







Noninvasive respiratory support after extubation: a systematic review and network meta-analysis

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Noninvasive respiratory support may be useful for preventing, but not treating, post-extubation respiratory failure in ICU patients. Prophylactic NIV and HFNO decreased the rate of extubation failure in high-risk and post-surgical patients, respectively. <https://bit.ly/3uSjXZG>

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Abstract

Background The effect of noninvasive respiratory support (NRS), including high-flow nasal oxygen, bi-level positive airway pressure and continuous positive airway pressure (noninvasive ventilation (NIV)), for preventing and treating post-extubation respiratory failure is still unclear. Our objective was to assess the effects of NRS on post-extubation respiratory failure, defined as re-intubation secondary to post-extubation respiratory failure (primary outcome). Secondary outcomes included the incidence of ventilator-associated pneumonia (VAP), discomfort, intensive care unit (ICU) and hospital mortality, ICU and hospital length of stay (LOS), and time to re-intubation. Subgroup analyses considered “prophylactic” *versus* “therapeutic” NRS application and subpopulations (high-risk, low-risk, post-surgical and hypoxaemic patients).

Methods We undertook a systematic review and network meta-analysis (Research Registry: [reviewregistry1435](https://www.researchregistry.com/registry/1435)). PubMed, Embase, CENTRAL, Scopus and Web of Science were searched (from inception until 22 June 2022). Randomised controlled trials (RCTs) investigating the use of NRS after extubation in ICU adult patients were included.

Results 32 RCTs entered the quantitative analysis (5063 patients). Compared with conventional oxygen therapy, NRS overall reduced re-intubations and VAP (moderate certainty). NIV decreased hospital mortality (moderate certainty), and hospital and ICU LOS (low and very low certainty, respectively), and increased discomfort (moderate certainty). Prophylactic NRS did not prevent extubation failure in low-risk or hypoxaemic patients.

Conclusion Prophylactic NRS may reduce the rate of post-extubation respiratory failure in ICU patients.

Introduction

Extubation failure, as defined by re-intubation secondary to post-extubation respiratory failure in a time interval varying from 48 h to 7 days among studies [1], has been described to occur in up to 23.5% of patients [2–6]. The incidence is even higher in high-risk patients, such as those aged >65 years or those affected by chronic cardiac disease, lung disease or other severe pulmonary disorders [6–8]. For surgical patients, the reported incidence of extubation failure varies between 5% and 10%, and depends on the patient’s underlying comorbidities, type of surgery and anaesthesia, and intra-operative settings of mechanical ventilation, which overall define the predictive post-operative risk profile of each patient [9–11].



Several studies showed that post-extubation respiratory failure affects patient prognosis [3, 4, 6, 12]. In fact, re-intubated patients are characterised by increased mortality (up to 50%), even after adjusting for clinical severity, suggesting a direct adverse effect of re-intubation on patient outcome [5, 6]. Furthermore, post-extubation respiratory failure usually leads to prolonged invasive mechanical ventilation and to a higher risk of ventilator-associated pneumonia (VAP), critical weakness and delirium [13–15]. Lastly, extubation failure increases resource utilisation and costs, and patient discomfort [13, 16].

Forms of noninvasive respiratory support (NRS), including high-flow nasal oxygen (HFNO), continuous positive airway pressure (CPAP) and bi-level positive airway pressure, commonly referred to as noninvasive ventilation (NIV) [5, 17, 18, 19], have been proposed for avoiding re-intubation secondary to post-extubation failure, by maintaining adequate gas exchange, breathing pattern, inspiratory effort and tracheobronchial secretion clearance [10–26].

NRS has been used for prevention (“prophylactic” NRS) or treatment (“therapeutic” NRS) of post-extubation respiratory failure [5, 18, 19, 20, 27]. The most recent 2017 European Respiratory Society (ERS)/American Thoracic Society (ATS) clinical practice guidelines recommend the use of NIV for preventing post-extubation respiratory failure in high-risk patients (moderate certainty of evidence), but not in low-risk patients (conditional recommendation, very low certainty of evidence) [5]. The 2022 ERS guidelines recommend the use of HFNO, over conventional oxygen therapy (COT), in surgical and nonsurgical patients at low risk (conditional recommendation, low certainty of evidence) [18].

