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# Post extubation non-invasive respiratory support effect on hospital mortality and length of stay: A systematic review

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## Abstract

**Background**: It is yet unknown how noninvasive ventilation affects the prevention and management of post-extubation respiratory failure. Our goal in doing this study was to present a current evaluation of post-extubation NIV effect on the rate of mortality, ventilator-associated pneumonia, pain, time spent re-intubating, and duration of stay in the hospital and ICU.

**Method**: This study was written using the PRISMA standards. To find, evaluate, and incorporate papers in the online databases from 2017 to 2022, we carried out a methodical search of the literature using Web of Science, Embase, Cochrane, Scopus, and PubMed. We also perused the necessary papers' reference lists. Articles written in the English language were considered.

**Result**: The mean age of the 1,014 patients who participated in the 7 randomized controlled trials varied from 61 to 77.9 years. Six studies employed NIV as a preventive measure, and one study used it as a therapy. The ICU served as the site of all the research.

**Conclusion**: In ICU patients, preventive NIV lower the post-extubation respiratory failure incidence.

**Keywords:** Non-Invasive Ventilation; Extubation Failure; Mechanical Ventilation; Respiratory Support; In Hospital Mortality; Reintubation.

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## 1. Introduction

When the acute phase of the disease has cleared and specific criteria are satisfied, extubation is performed in mechanically ventilated patients recovering from respiratory failure; however, this procedure is not always successful (1,2). About 15% of cases require reintubation, which is linked to a higher risk of complications and mortality (3,4). In such a situation, it is imperative to treat post-extubation hypoxemia, and oxygen treatment is frequently used to enhance oxygen supply (5).

In addition, invasive mechanical ventilation (IMV) for long time, ventilator-associated pneumonia (VAP), delirium and critical weakness, are common outcomes of post-extubation respiratory failure (PERF) (6). Finally, the inability to successfully extubate a patient results in higher resource usage, expenses, and discomfort (7).

In order to prevent re-intubation due to post-extubation failure, noninvasive invasive ventilation (NIV) techniques such as continuous positive airway pressure, bi-level positive airway pressure and high-flow nasal oxygen (HFNO) have been proposed (8). These techniques maintain adequate breathing pattern, gas exchange, tracheobronchial secretion clearance and inspiratory effort.

In high-risk patients, the most recent guidelines suggest using NIV to prevent PERF (9). The use of HFNO, as opposed to traditional oxygen therapy, is advised by the 2022 European Respiratory Society guidelines for low-risk ICU patients (10).

In this study, we aimed to provide a current assessment of NIV effects following extubation on the VAP rate, mortality in the hospital and ICU, pain, re-intubation time, and length of stay in the hospital and ICU.

## 2. Method

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was followed in the writing of this article. We conducted a systematic search of the literature to identify, screen, and include articles in the online databases from 2017 to 2022: PubMed, Embase, Cochrane, Scopus, and Web of Science were the online databases searched. We also looked through the reference lists of the relevant articles, as well as relevant reviews and guidelines. Only English-language articles were taken into consideration.

Four researchers chose relevant and irrelevant papers by separately examining the titles and abstracts of the selected papers. Full-text retrieval was used to examine every citation that might have been pertinent. Every study that satisfied the subsequent standards was incorporated into the analysis: Adult ICU patients; RCTs included one kind of NIV in randomization; PERF incidence, which is defined as the need for re-intubation; patient discomfort; VAP; re-intubation time; hospital mortality; ICU stay. Since there isn't a consensus definition for extubation failure time, we included all research that look into whether re-intubation with an endotracheal tube is necessary at any stage of the hospital stay.

Five researchers independently reviewed and evaluated each of the included papers after determining which ones met the inclusion criteria. Any disagreements about the choice of study and data extraction were discussed with the corresponding author. Two investigators independently gathered the following data: citation, year, inclusion criteria, exclusion criteria, sample size, age of patients, NIV modality, main findings and conclusion.

