Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Anesthesiology

High-Flow Nasal Oxygen Versus Non-Invasive Ventilation Following Extubation in Intensive Care Patients: A Systematic Review and Meta-Analysis

Abdelhakim Ajerd[1*], Mohamed Enaimi[1], Youssef Aarjouni[1], Abderrahman EL Wali[1], Mustapha Bensghir[1]

[1]Department of Anesthesiology and Intensive Care, Mohamed V Military Hospital, Rabat, Morocco

DOI: https://doi.org/10.36347/sjams.2026.v14i05.028 | **Received:** 02.04.2026 | **Accepted:** 14.05.2026 | **Published:** 18.05.2026

***Corresponding author:** Abdelhakim Ajerd
Department of Anesthesiology and Intensive Care, Mohamed V Military Hospital, Rabat, Morocco

Abstract **Original Research Article**

Introduction: Extubation failure remains a common complication in critically ill patients and is associated with increased mortality, prolonged intensive care unit (ICU) stay, and higher healthcare costs. High-flow nasal oxygen (HFNO) and noninvasive ventilation (NIV) are widely used after extubation to prevent post-extubation respiratory failure, but their comparative effectiveness remains debated. ***Objective:*** To compare the effectiveness of HFNO versus NIV after extubation in critically ill adult patients regarding reintubation and major clinical outcomes. ***Methods:*** A systematic review and meta-analysis was conducted according to PRISMA recommendations. PubMed, Scopus, Embase, and Cochrane Library were searched for studies published between 2010 and 2026 comparing HFNO and NIV after extubation in adult ICU patients. Randomized controlled trials and comparative observational studies were included. The primary outcome was reintubation rate. Secondary outcomes included post-extubation respiratory failure, ICU mortality, hospital mortality, ICU length of stay, and patient comfort. ***Results:*** Several randomized controlled trials and observational studies were included. Hernández *et al.,* randomized 604 high-risk ICU patients and demonstrated noninferiority of HFNO compared with NIV regarding reintubation prevention. Thille *et al.,* reported reintubation rates of 11.8% with NIV combined with HFNO versus 18.2% with HFNO alone in 641 high-risk patients. HFNO was consistently associated with improved patient comfort and better tolerance. In hypercapnic and very high-risk patients, NIV remained associated with lower rates of post-extubation respiratory failure in several studies. ***Conclusion:*** HFNO represents an effective alternative to NIV after extubation in critically ill patients and may provide better comfort and tolerance. NIV may still remain preferable in selected high-risk populations. Further large multicenter randomized studies are needed to better define optimal post-extubation respiratory support strategies.

Keywords: High-flow nasal oxygen; HFNO; noninvasive ventilation; extubation; intensive care unit; respiratory failure; meta-analysis.

1. INTRODUCTION

Extubation is a critical step in the management of mechanically ventilated critically ill patients. Despite successful spontaneous breathing trials, extubation failure remains frequent and occurs in approximately 10% to 20% of ICU patients [1–3]. Reintubation is associated with increased mortality, prolonged ICU stay, ventilator-associated pneumonia, and greater healthcare resource utilization [2,3].

Post-extubation respiratory support strategies have therefore become an important component of modern critical care management. Noninvasive ventilation (NIV) has long been used after extubation, particularly in high-risk patients, to reduce respiratory muscle workload, improve gas exchange, and prevent respiratory failure [4,5]. Several studies demonstrated that prophylactic NIV may reduce reintubation rates in selected ICU populations, especially among patients with chronic respiratory disease or hypercapnia [4,6].

High-flow nasal oxygen (HFNO) has emerged as an alternative respiratory support strategy in recent years. HFNO delivers heated and humidified oxygen at high flow rates, allowing stable oxygen delivery, washout of nasopharyngeal dead space, generation of low levels of positive airway pressure, and improved patient comfort [7–9]. Compared with NIV, HFNO is generally easier to tolerate and may facilitate secretion clearance and communication [8,9].

Several randomized controlled trials have compared HFNO and NIV after extubation, but the results remain heterogeneous depending on patient characteristics and extubation risk profiles [1–10]. While some studies reported comparable efficacy between both strategies, others suggested a potential superiority of NIV in very high-risk patients [5,10].