The purpose of this systematic review and network meta-analysis of randomised controlled trials (RCTs) is to provide an updated assessment of the effects of post-extubation NRS application on the rate of extubation failure (primary outcome), and on the incidence of VAP, patient discomfort, ICU and hospital mortality, ICU and hospital length of stay (LOS), and time to re-intubation (secondary outcomes). Additional subgroup analyses were planned for investigating, separately, the effect of “prophylactic” and “therapeutic” NRS application on the rate of extubation failure and the impact of NRS on predefined ICU subpopulations (high-risk, low-risk, post-surgical and hypoxaemic patients).

Methods

This article was written following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement extension for network meta-analysis [28–30]. The PRISMA checklist is available as supplementary table S1. A review protocol was written before conducting this study and prospectively registered at Research Registry (reviewregistry1435) on 22 June 2022.

Search strategy

We performed a systematic research of the medical literature for the identification, screening and inclusion of articles in the following databases from inception until 20 June 2022: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus and Web of Science. To take into account possible publication biases, ongoing trials at ClinicalTrials.gov were also retrieved. In addition, backward snowballing (*i.e.* checking the reference lists of included studies, and of pertinent reviews and guidelines) was employed. Abstracts and conference proceedings were excluded. Further detailed information about the search strategy is available in supplementary table S2. No restrictions on language and year of publication were applied.

Study selection

Two researchers (A. Boscolo and T. Pettenuzzo) independently screened titles and abstracts of the identified papers to select relevant and nonrelevant papers. Each potentially relevant citation was reviewed with full-text retrieval. All studies meeting the following PICOS (Population, Intervention, Control, Outcomes, Study) criteria were included in the analysis: P) adult ICU patients (≥ 18 years old); I) randomisation for COT or one type of NRS (*i.e.* CPAP, NIV or HFNO); C) randomisation for COT or NRS, different from the one tested as intervention; O) incidence of post-extubation respiratory failure, defined as re-intubation (primary outcome) [1] and/or VAP, patient discomfort, ICU and hospital mortality, ICU and hospital LOS, and time to re-intubation (secondary outcomes); S) only RCTs. Note that CPAP was classified as NIV in the analysis.

Trials were excluded when focused on patients developing self-extubation, requiring palliative care, or when NRS had been used before the first cycle of invasive mechanical ventilation or as a “weaning” approach to allow early extubation after a failed spontaneous breathing trial (SBT) [31, 32].

With regard to the primary outcome, in the absence of a clearly accepted definition of extubation failure timing, we included all studies investigating the need for re-intubation, using an endotracheal tube, at any point during the hospital stay [27].

Moreover, we excluded from the quantitative analysis all studies investigating combinations of NRS devices administered in sequence, as reported by THILLE *et al.* [33].

Data extraction

After identifying those studies meeting the inclusion criteria, three researchers (M. Zatta, A. De Cassai and A. Bruni) independently reviewed and assessed each of the included studies. Any disagreement on both study selection and data extraction was resolved by discussion with a further author (F. Zarantonello) or by contacting the corresponding author. The following information was independently collected by two investigators (A. De Cassai and A. Bruni): first author, year of study, eligibility criteria, exclusion criteria, total number of ICU patients per group and subgroups (classified as high-risk, low-risk, post-surgical and hypoxaemic), patients' age and gender, "prophylactic" or "therapeutic" NRS modality, and primary and secondary outcomes.

Quality assessment and certainty of evidence assessment

Two researchers (M. Zatta and C. Pretto) independently evaluated the quality of included RCTs by using the Cochrane Collaboration's Risk of Bias 2 tool [34]. The study-level risk of bias was expressed on a three-grade scale ("low risk of bias", "high risk of bias" or "some concerns"). Disagreements were resolved by discussion with a third researcher (F. Geraldini). The GRADE (Grading of Recommendations Assessment, Development and Evaluations) approach was used to assess the certainty of evidence related to the outcomes [35]. GRADE addresses the domains of risk of bias, inconsistency, indirectness, publication bias, intransitivity, incoherence and imprecision. Imprecision for each comparison was only incorporated at the network level, not at the level of the direct or indirect estimate. A minimally contextualised approach, considering COT as reference, was applied to evaluate the magnitude of the intervention effect [36, 37].