## 3. Result

We included 7 randomized controlled trials (Fig 1) with a total of 1,014 patients, participant mean age ranged from 61 to 77.9 years. NIV was used as prophylactic in 6 studies (11–16), and treatment in one study (17) (Table 1). All of studies were conducted in ICU. According to Jing et al., 2019 (11), before extubation, ABGs and vital signs were similar in both groups. Three hours after extubation, the pH in NIV group was lower than in HFNC group. Twenty-four hours after extubation, the mean arterial pressure and pH of the patients in NIV group were lower than in HFNC group. Forty-eight hours after extubation, no significant changes were found. Patients in HFNC group had more comfort ratings, and fewer of them underwent a bronchoscopy within 48 hours of being extubated to control secretion. According to the Maggiore et al., 2022 study, 13% of high-flow group patients and 11% of VenturiMask group required re-intubation 72 hours after the intubation criteria was assessed.

According to Sahin et al., 2018 (13) study, the HFO group's mean hospital stay was much shorter—6.5 days—than that of the mask O2 group, which showed a mean stay of 6.9 days. Patients with significantly lower $PaCO_2$ values and significantly higher PaO2 and SpO2 values were those who got HFO after the fourth, 24th, and 36th hours. Postoperative FVC is improved in patients who receive HFO during the postoperative phase. Furthermore, dyspnea and comfort scores were noticeably better in patients who received HFO on both the first and second postoperative postoperative days.

Tan et al., 2020 (14) study found that, with a rate of 28.6% for NIV group and a rate of 22.7% for HFNC group, the treatment failure rate was much lower than 9%. A study of the reasons why treatments failed revealed that HFNC group had considerably lower treatment intolerance compared to NIV group, and a risk difference of - 50.0%. An hour after extubation, both groups' mean respiratory rates were higher than they were at baseline. 2 days after extubation, there was no statistically significant difference in the rates of respiration of either group (Table 2).

