Journal of Critical Care 50 (2019) 250–256

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

High flow nasal therapy in immunocompromised patients with acute respiratory failure: A systematic review and meta-analysis

Andrea Cortegiani [a,*], Claudia Crimi [b], Filippo Sanfilippo [c], Alberto Noto [d], Davide Di Falco [e], Giacomo Grasselli [f,g], Cesare Gregoretti [a], Antonino Giarratano [a]

[a] Department of Surgical, Oncological and Oral Science (Di.Chir.On.S.), Section of Anesthesia, Analgesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, University of Palermo, Palermo, Italy
[b] Respiratory Medicine Unit, AOU "Policlinico-Vittorio Emanuele", Catania, Italy
[c] Department of Anesthesia and Intensive Care, AOU Policlinico Vittorio Emanuele, Catania, Italy
[d] Anesthesia and Intensive Care Unit, AOU Policinico "G. Martino", Messina, Italy
[e] Department of Anesthesia and Intensive Care, School of Anesthesia and Intensive Care, University of Catania, 95100 Catania, Italy
[f] Department of Anesthesiology, Intensive Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Francesco Sforza 35, 20122, Milan, Italy
[g] Department of Pathophysiology and Transplantation, University of Milan, Via Festa del Perdono 1, 20122, Milan, Italy

ARTICLE INFO

Keywords:
High flow nasal therapy
Acute respiratory failure
High flow nasal cannula
Oxygen therapy
Immunocompromised patients
Mechanical ventilation
Noninvasive ventilation

ABSTRACT

Purpose: The role of high-flow nasal therapy (HFNT) as compared to conventional oxygen therapy (COT) in immunocompromised patients admitted to intensive care unit (ICU) with acute respiratory failure (ARF) remains unclear. We conducted a systematic review and meta-analysis in order to address this issue.
Methods: We searched PubMed, Medline and Embase until November 7th, 2018. Randomized controlled trials (RCTs), non-randomized prospective and retrospective evidence were selected. Observational studies were considered for sensitivity analysis. Primary outcome was mortality rate; intubation rate was a secondary outcome.
Results: We included four studies in the primary analysis: one RCT, two RCT's post-hoc analyses and one retrospective study. We found no significant difference in short-term mortality comparing HFNT vs. COT: 1) ICU: n = 872 patients, odds ratio (OR) = 0.80 [0.44,1.45], p = 0.46, I^2 = 30%, p = 0.24; 2) 28-day: n = 996 patients, OR = 0.79 [0.45,1.38], p = 0.40, I^2 = 52%, p = 0.12). Conversely, we found a reduction of intubation rate in the HFNT group (n = 1052 patients, OR = 0.74 [0.55,0.98], p = 0.03, I^2 = 7%, p = 0.36). The inclusion of one observational study for sensitivity analysis did not grossly change results.
Conclusions: We found no benefit of HFNT over COT on mortality in immunocompromised patients with ARF. However, HFNT was associated with a lower intubation rate warranting further research.

1. Introduction

Acute respiratory failure (ARF) represents a leading cause of Intensive Care Unit (ICU) admission and death in immunocompromised patients [1]. However, the best respiratory management strategy to avoid endotracheal intubation and decrease mortality in this patient population is unclear [1-5]. High flow nasal therapy (HFNT) is a relatively novel strategy of respiratory support that supplies high flow (up to 60 L/min) of heated and humidified gas with a controlled and adjustable inspiratory fraction of oxygen (FiO_2) up to 100% through a dedicated nasal cannula [6]. Several mechanisms explain the effect of HFNT on gas exchange and respiratory function, including a more stable pharyngeal fraction of inspired oxygen, the generation of a small positive end-expiratory pressure (PEEP), washout of nasopharyngeal dead space and greater patient's comfort as compared to noninvasive ventilation (NIV) or conventional oxygen therapy (COT). In addition, as opposed to NIV, since HFNT does not deliver positive pressure breaths, the risk of delivering high tidal volumes and consequently excessive transpulmonary pressure may be reduced [7,8].