Statistical methods

Meta-analysis of data was performed using R version 4.1 "Camp Pontanezen" (R Foundation for Statistical Computing, Vienna, Austria) and the package "netmeta". A random effects model was used for all outcomes.

The primary outcome, *i.e.* extubation failure, as defined by need for re-intubation consequent to post-extubation respiratory failure, was investigated in the overall population and through subgroup analyses (*i.e.* "prophylactic" versus "therapeutic" NRS and in pre-registered subpopulations (see Subgroup analyses section)). The secondary outcomes (VAP, patient discomfort, ICU and hospital mortality, ICU and hospital LOS (days), and time to re-intubation (days)) were investigated only in the overall population. The treatment effect for continuous outcomes was expressed as mean difference with 95% confidence interval. The treatment effect for dichotomous outcomes was expressed as odds ratio with 95% confidence interval. A ranking among treatments was performed based on the frequentist analogue of the surface under the cumulative ranking curve (SUCRA). SUCRA represents the overall ranking of each treatment for the specified outcome and ranges from 0 (minimum) to 1 (maximum) [38, 39]. Wherever necessary, we converted reported median and interquartile range to estimated mean and standard deviation using the method of Hozo *et al.* [40] or Luo *et al.* [41] as appropriate. No continuity correction was applied in case of zero events.

Subgroup analyses

Additional pre-registered analyses were performed according to the following subgroups: 1) "prophylactic" (applied immediately after extubation) versus "therapeutic" support (defined as NRS application only after evidence of respiratory deterioration) [27], and 2) ICU high-risk and low-risk patients, post-surgical patients (undergoing NRS exclusively in the ICU), and hypoxaemic patients.

Patients were classified at high risk when aged >65 years or affected by heart disease, respiratory disease or other severe pulmonary disorders [6–8], otherwise they were classified at low risk of post-extubation respiratory failure.

Patients were defined as hypoxaemic when the arterial oxygen tension/inspiratory oxygen fraction (P_{aO_2}/F_{iO_2}) ratio at the end of the SBT was <300 mmHg [42].

Regarding ICU post-surgical patients, we excluded studies enrolling patients undergoing NRS in the operating room, in the post-anaesthesia care unit or in medical/surgical wards.

Inconsistency and heterogeneity analysis

For assessment of study heterogeneity, the Chi-squared test and I^2 -statistic were used. Heterogeneity was defined as low for $I^2 < 25\%$, moderate for $I^2 = 25\text{--}50\%$ and high for $I^2 > 50\%$ [43]. Within-design heterogeneity and between-design inconsistency were evaluated using τ^2 .

Results

Study selection, characteristics and risk of bias assessment

Bibliographic search results are shown in the study flowchart (figure 1). The initial screening found 14 598 studies. Of those, 33 (5711 patients) entered the qualitative analysis and 32 (5063 patients) entered the quantitative analysis. Characteristics of the included trials are available for consultation as supplementary table S3 and supplementary figure S1 [8, 33, 24, 26, 42, 44–71].

Overall, 12 (36%) studies (1955 patients (34%)) compared HFNO to COT [24, 26, 42, 44–49, 69–71], while five (15%) studies (1104 patients (19%)) compared HFNO to NIV [50–54]. 15 (46%) studies (2004 patients (35%)) investigated NIV *versus* COT [8, 55–68] (figure 1). Finally, one (3%) study (648 patients (11%)) comparing HFNO to NIV plus HFNO (administered in sequence) was excluded from the quantitative analysis for limited comparability [33].

Risk of bias assessments are shown in figure 2 and supplementary table S4. The majority of trials were considered at low or moderate risk of bias. Only four studies were considered at high risk of bias due to questionable randomisation processes [56, 63, 66, 69].

Primary outcome in the overall population

As shown in figure 3, in the overall population, both HFNO (OR 0.60, 95% CI 0.43–0.84; $p=0.003$) and NIV (OR 0.61, 95% CI 0.46–0.81; $p<0.001$) reduced the incidence of extubation failure compared with COT (moderate certainty) (table 1, and supplementary tables S5 and S6). Moreover, no differences were found between HFNO *versus* NIV ($p=0.844$). Heterogeneity was moderate ($I^2=36\%$).