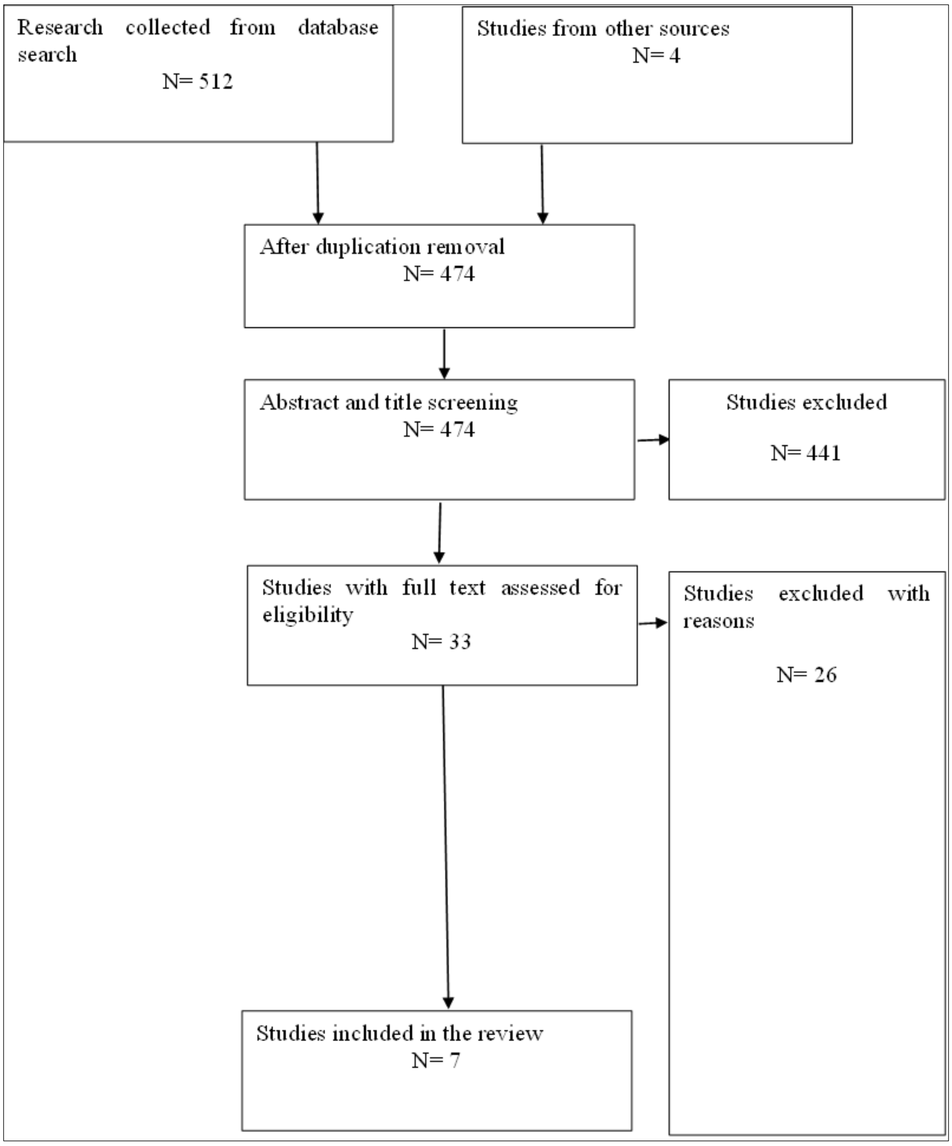


**Figure 1** PRISMA consort chart of selection process

**Table 1** Characteristics of the included studies

| Citation | Sample size | Inclusion criteria | Indication | Setting | Exclusion criteria | Mean age of the population (Years) |
|---|---|---|---|---|---|---|
| Jing et al., 2019 (11) | 42 | Adult with hypercapnia and COPD exacerbation | Prophylactic | ICU | Severe dysfunction of other organs; Tracheostomy; hemodynamic instability; burns or facial injury, uncooperative; deformities; copious secretions; rhinitis weak; cough | 75.5 |
| Maggiore et al., 2022 (12) | 492 | Adult; PaO2/FiO2 < 300; IMV > 48hrs | Prophylactic | ICU | Pregnancy; Tracheostomy; planned use of NIV after extubation | 62.5 |
| Matsuda et al., 2020 (17) | 69 | Adult; PaO2/FiO2 < 300; IMV >24hrs | Treatment | ICU | Do-not intubate order; Tracheostomy; Pneumothorax; pregnancy | 71.4 |
| Sahin et al., 2018 (13) | 100 | Adult; cardiopulmonary bypass; BMI > 30 | Prophylactic | ICU | tracheostomy, Hemodynamic instability, obstructive sleep apnea, low cardiac output, active pulmonary disease, emergency surgery | 61 |
| Tan et al., 2020 (14) | 96 | Adult; hyoercapnia; COPD exacerbation; bronchopulmonary infection | Prophylactic | ICU | Contraindications to NIV; weak cough; palliative care; kidney failure | 69.9 |
| Cho et al., 2020 (15) | 60 | Adult; IMV > 12hrs | Prophylactic | ICU | Not available | 77.9 |
| Fernandez et al., 2017 (16) | 155 | Adult; IMV > 12hrs | Prophylactic | ICU | Tracheostomy; hypercapnia during SBT; ; do-Not Reintubate order; | 68.5 |