Over the past five years, some studies have compared HFNT *vs.* COT and/or NIV, with considerable heterogeneity in their design, being prospective observational [9,10], post-hoc analyses [11,12], retrospective [13,14], and in groups' comparison. The most recent meta-analysis included six studies with a total population of almost 600 patients [15].

Abbreviations: ARF, Acute respiratory failure; ICU, Intensive Care Unit; HFNT, High flow nasal therapy; FiO_2, inspiratory fraction of oxygen; PEEP, positive end-expiratory pressure; COT, conventional oxygen therapy; NIV, noninvasive ventilation; RCT, randomized controlled trial; NOS, Newcastle-Ottawa Assessment Scale; OR, odds ratio; CI, Confidence Intervals; SMD, standard mean difference; SOFA, Sequential Organ Failure Assessment.

* Corresponding author at: Department of Surgical, Oncological and Oral Science (Di.Chir.On.S.), Section of Anesthesia, Analgesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, University of Palermo, Via del vespro 129, 90127 Palermo, Italy.
E-mail address: andrea.cortegiani@unipa.it (A. Cortegiani).

https://doi.org/10.1016/j.jcrc.2018.12.015
0883-9441/

The authors identified beneficial effects with the use of HFNT in immunocompromised patients with ARF, showing a significant reduction in short-term mortality and intubation rate. However, it should be noted that three studies compared HFNT *vs.* COT, while in the other three included studies the control group received NIV [9,14,16]. A recent very large and rigorous randomized controlled trial (RCT) compared HFNT *vs.* COT in almost 800 immunocompromised patients [17]. Indeed, such study found no statistically significant differences for any of the predetermined outcomes, including mortality as primary outcome, thus leaving uncertainty on the role of HFNT in this patient's population [17].

We conducted a systematic review and meta-analysis with the aim of summarizing the recently growing evidence and evaluating the effectiveness of HFNT compared to COT in immunocompromised patients.

2. Methods

The protocol of our systematic review and meta-analysis was prospectively registered in PROSPERO database (CRD number 42018115984). We conducted a web-based literature search of three electronic databases (Pubmed, Medline, EMBASE) using the *NHS Library Evidence tool*, from inception until 7th November 2018. We followed the approach suggested by the PRISMA statement for reporting systematic reviews and meta-analyses, and the PRISMA checklist is provided in Supplemental Digital Content 1 [18]. Inclusion criteria were prespecified according to the PICOS approach (Table 1). The primary outcome was mortality, which analysis was prospectively planned in short-term (ICU, 28-day, 30-day), midterm (between 31 and 90 day, or hospital) and long-term (anything longer than 90 day). We chose as secondary outcomes the intubation rate and the ICU length of stay.

The core search was structured by the combination of terms obtained from the following two groups. The first one included in alphabetical order: “cancer” or “hematologic” or “hematological” or “immunocompromised” or “immunosuppression” or “transplant” or “transplantation”. The second group consisted of the following: “HFNC” or “high-flow nasal cannula oxygen” or “high flow oxygen” or “high flow therapy” or “humidified high-flow” or “high flow nasal”. Study selection for eligibility of inclusion in the systematic review was performed independently by two reviewers (CC, AN). Discrepancies were resolved involving other authors (AC, FS, GG, CG, AG) and/or by consensus. Three authors (AC, FS, DDF) conducted a further manual search exploring the list of references of the included studies. When needed, we contacted via email the corresponding authors for retrieving available data. Data extraction from selected studies was performed independently by two authors (FS, DDF) and a final check was conducted by a third one (AC). Meta-analysis was performed independently by two experienced authors (AC, FS). We excluded articles referring to the paediatric population.

Table 1
“PICOS” approach for selecting clinical studies in the systematic search. ICU: intensive care unit.