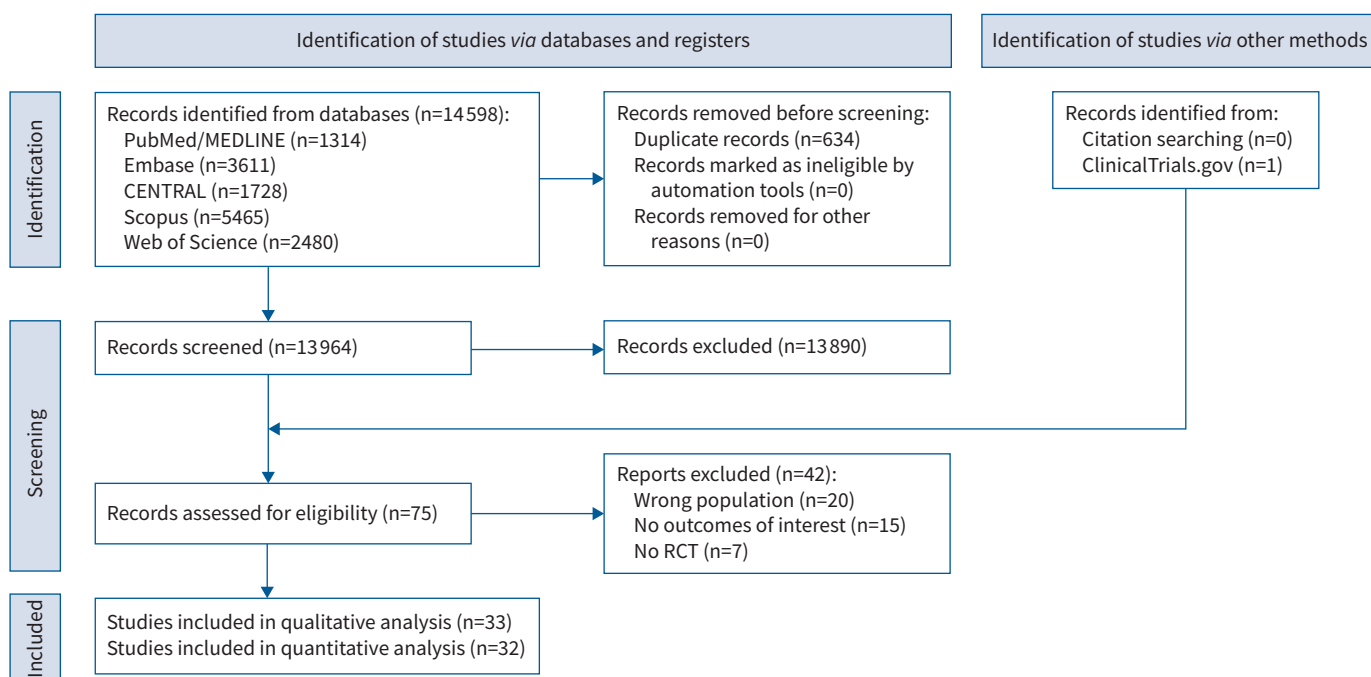


FIGURE 1 PRISMA flowchart. RCT: randomised controlled trial.

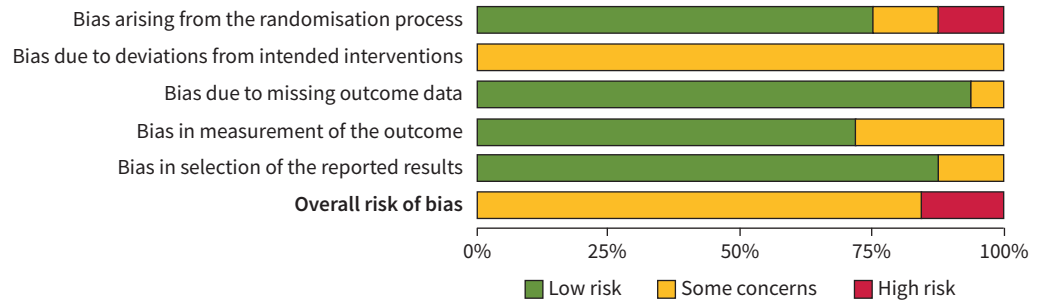


FIGURE 2 Risk of bias assessments.