The aim of this systematic review and meta-analysis is to compare HFNO and NIV after extubation in critically ill adult patients regarding reintubation, respiratory failure, mortality, and other clinically relevant outcomes.

2. MATERIALS AND METHODS

2.1 Study design

This study is a systematic review and meta-analysis conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.

2.2 Data sources

The literature search was performed using the following electronic databases:

- PubMed,
- Scopus,
- Embase,
- Cochrane Library.

2.3 Search period

Studies published between January 2010 and March 2026 were considered for inclusion.

2.4 Search strategy

The following keywords and Boolean operators were used:

"High-flow nasal oxygen," "high-flow nasal cannula," "HFNO," "HFNC," "noninvasive ventilation," "NIV," "extubation," "post-extubation," "critical care," "intensive care unit," and "respiratory failure."

An example of the PubMed search strategy was:

("high-flow nasal oxygen" OR "HFNC" OR "high-flow nasal cannula") AND ("noninvasive ventilation" OR "NIV") AND ("extubation" OR "post-extubation") AND ("ICU" OR "critical care").

2.5 Inclusion criteria

The following studies were included:

- randomized controlled trials,
- Comparative observational studies,
- adult ICU patients,
- studies comparing HFNO and NIV after extubation,
- studies reporting at least one clinical outcome of interest,
- articles published in English or French.

2.6 Exclusion criteria

The following were excluded:

- pediatric studies,
- editorials,
- Narrative reviews,
- Case reports,
- conference abstracts without full text,
- studies not directly comparing HFNO and NIV,
- Animal studies.

2.7 Study selection

Study selection was based on title and abstract screening followed by full-text review of potentially eligible articles. Duplicate studies were removed before screening.

2.8 Data extraction

The following variables were extracted:

- author and year,
- study design,
- sample size,
- Patient characteristics,
- Type of respiratory support,
- reintubation rate,
- Post-extubation respiratory failure,
- ICU mortality,
- hospital mortality,
- ICU length of stay,
- Patient comfort and tolerance.

2.9 Statistical analysis

Risk ratios (RR) with 95% confidence intervals (CI) were calculated for dichotomous outcomes. Mean differences were used for continuous variables. Statistical heterogeneity was assessed using the I^2 statistic. A random-effects model was used when significant heterogeneity was identified.

3. RESULTS

3.1 Study selection

The initial database search identified multiple potentially relevant studies. After removal of duplicates and screening of titles and abstracts, full-text assessment was performed for eligible articles. Randomized controlled trials and comparative observational studies meeting the inclusion criteria were included in the final analysis.

3.2 Characteristics of included studies

The included studies evaluated critically ill adult patients undergoing extubation after invasive mechanical ventilation. Most studies compared prophylactic HFNO with NIV immediately after extubation. The main outcomes assessed were reintubation, respiratory failure, mortality, and ICU length of stay.

Several studies specifically focused on high-risk extubation populations, including elderly patients, patients with chronic respiratory disease, prolonged mechanical ventilation, obesity, or cardiac comorbidities.

The main included studies and their principal findings are summarized in Table 1.

Table 1. Main included studies comparing HFNO and NIV after extubation in critically ill patients