PICOS	
1. Participants	Immunocompromised patients with Acute Hypoxemic Respiratory Failure
2. Intervention	High Flow Nasal Oxygen Therapy
3. Comparison	Conventional Oxygen Therapy
4. Outcomes	Primary outcomes: mortality at short term (ICU, 28-day), mid-term (90 day and hospital), long-term (>90 days). Secondary outcomes: intubation rate, length of stay in ICU and hospital (secondary)
5. Study design	Prospective (RCT, non-RCT); Retrospective; Post-hoc analyses; pair-matching studies. Observational prospective studies were included only for sensitivity analysis

RCT: randomized controlled trial.

Since we did not expect enough RCTs we decided to include also non-randomized prospective and retrospective evidence, including also studies with pair-matching analysis strategy. However, we prospectively decided to include observational studies only in a sensitivity analysis because of their high risk of selection bias, while case reports and case series were excluded. Language restrictions were applied: only articles published in English, Spanish, German, French or Italian were considered.

2.1. Risk of bias assessment

Two authors (AN, FS) independently assessed the methodological quality of the included studies. Methodological quality of included RCTs was performed using the Cochrane Collaboration tool which incorporated the following domains: selection, performance, detection, attrition, reporting and other potential sources of bias [19]. The quality of non-randomized studies was assessed using the Newcastle-Ottawa Assessment Scale (NOS), as recommended by the Cochrane collaboration [20]. This scale has three main domains and assigns one point for each subset of assessment criteria within the selection and exposure domains. Studies can obtain up to two points within the comparability domain. We then classified studies as high risk (1-3 points), intermediate risk (4-5 points) and low risk of bias (6-9 points).

2.2. Statistical analysis

The Mantel–Haenszel method was used to analyse dichotomous outcomes such as mortality and intubation rate. Results are reported as odd ratios (OR) with 95% Confidence Intervals (CI). Continuous outcome differences (length of stay) were analysed using an inverse variance model with a 95% CI. Values are reported as standard mean difference (SMD). In both analyses p values were two-tailed and considered significant if <0.05. The presence of statistical heterogeneity was assessed using the X2 (Cochran Q) test. Heterogeneity was likely if $Q>df$ (degrees of freedom) suggested and confirmed if $P \leq 0.10$. Quantification of heterogeneity performed using I^2 statistic. Values of 0-24.9%, 25-49.9%, 50-74.9% and >75% were considered as none, low, moderate and high heterogeneity respectively [19]. If heterogeneity was quantified as low or above, a random model was used. A sensitivity analyses was planned excluding studies with high risk of bias, providing at least three studies remained for analysis. Another sensitivity analysis was planned adding prospective observational studies.

3. Results

3.1. Study selection

The literature search produced 414 titles on Medline, 53 on Pubmed and 104 on EMBASE. After removal of duplicates, 535 titles and abstracts were identified as potentially relevant and were appraised against inclusion criteria. As shown in the flowchart (Fig. 1), 476 articles were excluded because not relevant and 38 because they were not clinical studies on HFNT (n=21 review/meta-analysis; n=1 letter/reply/editorial; n=7 case report/series; n=4 paediatric population; n=5 study protocol), leaving 21 articles included initially. However, we subsequently excluded 16 studies as not providing data on mortality or any of the secondary outcomes comparing HFNT with COT. Of these studies 7 were single arm observational retrospective studies or HFNT case series; 3 studies evaluated different outcomes (i.e. reduction in dyspnoea in non-ICU patients); one study [21] compared HFNT *vs.* COT but was excluded because treatment was applied only for a two-hour period; two studies [9,16] and one conference abstract [22] compared patients receiving HFNT *vs.* NIV. Another study [10] was a post-hoc joint analysis pooling data from three other studies and investigating the risk of intubation according to the initial strategy of ventilatory management. One study [14] including patients on HFNT, COT and NIV and a mix of these