Secondary outcomes in the overall population

Incidence of VAP

Both HFNO (OR 0.36, 95% CI 0.18–0.71; p=0.003) and NIV (OR 0.49, 95% CI 0.34–0.73; p<0.001) were associated to a lower rate of VAP (moderate certainty) compared with COT (table 1, and supplementary tables S5 and S6). Heterogeneity was very low (I²=0%).

Discomfort

NIV (OR 13.14, 95% CI 5.94,29.04; p<0.001, moderate certainty), but not HFNO, was associated with a higher patient discomfort compared with COT (table 1, and supplementary tables S5 and S6). Heterogeneity was moderate (I²=49%).

ICU and hospital mortality

Neither HFNO nor NIV affected ICU mortality compared with COT. NIV, but not HFNO, reduced hospital mortality (OR 0.64, 95% CI 0.47–0.87; p=0.004, moderate certainty) compared with COT (table 1, and supplementary tables S5 and S6). Heterogeneity was low (I²=6%).

ICU and hospital LOS

NIV shortened ICU LOS (days) (MD -0.72, 95% CI -1.44–0.00; p=0.049, very low certainty), despite a high heterogeneity (I²=87%), compared with COT. HFNO did not show any benefit (table 1, and supplementary tables S5 and S6).

Time to re-intubation

Neither HFNO nor NIV affected the time to re-intubation (days) compared with COT. Heterogeneity was very high (I²=89%) (table 1, and supplementary tables S5 and S6).

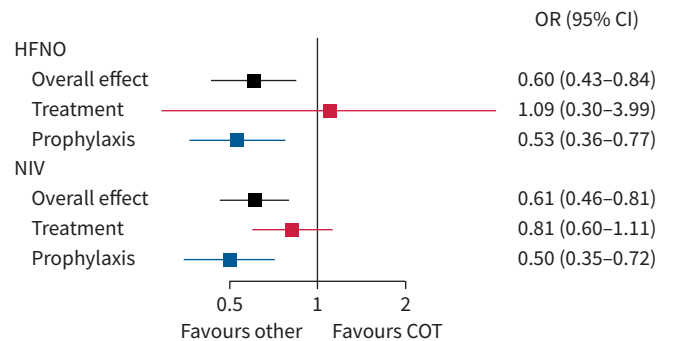


FIGURE 3 Impact of overall, “therapeutic” and “prophylactic” noninvasive respiratory support on primary outcome (re-intubation). COT: conventional oxygen therapy; HFNO: high-flow nasal oxygen; NIV: noninvasive ventilation.

TABLE 1 Network estimates evaluating the impact of the interventions on primary and secondary outcomes in the overall population

