during the current study are available in the MIMIC-IV database (https://physionet.org/content/mimiciv/1.0/).

ORCID iD

Dongmin Zhou http://orcid.org/0000-0002-6005-9405

REFERENCES

1 Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care* 2013;58:1621–4.
2 Riera J, Pérez P, Cortés J, *et al*. Effect of high-flow nasal cannula and body position on end-expiratory lung volume: a cohort study using electrical impedance tomography. *Respir Care* 2013;58:589–96.
3 Lee JH, Rehder KJ, Williford L, *et al*. Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. *Intensive Care Med* 2013;39:247–57.
4 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.
5 Maggiore SM, Idone FA, Vaschetto R, *et al*. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med* 2014;190:282–8.
6 Hernández G, Vaquero C, González P, *et al*. Effect of Postextubation high-flow nasal Cannula vs Conventional oxygen therapy on reintubation in low-risk patients: a randomized clinical trial. *JAMA* 2016;315:1354–61.
7 Pépin JL, Timsit JF, Tamisier R, *et al*. Prevention and care of respiratory failure in obese patients. *Lancet Respir Med* 2016;4:407–18.
8 Kress JP, Pohlman AS, Alverdy J, *et al*. The impact of morbid obesity on oxygen cost of breathing (VO(2Resp)) at rest. *Am J Respir Crit Care Med* 1999;160:883–6.
9 Frat J-P, Gissot V, Ragot S, *et al*. Impact of obesity in mechanically ventilated patients: a prospective study. *Intensive Care Med* 2008;34:1991–8.
10 Sreenan C, Lemke RP, Hudson-Mason A, *et al*. High-flow nasal cannulae in the management of apnea of prematurity: a comparison with conventional nasal continuous positive airway pressure. *Pediatrics* 2001;107:1081–3.
11 Liu T, Zhao Q, Du B. Effects of high-flow oxygen therapy on patients with hypoxemia after extubation and predictors of reintubation: a retrospective study based on the MIMIC-IV database. *BMC Pulm Med* 2021;21:160.

12 Giesa N, Heeren P, Klopfenstein S, *et al*. MIMIC-IV as a clinical data schema. *Stud Health Technol Inform* 2022;294:559–60.
13 El-Solh AA, Aquilina A, Pineda L, *et al*. Noninvasive ventilation for prevention of post-extubation respiratory failure in obese patients. *Eur Respir J* 2006;28:588–95.
14 De Jong A, Wrigge H, Hedenstierna G, *et al*. How to ventilate obese patients in the ICU. *Intensive Care Med* 2020;46:2423–35.
15 Hernández G, Vaquero C, Colinas L, *et al*. Effect of Postextubation high-flow nasal Cannula vs Noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial. *JAMA* 2016;316:1565.
16 Thille AW, Coudroy R, Nay M-A, *et al*. Beneficial effects of noninvasive ventilation after extubation in obese or overweight patients: a post hoc analysis of a randomized clinical trial. *Am J Respir Crit Care Med* 2022;205:440–9.
17 Nava S, Gregoretti C, Fanfulla F, *et al*. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med* 2005;33:2465–70.
18 Ross RK, Breskin A, Breger TL, *et al*. Reflection on modern methods: combining weights for confounding and missing data. *Int J Epidemiol* 2022;51:679–84.
19 Cole SR, Hernán MA. Constructing inverse probability weights for marginal structural models. *Am J Epidemiol* 2008;168:656–64.
20 Funk MJ, Westreich D, Wiesen C, *et al*. Doubly robust estimation of causal effects. *Am J Epidemiol* 2011;173:761–7.
21 Fisher ES, Welch HG. Avoiding the unintended consequences of growth in medical care: how might more be worse *JAMA* 1999;281:446–53.
22 Miltiades AN, Gershengorn HB, Hua M, *et al*. Cumulative probability and time to reintubation in U.S. *Crit Care Med* 2017;45:835–42.
23 Thille AW, Muller G, Gacouin A, *et al*. Effect of Postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: a randomized clinical trial. *JAMA* 2019;322:1465–75.
24 Thille AW, Harrois A, Schortgen F, *et al*. Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med* 2011;39:2612–8.
25 Funk G-C, Anders S, Breyer M-K, *et al*. Incidence and outcome of weaning from mechanical ventilation according to new categories. *Eur Respir J* 2010;35:88–94.
26 Ferrer M, Valencia M, Nicolas JM, *et al*. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med* 2006;173:164–70.
27 Doshi P, Whittle JS, Bublewicz M, *et al*. High-velocity nasal Insufflation in the treatment of respiratory failure: a randomized clinical trial. *Ann Emerg Med* 2018;72:73–83.
28 Sun J, Li Y, Ling B, *et al*. High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: an observational cohort study. *Int J Chron Obstruct Pulmon Dis* 2019;14:1229–37.
29 Spoletini G, Garpestad E, Hill NS. High-flow nasal oxygen or noninvasive ventilation for Postextubation hypoxemia: Flow vs Pressure *JAMA* 2016;315:1340–2.
30 Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure during nasal high-flow oxygen therapy. *Respir Care* 2011;56:1151–5.
31 Roca O, Hernández G, Díaz-Lobato S, *et al*. Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. *Crit Care* 2016;20:109.
32 Stéphan F, Bérard L, Rézaiguia-Delclaux S, *et al*. High-flow nasal cannula therapy versus intermittent noninvasive ventilation in obese subjects after cardiothoracic surgery. *Respir Care* 2017;62:1193–202.
33 Corley A, Caruana LR, Barnett AG, *et al*. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth* 2011;107:998–1004.
34 Schutzer-Weissmann J, Wojcikiewicz T, Karmali A, *et al*. Apnoeic oxygenation in morbid obesity: a randomised controlled trial comparing facemask and high-flow nasal oxygen delivery. *Br J Anaesth* 2023;130:103–10.
35 Achar SK, Pai AJ, Shenoy UK. Apneic oxygenation during simulated prolonged difficult laryngoscopy: comparison of nasal prongs versus nasopharyngeal catheter: a prospective randomized controlled study. *Anesth Essays Res* 2014;8:63–7.
36 Sztrymf B, Messika J, Mayot T, *et al*. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. *J Crit Care* 2012;27:324.
37 Kang BJ, Koh Y, Lim C-M, *et al*. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. *Intensive Care Med* 2015;41:623–32.