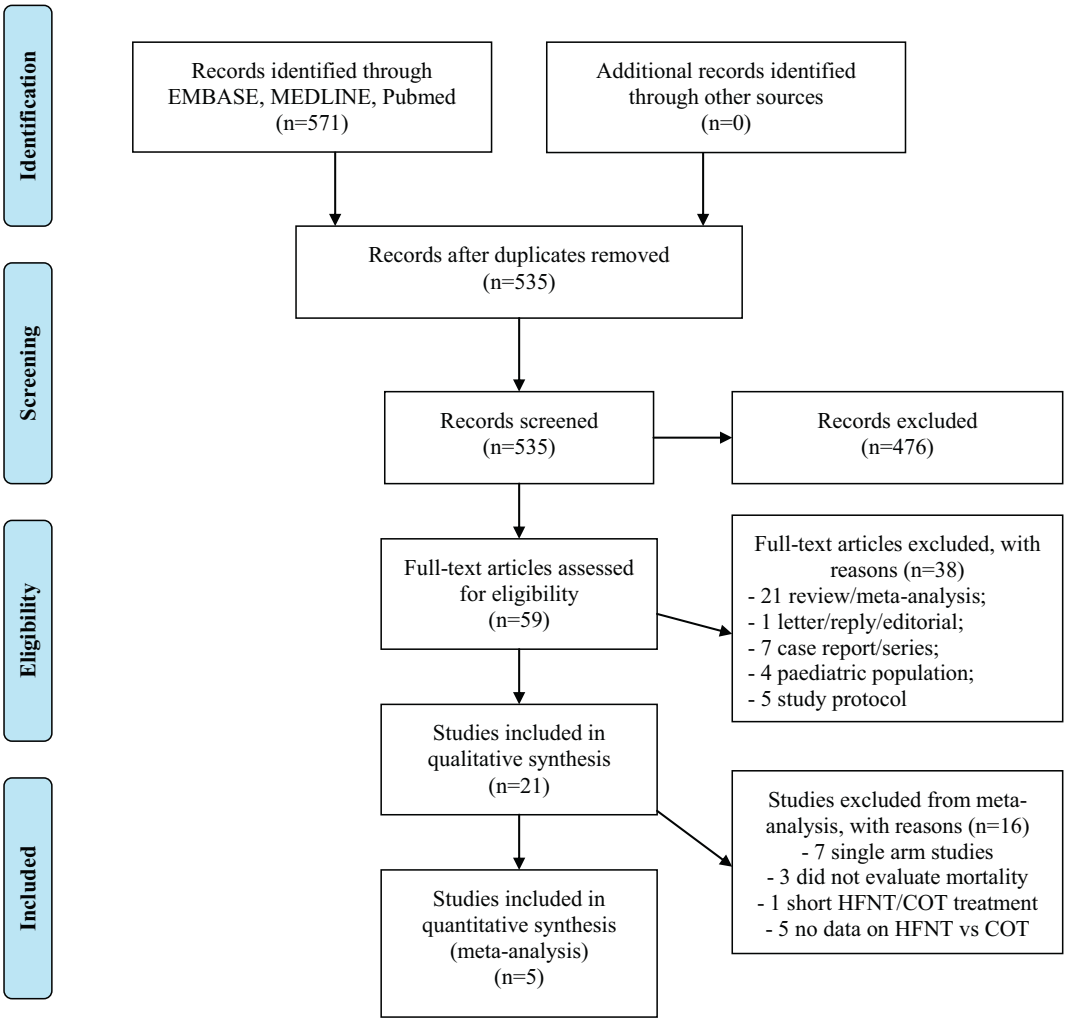

Fig. 1. PRISMA flow chart. HHFT: High flow nasal therapy: COT: conventional oxygen therapy.

approaches did not explicitly report the outcomes of the populations of interest in our meta-analysis. We attempted to contact the corresponding author but unfortunately data were not available. Finally, we identified four studies [11-13,17] as suitable for the meta-analysis, with one additional observational study [4] for sensitivity analysis. Table 2 shows characteristics of included studies and also summarizes other non-included studies (i.e. those comparing HFNT to NIV).