Comparison	MD or OR (95% CI)	p-value	I ² (%)	τ ²	K	GRADE [#]	Classification of intervention [¶]
Re-intubation			36	0.120			
HFNO versus COT	0.60 (0.43–0.84)	0.003			11	Moderate ^a	Large beneficial effect
NIV versus COT	0.61 (0.46–0.81)	<0.001			15	Moderate ^a	Large beneficial effect
NIV versus HFNO	0.98 (0.69–1.40)	0.844			5	Moderate ^b	
VAP			0	0			
HFNO versus COT	0.36 (0.18–0.71)	0.003			3	Moderate ^a	Large beneficial effect
NIV versus COT	0.49 (0.34–0.73)	<0.001			7	Moderate ^a	Large beneficial effect
NIV versus HFNO	0.74 (0.39–1.38)	0.855			1	Moderate ^b	
Discomfort			49	0.493			
HFNO versus COT	2.60 (0.79–8.60)	0.117			7	Low ^{a,b}	Large harmful effect
NIV versus COT	13.14 (5.94–29.04)	<0.001			1	Moderate ^a	Large harmful effect
NIV versus HFNO	0.20 (0.06–0.62)	0.050			1	High	
ICU mortality			6	0.017			
HFNO versus COT	0.81 (0.44–1.48)	0.489			5	Low ^{a,b}	Small beneficial effect
NIV versus COT	0.64 (0.39–1.05)	0.075			8	Moderate ^a	Large beneficial effect
NIV versus HFNO	1.26 (0.63–2.52)	0.834			1	Low ^{a,b}	
Hospital mortality			6	0.017			
HFNO versus COT	0.86 (0.62–1.18)	0.431			5	Moderate ^a	Small beneficial effect
NIV versus COT	0.64 (0.47–0.87)	0.004			11	Moderate ^a	Large beneficial effect
NIV versus HFNO	1.35 (0.97–1.86)	0.194			4	Moderate ^b	
ICU length of stay			87	1.048			
HFNO versus COT	−0.12 (−0.85–0.61)	0.741			9	Very low ^{a,b,c,d}	Trivial beneficial effect
NIV versus COT	−0.72 (−1.44–0.00)	0.049			14	Very low ^{a,c,d}	Small beneficial effect
NIV versus HFNO	0.60 (−0.33–1.53)	0.320			4	Very low ^{b,c,d}	
Hospital length of stay			86	2.230			
HFNO versus COT	−0.04 (−1.27–1.18)	0.264			8	Very low ^{a,b,c}	Trivial beneficial effect
NIV versus COT	−2.38 (−3.69–−1.07)	<0.001			10	Low ^{a,c}	Large beneficial effect
NIV versus HFNO	2.34 (0.80–3.88)	0.189			3	Very low ^{a,b,c}	
Time to re-intubation			89	87.485			
HFNO versus COT	2.99 (−8.13–14.10)	0.564			3	Very low ^{a,b,c}	Trivial harmful effect
NIV versus COT	9.17 (−1.06–19.40)	0.105			4	Very low ^{a,b,c}	Small harmful effect
NIV versus HFNO	−6.18 (−18.86–6.5)	0.371			1	Very low ^{a,b,c}	

MD: mean difference; OR: odds ratio; τ² and I²: loop heterogeneity; K: number of studies providing direct evidence; GRADE: Grading of Recommendations Assessment, Development and Evaluations; HFNO: high-flow nasal oxygen; COT: conventional oxygen therapy; NIV: noninvasive ventilation; VAP: ventilator-associated pneumonia; ICU: intensive care unit. #: GRADE certainty of evidence: ^a: lowered one level for risk of bias; ^b: lowered one level for imprecision as confidence intervals do not allow excluding harm; ^c: lowered one level for inconsistency; ^d: lowered one level for incoherence. ¶: for dichotomous outcome variables, large intervention effects were considered for OR >1.3 or <0.7, moderate intervention effects for 1.2<OR≤1.3 or 0.7≤OR<0.8, small intervention effects for 1.1<OR≤1.2 or 0.8≤OR<0.9 and trivial intervention effects for 1.0<OR≤1.1 or 0.9≤OR<1.0; for length of stay, large intervention effects were considered for MD>2, moderate intervention effects for 1<MD≤2, small intervention effects for 0.5<MD≤1 and trivial intervention effects for 0<MD≤0.5; for time to re-intubation, large intervention effects were considered for MD>24, moderate intervention effects for 12<MD≤24, small intervention effects for 6<MD≤12 and trivial intervention effects for 0<MD≤6. COT was considered as the reference intervention. Bold indicates p<0.05.

Subgroup analysis Prophylactic NRS

As shown in figure 3, in the overall population, both prophylactic HFNO (OR 0.53, 95% CI 0.36–0.77; p=0.001) and NIV (OR 0.50, 95% CI 0.35–0.72; p<0.001) were significantly correlated to a lower risk of extubation failure compared with COT [8, 25, 38, 40–51, 53, 54, 57–63, 65–67]. Heterogeneity was moderate (I²=39%) (supplementary tables S5–S7).

In high-risk patients (12 studies (1702 patients)), only prophylactic NIV significantly reduced the risk of extubation failure (OR 0.50, 95% CI 0.33–0.75; p<0.001) compared with COT (figure 4). Heterogeneity was very low (I²=0%) (supplementary tables S5–S7).

In low-risk patients (seven studies (1433 patients)), neither prophylactic HFNO nor NIV affected the primary outcome compared with COT (figure 4). Heterogeneity was high (I²=61%) (supplementary tables S5–S7).