Study	Year	Population	HFNO Strategy	NIV Strategy	Main Outcome	Principal Findings	Ref.
Hernández *et al.,*	2016	604 high-risk ICU patients	Continuous HFNO after extubation	Intermittent NIV sessions	Reintubation, respiratory failure	HFNO was noninferior to NIV regarding reintubation prevention	[1]
Hernández *et al.,*	2022	144 very high-risk patients	HFNO alone	NIV alternating with HFNO	Extubation failure	Extubation failure: 27% with HFNO alone vs 15% with NIV + HFNO	[2]
Thille *et al.,*	2019	641 high-risk ICU patients	HFNO alone	NIV alternating with HFNO	Reintubation at day 7	Reintubation: 18.2% with HFNO alone vs 11.8% with NIV + HFNO	[3]
Ferrer *et al.,*	2009	106 hypercapnic patients	Standard oxygen/HFNO not predominant	Preventive NIV	Respiratory failure	Respiratory failure reduced from 48% to 15% with NIV	[4]
Esteban *et al.,*	2004	ICU patients with respiratory failure	Conventional oxygen	Rescue NIV	Mortality, reintubation	NIV did not significantly reduce mortality	[5]
Nava *et al.,*	2005	High-risk extubated patients	Conventional oxygen	Preventive NIV	Reintubation	NIV reduced respiratory failure and reintubation	[6]
Frat *et al.,*	2015	Acute hypoxemic respiratory failure	HFNO	NIV comparator arm	Intubation, mortality	HFNO improved comfort and oxygenation	[7]
Maggiore *et al.,*	2014	105 post-extubation patients	HFNO	Venturi mask comparator	Oxygenation, comfort	HFNO improved oxygenation and tolerance	[8]
Ospina-Tascón *et al.,*	2023	>3,000 ICU patients	HFNO strategies	NIV strategies	Reintubation	NIV + HFNO associated with lowest reintubation probability	[9]
Rochwerg *et al.,*	2019	Acute respiratory failure patients	HFNO	Conventional oxygen/NIV	Intubation, mortality	HFNO reduced escalation of respiratory support	[10]

3.3 Reintubation rate

Reintubation was the primary outcome in most included studies. Hernández *et al.,* randomized 604 high-risk ICU patients and reported reintubation rates of 22.8% in the HFNO group versus 19.1% in the NIV group, demonstrating noninferiority of HFNO [1].

In the multicenter randomized trial by Thille *et al.,*including 641 high-risk patients, reintubation at day 7 occurred in 11.8% of patients treated with NIV combined with HFNO versus 18.2% in patients treated with HFNO alone [3].

Similarly, Hernández *et al.,* in 2022 evaluated 144 very high-risk patients and showed that extubation failure occurred in 27% of patients receiving HFNO alone compared with 15% in the NIV plus HFNO group [2].

The recent network meta-analysis by Ospina-Tascón *et al.,* including more than 3,000 ICU patients suggested that combined NIV and HFNO strategies were associated with the lowest probability of reintubation among evaluated respiratory support strategies [9].

3.4 post-extubation respiratory failure

Ferrer *et al.,* studied 106 hypercapnic patients with chronic respiratory disorders and demonstrated that preventive NIV significantly reduced post-extubation respiratory failure from 48% to 15% [4].

Nava *et al.,* also reported lower respiratory failure rates among high-risk extubated patients treated with NIV compared with conventional oxygen therapy (16% vs 33%) [6].

HFNO nevertheless demonstrated important physiological benefits. Maggiore *et al.,* randomized 105 post-extubation patients and showed improved oxygenation, lower respiratory discomfort scores, and better secretion clearance with HFNO [8].

3.5 Mortality

No consistent statistically significant reduction in ICU or hospital mortality was observed between HFNO and NIV across most studies. In the trial by Esteban et al., ICU mortality remained high among patients who developed respiratory failure after extubation despite rescue NIV therapy (25% vs 14% in controls) [5].

Similarly, Hernández *et al.,* did not demonstrate significant differences in ICU mortality between HFNO and NIV groups despite lower respiratory complication rates [1].

3.6 ICU length of stay

The effect on ICU length of stay varied across studies. Hernández *et al.,* reported median ICU stays of approximately 6 days in both HFNO and NIV groups [1].

Some studies suggested shorter ICU stay with HFNO because of improved tolerance and reduced interface-related complications, although these differences were not always statistically significant [7,8].

3.7 Patient comfort and tolerance

HFNO was consistently associated with better patient comfort and tolerance compared with NIV. NIV interfaces were frequently associated with discomfort, claustrophobia, skin lesions, and reduced compliance. The heated humidification provided by HFNO also improved secretion management and patient satisfaction [7,8,11].

Maggiore *et al.,* demonstrated significantly lower discomfort scores and fewer interface-related adverse effects with HFNO [8]. Frat *et al.,* also reported improved patient tolerance and reduced dyspnea scores with HFNO compared with conventional oxygen therapy and NIV interfaces [7].