3.2. Primary outcome (mortality)

1. Short term mortality

Mortality was reported at different time points by the included studies: ICU [4,11,13,17], 28-day [12,13,17], hospital [13,17] and 90-day [11]. The analyses of short term mortality - ICU or 28-day - included three studies each, and both analyses did not show significant differences: 1) ICU [11,13,17]: n=872 patients, OR=0.80 [0.44, 1.45] p=0.46, I^2=30%, p=0.24 (Fig. 2a); 2) 28-day [12,13,17]: n=996 patients, OR=0.79 [0.45, 1.38] p=0.40, I^2=52%, p=0.12 (Fig. 2b).

2. Midterm Mortality

The analysis of midterm mortality was conducted pooling the results of hospital and 90-day mortality from a total of three [11,13,17] studies, including 872 patients. Such analysis showed no significant differences between HFNT and COT: OR=0.58 [0.23, 1.45] p=0.24, I^2=60%, p=0.08 (Fig. 3).

The observational study conducted by Azoulay et al in 2017 [4] reported data on ICU mortality only and its inclusion in the sensitivity analysis did not change the overall result ICU: n=1555 patients, OR=1.03 [0.66, 1.61] p=0.88, I^2=55%, p=0.08.

3.3. Secondary outcomes

1. Intubation rate

The need for intubation was reported by four studies [11-13,17] included in the primary analysis and pooling these results showed a significantly lower intubation rate in the HFNT group: n=1052 patients, OR=0.74 [0.55, 0.98] p=0.03, I^2=7%, p=0.36 (Fig. 4). When we added the prospective observational study of Azoulay et al. [4] for the sensitivity analysis, the overall results showed no significant differences between groups (n=1735 patients, OR=0.81 [0.63, 1.05] p=0.12, I^2=24%, p=0.26).

2. ICU Length of stay

Three studies [12,13,17] reported the length of stay in ICU and were included in the primary analysis, which showed no significant

Table 2
Studies included in the meta-analysis (upper part) and studies excluded from the meta-analysis but of some interest (lower part).

Studies included in the meta-analysis

Study, year	Study design	Setting	Population characteristics						Primary outcome
		Case-mix	N	Age (y)	Cancer %	Severity scores	RR/min	PaO_2/FiO_2	
Azoulay et al. [17]	RCT	ICU Mixed	388 HFNT 388 COT	64 vs 63	76 vs 82	SOFA 6 (4) vs 6 (4) SAPS II 36 (18) vs 37 (20)	33 vas 32	136 vs 128	28-Days mortality
Azoulay et al. 2017[a]	Prospective observational	ICU/ED/ward Mixed	187 HFNT 496 COT	62 vs 64	88 vs 87	SOFA 6 (4) vs 5 (5)	–	150 vs 173	ICU mortality
Lemiale et al. [12][b]	Post-hoc analysis	ICU Mixed	90 HFNT 90 COT	64 vs 63	87 vs 85	SOFA 4 (4) vs 3 (4)	28 vs 25	—	28-Days mortality
Frat et al. [11]	Post-hoc analysis	ICU Mixed	26 HFNT 30 COT	62 vs 63	38 vs 50	SAPS II 29 (11) vs 30 (17)	32 vs 32	138 vs 155	Rate of intubation
Roca et al. [13]	Retrospective	ICU Lung Tx	22 HFNT 18 COT	56 vs 53	0 vs 0	APACHE II 21 (7) vs 20 (6)	28 vs 20	—	Rate of intubation