**Table 2** Main findings and conclusion

| **Citation** | **Main findings** | **Conclusion** |
|---|---|---|
| 54 Jing et al., 2019 (11) | Randomly chosen COPD patients who had prolonged hypercapnia at extubation were given either NIV or HFNC. Each group comprised twenty patients who were enrolled for analysis concerning primary outcomes. Before extubation, ABGs and vital signs were comparable among groups. NIV group pH was lower than HFNC group three hours after extubation. The mean arterial pressure and pH of the patients in NIV group were lower than those in HFNC group 24 hours after extubation. 2 days after extubation, no discernible changes were discovered. Comfort ratings were higher and fewer patients in HFNC group had a bronchoscopy within 48 hours of being extubated in order to manage secretion. | Regarding vital signs and ABGs, HFNC is a viable substitute for NIV in the weaning of hypercapnic COPD patients. Additionally, HFNC enhanced patient comfort and secretion clearance. |
| 26 Maggiore et al., 2022 (12) | 13% of patients in the high-flow group and 11% of patients in the VenturiMask group needed reintubation at 72 hours following the assessment of the intubation criteria. In high-flow group, the reintubation rate was 21%, whereas in VenturiMask group, it was 23% after 28 days. When compared to the VenturiMask group, the high-flow group required much less noninvasive rescue breathing after 3 days and 28 days. | Following extubation, VenturiMask group and high-flow oxygen did not significantly differ in their reintubation rate. Less frequently, high-flow oxygen resulted in the need for noninvasive rescue ventilation. |
| 24 Matsuda et al., 2020 (17) | There was no significant difference in the re-intubation rate within 7 days between the HFNC and nebulizer groups. | Within seven days, the re-intubation rate may not be decreased by HFNC in comparison to a humidifier. |
| 70 Sahin et al., 2018 (13) | The mask O2 group experienced a mean hospital stay of 6.9 days, while the HFO group saw a considerably shorter stay of 6.5 days. Patients who received HFO after the fourth, 24th, and 36th hours had considerably higher PaO2 and SpO2 values and significantly lower PaCO2 values. Patients that get HFO during the postoperative course experience improved postoperative FVC. In addition, patients who received HFO on both the first and second postoperative postoperative days had significantly improved dyspnea and comfort levels. | When compared to mask O2, HFO after CPB in obese individuals reduced the incidence of atelectasis, reintubation, and death while increasing postoperative SpO2, PaCO2, and PaO2. |
| 51 Tan et al., 2020 (14) | Treatment failure rate was considerably lower than 9%, with HFNC group experiencing a rate of 22.7% and NIV group experiencing a rate of 28.6%. Treatment intolerance was shown to be much lower in HFNC group compared to NIV group, with a risk difference of - 50.0%, according to an analysis of the reasons why treatments failed. The respiratory rates mean of both groups were higher an hour after extubation than they were at baseline. HFNC group's respiratory rate had reverted to baseline 24 hours following extubation, however the NIV group's respiratory rate remained higher than baseline. The respiration rate in both groups were not statistically different from 2 days after extubation. | When using HFNC following extubation in COPD patients with HRF receiving invasive ventilation, the rates of treatment failure were not higher than when using NIV. NIV was less comfortable and had less tolerance than HFNC. |
| 44 Cho et al., 2020 (15) | 29 people got COT, while 31 people got HFNC. The rates of re-intubation after 72 hours were the same for all groups. Patients who got COT required less time for re-intubation than patients who received HFNC, although this difference was not statistically significant. There was no difference in ICU duration across the groups. | HFNC did not lower the likelihood of reintubation within 3 days among patients at high risk, when compared to COT. |
| 46 Fernandez et al., 2017 (16) | At enrollment, the groups were similar, and every patient could tolerate 24-hour HFNC. Twenty percent of HFNC patients and twenty-seven percent of conventional patients suffered RF post-extubation. In 11% of HFNC patients and 16% of conventional patients, re-intubation | Regarding the possible advantage of HFNC over traditional oxygen in preventing RF in non- |

| | | |
|---|---|---|
| | was required. Mortality or length of stay in the ICU or hospital did not differ. According to logistic regression models, postextubation RF may be independently correlated with HFNC and cancer. | hypercapnic patients at high extubation failure risk, this study is equivocal. |

## 4. Discussion

Our goal in this study was to present an updated evaluation of the impact of post-extubation NIV use on the incidence of VAP, hospital and ICU mortality, pain, time to re-intubation, and duration of stay in the hospital and ICU.