In ICU post-surgical patients (five studies (544 patients)), prophylactic HFNO (OR 0.13, 95% CI 0.04–0.45; p=0.001), but not prophylactic NIV (OR 0.27, 95% CI 0.04–1.69; p=0.162), decreased the incidence of extubation failure compared with COT. Heterogeneity was very low (I²=0%) (supplementary tables S5–S7).

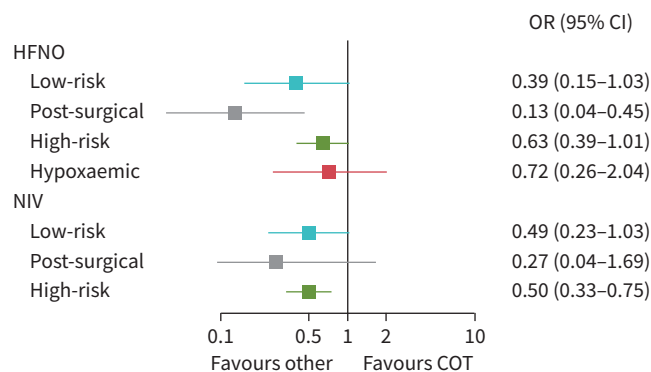


FIGURE 4 Impact of “prophylactic” noninvasive respiratory support on predefined subgroups (re-intubation). COT: conventional oxygen therapy; HFNO: high-flow nasal oxygen; NIV: noninvasive ventilation.

In hypoxaemic patients (three studies (663 patients)), prophylactic HFNO did not affect the rate of post-extubation respiratory failure (figure 4). Heterogeneity was high ($I^2=69\%$) (supplementary tables S5–S7).

Therapeutic NRS

The application of HFNO or NIV, as treatment for established post-extubation respiratory failure, showed no benefits in the overall population compared with COT [23, 52, 55, 56, 64]. Heterogeneity was very low ($I^2=0\%$) (supplementary tables S5–S7).

Additional subgroup analyses were not feasible due to the limited number of RCTs investigating the use of NRS for treating established post-extubation respiratory failure in medical and post-surgical populations.

Discussion

In this network meta-analysis, we found that: 1) HFNO and NIV reduced the rate of extubation failure and VAP compared with COT; 2) NIV, but not HFNO, reduced hospital mortality and ICU and hospital LOS; 3) neither HFNO nor NIV showed any benefit on ICU mortality or time to re-intubation; 4) patient discomfort was worsened by NIV compared with COT and HFNO; 5) prophylactic NIV, but not HFNO, reduced the rate of extubation failure in high-risk patients compared with COT; 6) prophylactic HFNO, but not NIV, reduced the rate of post-extubation respiratory failure in post-surgical patients compared with COT; 7) neither prophylactic NIV nor HFNO reduced the rate of extubation failure in low-risk or hypoxaemic patients; and 8) the therapeutic use of NIV or HFNO showed no benefits compared with COT.

Our results are consistent with those of another recent network meta-analysis on 36 RCTs (6806 patients) showing that, compared with COT, NRS overall reduced the rate of re-intubation when applied to prevent post-extubation respiratory failure, but it did not improve hospital mortality [27]. Nonetheless, the two network meta-analyses present several differences. First, the previous meta-analysis was more focused on low-risk patients (14 (39%) studies) rather than on patients at high risk of extubation failure (seven (19%) studies), as opposed to the present meta-analysis (eight (25%) low-risk studies and 13 (41%) high-risk studies). Second, despite a higher number of patients included (6806 versus 5063 patients), the previous network meta-analysis enrolled 2259 (33%) surgical patients undergoing NRS not exclusively in the ICU, but also in the operating room, post-anaesthesia care unit or medical/surgical wards [62–75]. On the contrary, we considered only post-operative patients admitted to the ICU. Third, three studies included in the previous network meta-analysis investigated NRS application as a “weaning” strategy to allow early extubation after failed SBT [20, 31, 32, 76], which is, in our opinion, a quite different population of patients than that of patients extubated after a successful SBT. Finally, some of our secondary outcomes, such as time to re-intubation and ICU or hospital LOS, were not considered in the previous meta-analysis [27].