Studies not included in the meta-analysis

Study, year	Study design	Setting	Population characteristics						Primary outcome
		Case-mix	N	Age (y)	Cancer %	Severity scores	RR/min	PaO_2/FiO_2	
Coudroy et al. [9]	Retrospective	ICU Mixed	60 HFNT 55 NIV	45 vs 44	65 vs 80	SAPS II 46 (13) vs 42 (11)	29 vs 30	149 vs 141	28-Days mortality
Gupta et al. [22][c]	RCT	ICU Liver Tx	10 HFNT 10 NIV	–	–	–	–	–	Intubation rate
Lemiale et al. [21][d]	RCT	ICU Mixed	52 HFNT 48 COT	50 vs 49	88 vs 79	SAPS II 42 (22) vs 38 (15)	26 vs 27	128 vs 100	Rate of intubation or NIV
Mokart et al. [14][e]	Propensity analysis	ICU, Cancer	69 HFNT +NIV 69 Others	56 vs 59	100 vs 100	SAPS II 47 (18) vs 42 (21)	—	128 vs 116	28-Days mortality
Tu et al. [16]	Retrospective	ICU Renal Tx	20 HFNT 18 NIV	47 vs 47	0 vs 0	APACHE II 20 (4) vs 19 (4)	32 vs 30	150 vs 148	Rate of intubation

APACHE: acute physiology and chronic health evaluation. COT: conventional oxygen therapy. ED: emergency department. HFNT: high flow nasal therapy. ICU: intensive care unit. NIV: noninvasive ventilation. RCT: randomized controlled trial. RR: respiratory rate. SAPS: simplified acute physiology score. SOFA: sequential organ failure assessment. Tx: Transplant.
[a] Evaluated also NIV and NIV-HFNT patient.
[b] The HFNT and COT groups received also NIV at day 1 (44% vs 55%, respectively).
[c] Conference abstract (Intensive Care Medicine Experimental; Sep 2016; vol. 4).
[d] The study was not included in the meta-analysis because patients were randomized to two hours only of HFNT or COT.
[e] The group "others" includes COT alone, HFNT alone and HFNT-COT.