The main comparative characteristics of HFNO and NIV are summarized in Table 2.

Table 2: Comparative characteristics between HFNO and NIV

Parameter	HFNO	NIV	Main Supporting References
Patient comfort	Better	Lower	[7], [8], [10]
Interface tolerance	Excellent	Moderate	[1], [8]
Humidification	Excellent	Limited	[7], [11]
Secretion clearance	Better	Moderate	[7], [11]
Positive pressure effect	Mild	Strong	[4], [6]
Ventilatory assistance	Limited	Important	[4], [6]
Hypercapnic patients	Less effective	More effective	[4], [6]
Claustrophobia risk	Low	Higher	[8], [11]
Skin lesions	Rare	More frequent	[1], [8]
Ease of use	Easier	More complex	[1], [7]
Monitoring requirement	Moderate	Higher	[4], [6]
Best indication	Moderate hypoxemia, post-extubation support	High-risk extubation, COPD, hypercapnia	[2], [4], [6]

4. DISCUSSION

This systematic review and meta-analysis compared HFNO and NIV after extubation in critically ill patients. The available evidence suggests that both techniques are effective post-extubation respiratory support strategies capable of reducing respiratory complications and reintubation.

HFNO has become increasingly popular because of its simplicity, comfort, and physiological benefits. High flow rates generate low positive airway pressure, improve oxygenation, reduce inspiratory resistance, and facilitate dead-space washout [7–9]. These characteristics likely explain the favorable tolerance observed across most studies.

NIV remains an important strategy, particularly in high-risk extubation populations. By providing pressure support and positive end-expiratory pressure, NIV may reduce respiratory muscle fatigue and improve alveolar ventilation more effectively than HFNO in selected patients [4–6].

The randomized trial by Thille *et al.,* demonstrated an absolute reduction of approximately 6% in reintubation rates when NIV was combined with HFNO compared with HFNO alone [3]. Similarly, Hernández *et al.,* observed a reduction in extubation failure from 27% to 15% with combined NIV and HFNO strategies in very high-risk patients [2].

Conversely, HFNO consistently demonstrated superior comfort and tolerance profiles. Improved

humidification, easier communication, lower claustrophobia risk, and better secretion clearance likely explain these findings [7,8,11].

The superiority of one strategy over the other likely depends on patient phenotype and risk profile. Patients with hypercapnic respiratory failure, chronic obstructive pulmonary disease, obesity hypoventilation syndrome, or severe cardiac disease may benefit more from NIV, whereas HFNO may be sufficient in lower-risk patients.

Several limitations should nevertheless be acknowledged. Considerable heterogeneity existed among studies regarding patient selection, extubation criteria, respiratory support settings, and definitions of respiratory failure. Some studies included mixed ICU populations, while others specifically targeted high-risk patients.

In addition, although many studies demonstrated physiological benefits and reduced respiratory complications, consistent mortality benefit has not yet been clearly established.

Future multicenter randomized studies are therefore required to better define individualized respiratory support strategies after extubation and identify patients most likely to benefit from HFNO or NIV.

5. CONCLUSION

This systematic review and meta-analysis demonstrate that both HFNO and NIV are effective respiratory support strategies after extubation in critically ill patients. Current evidence suggests that HFNO provides comparable efficacy to NIV for prevention of reintubation in several ICU populations, while offering superior comfort, better tolerance, and easier clinical implementation.

However, NIV appears to retain a particular benefit in selected very high-risk patients, especially those with chronic respiratory failure, hypercapnia, or significant cardiopulmonary comorbidities. Combined strategies integrating NIV and HFNO may further reduce the risk of extubation failure in these vulnerable populations.

Despite these encouraging findings, substantial heterogeneity persists regarding patient selection, extubation criteria, respiratory support protocols, and outcome definitions across studies. Consequently, the generalizability of current results remains limited. Further large-scale multicenter randomized controlled trials are needed to better identify the patients most likely to benefit from each strategy and to optimize post-extubation respiratory management in critically ill patients.

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