We found that in hypercapnic COPD patients weaning, HFNC is a good alternative to NIV; after extubation, patients treated with VenturiMask or high-flow oxygen did not significantly differ in their re-intubation rate; HFNC may not reduce the re-intubation rate more than a humidifier; HFO following CPB decreased the risk of atelectasis, re-intubation, and death in obese patients as compared to mask O2; NIV was less comfortable and had lower tolerance than HFNC.

In contrast to VenturiMask oxygen therapy, the use of high-flow nasal oxygen did not reduce the rate of extubation failure in patients who developed hypoxemia following scheduled extubation in the ICU, according to a 2022 study by Maggiore et al. There was consistently no discernible impact on the duration of hospital stays and intensive care, as well as all-cause death. However, rescue noninvasive ventilation was more frequently needed for patients in the VenturiMask group. High-flow nasal oxygen is becoming more and more popular. It uses a specially constructed nasal cannula to deliver an air/oxygen combination that is actively conditioned by a heated humidifier at a rate of up to 60 L/min (18,19). The system produces a flow-dependent upper airways washout effect that enhances CO2 clearance in the anatomical dead space (20) and optimizes tolerance through full gas conditioning and the comfortable interface (21,22). It also matches patients' peak inspiratory flow, which ensures accurate delivery of the set FiO2 (23,24). Furthermore, a nasopharyngeal flow-dependent positive pressure is created by the air entrainment effect caused by a patient expiring against the continuous gas flow; values as high as 5.6 cm H2O are attained at the conclusion of expiration and when the mouth is closed (25,26).

In COPD patients who had just been extubated due to HRF, HFNC and NIV perform good in prevention of re-intubation and post-extubation treatment failure, per the Cho et al., 2020 study. HFNC was well-tolerated and more comfortable than NIV. Compared to NIV, HFNC was linked with a considerably decreased nasofacial skin breakdown and fewer airway care interventions. For COPD patients who have been extubated following severe HRF, HFNC seems to be a useful respiratory support technique.

In COPD patients with HRF, the use of HFNC is becoming more recommended. Bräunlich et al. found that HFNC raised pH and decreased carbon dioxide by in 38 patients with an acute COPD exacerbation and a pH $<$7.38 (27). The pH of the patients improved and their respiratory rate reduced with HFNC treatment in a previous research involving patients with moderate HRF who were intolerant to NIV (28). The HFNC non-response rate was only 13.3%. Similar fatality rates and tracheal intubation were seen between NIV and HFNC for COPD patients with acute moderate HRF, although HFNC was better tolerated, according to two cohort studies (29,30).

A recent meta-analysis demonstrating that NIV did not increase hospital mortality but did, generally, lower the rate of re-intubation when used to avoid PERF when compared to COT (31).

Our findings regarding HFNO are consistent with the recommendations made in the 2022 ERS guidelines, which stipulate that in patients at low and high risk of extubation failure, prophylactic HFNO should be performed (10).

### *List of abbreviation*

- BMI, body mass index
- COPD, chronic obstructive pulmonary disease
- COT, conventional oxygen therapy
- CPB, cardiopulmonary bypass
- HFNO, high-flow nasal oxygen
- HFNC, high-flow nasal cannula
- HRF, hypercapnic respiratory failure
- ICU, intensive care unit
- IMV, invasive mechanical ventilation
- NIV, noninvasive ventilation

- PaO2/FiO2, arterial partial pressure of oxygen/inspiratory oxygen concentration
- PERF, post-extubation respiratory failure
- SBT, spontaneous breathing trial
- VAP, ventilator-associated pneumonia

## 5. Conclusion

We conclude that, for hypercapnic COPD patients weaning, HFNC is a good substitute for NIV; following CPB, HFO reduced the risk of atelectasis, re-intubation, and death in obese patients as compared to mask O2; following extubation, patients treated with VenturiMask or high-flow oxygen did not significantly differ in their re-intubation rate; and HFNC may not reduce the re-intubation rate more than a humidifier.

## Compliance with ethical standards

*Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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