With respect to HFNO in surgical patients, our results are in accordance with the statements of the 2022 ERS guidelines, which recommend prophylactic HFNO, over COT, after extubation in surgical patients both at low and high risk of extubation failure (conditional recommendation, low certainty of evidence) [18]. While different from those guidelines, recommending the prophylactic use of HFNO also in nonsurgical patients at low risk of failure (conditional recommendation, low certainty of evidence) [18], our analysis did not observe a significant difference between HFNO and COT in nonsurgical low-risk patients ($p=0.057$, $I^2=61\%$).

With respect to the impact of prophylactic HFNO on hypoxaemic patients, our network meta-analysis did not show any difference on the rate of post-extubation respiratory failure between HFNO and COT, as recently reported by MAGGIORE *et al.* [42].

In keeping with the statements of the 2017 ERS/ATS guidelines, our network meta-analysis showed that prophylactic, but not therapeutic, NIV decreased the rate of post-extubation respiratory failure in high-risk patients, but not in low-risk patients, compared with COT [5].

With regard to surgical patients, the 2017 ERS/ATS guidelines discussed the possible therapeutic application of NIV in post-surgical patients with established respiratory failure (conditional recommendation, moderate certainty of evidence) [5]. Based on our network meta-analysis, we showed that the therapeutic use of NIV did not reduce the rate of extubation failure in the overall population compared with COT. However, a subgroup analysis, exclusively focused on ICU patients, after surgery was not feasible due to the limited number of RCTs available ($n=2$ [59, 68]).

Finally, in accordance with the 2022 ERS guidelines, our analysis confirmed that NIV, but not HFNO, reduced the rate of post-extubation respiratory failure in high-risk nonsurgical patients [18]. With respect to surgical patients, conversely, our network meta-analysis showed that only prophylactic HFNO reduced the risk of extubation failure, while the 2022 ERS guidelines stated that either HFNO or NIV may reduce the rate of extubation failure in surgical patients at high risk of post-operative respiratory complications (conditional recommendation, low certainty of evidence) [18]. It is worth emphasising, as already mentioned, that we considered only surgical patients exclusively treated with NRS after extubation in the ICU, without any stratification between patients at low or high risk of post-operative respiratory failure. Therefore, we cannot exclude that the use of NIV may have a different impact on surgical patients enrolled in the operating room or post-anaesthesia care unit.

Finally, we did not find any difference between NRS modalities with respect to time to re-intubation. However, the very low certainty of evidence limits the robustness of this finding. It is worth remarking that longer time to re-intubation may result in delayed intubation in the patients who need it more, such as those experiencing post-extubation respiratory failure and receiving therapeutic NRS.

Study strengths and limitations

This review has some points of strength since it included: 1) a broad and systematic search of five different databases; 2) a pre-planned network meta-analysis with rigorous subset analyses to investigate the impact of post-extubation NRS in different subpopulations; and 3) a large number of studies, including more than 5000 enrolled patients. Moreover, our network analysis showed a relatively low incoherence between direct and indirect findings. Despite these assumptions, some limitations require discussion. First, we included several studies published more than 10 years ago and, in the meantime, clinical practice may have changed, thus introducing potential intransitivity. Second, we could not account for the heterogeneity attributable to the different outcome definitions among studies. Third, only 24% (eight out of 33) of trials included more than 100 patients per group, which may introduce bias due to small-study effects.

Points for clinical practice

- NRS may be useful for preventing, but not for treating, post-extubation respiratory failure in ICU patients.
- Prophylactic NIV decreased the rate of extubation failure in ICU high-risk patients; prophylactic HFNO decreased the rate of extubation failure in ICU post-surgical patients.

Conclusions

In the overall population, NRS reduced the rate of post-extubation respiratory failure and VAP compared with COT. NIV, but not HFNO, improved hospital mortality, and ICU and hospital LOS, despite worsened patient discomfort. Prophylactic, but not therapeutic, NRS decreased the rate of extubation failure in high-risk patients (NIV) and in post-surgical patients (HFNO), but not in the low-risk and hypoxaemic subgroups of patients.

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Previous articles in this series: No. 1: Bureau C, Van Hollebeke M, Dres M. Managing respiratory muscle weakness during weaning from invasive ventilation. *Eur Respir Rev* 2023; 32: 220205. No. 2: van den Biggelaar R, Hazenberg A, Duiverman ML. The role of telemonitoring in patients on home mechanical ventilation. *Eur Respir Rev* 2023; 32: 220207.

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