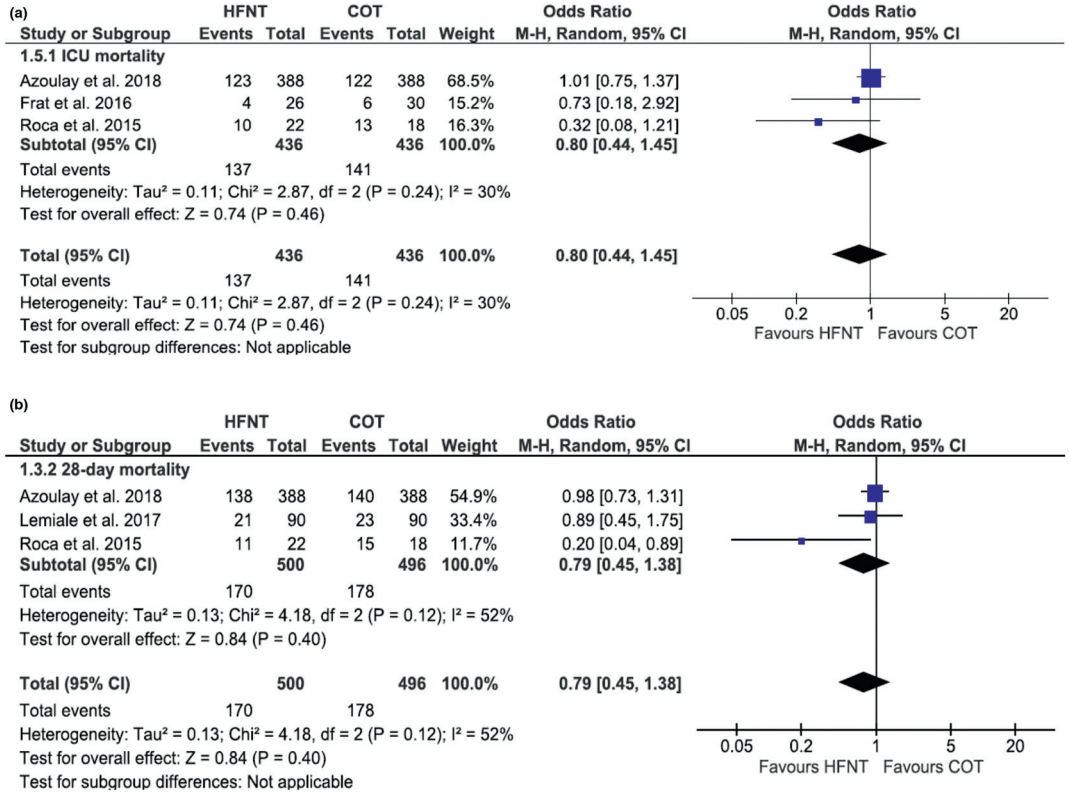

Fig. 2. Forest plot analyzing the risk of ICU mortality (a - upper) and 28-day mortality (b - lower) in immunocompromised patients with acute respiratory failure treated high flow nasal therapy (HFNT) or conventional oxygen therapy (COT).

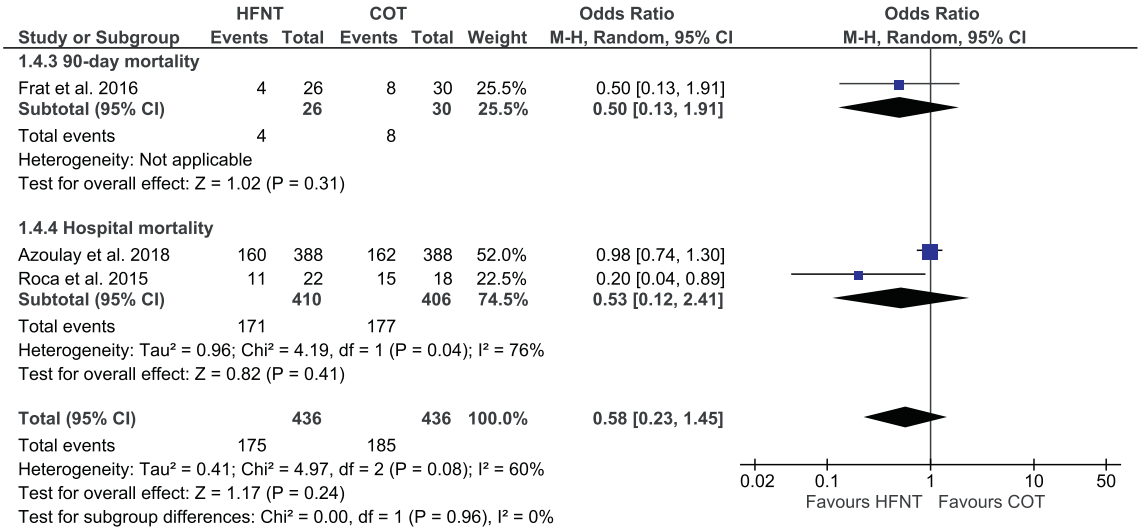

Fig. 3. Forest plot analyzing the risks of 90-day and hospital mortality in immunocompromised patients with acute respiratory failure treated high flow nasal therapy (HFNT) or conventional oxygen therapy (COT).

differences between groups: n=996 patients, SMD=0.53 [-0.19, 1.25] p=0.15, I^2=94%, p<0.0001 (Supplemental Digital Content 2).

3.4. Risk of bias assessment

The only RCT [17] included was evaluated against the Cochrane Collaboration criteria and was judged of high quality (six domains at low risk of bias and one at high risk). The other included studies were judged of low risk of bias according to the NOS scale, scoring 7 points [12], 8 points [11,13] and 9 points [4]. Detailed assessment is provided as Supplemental Digital Content 3.

4. Discussion

The main findings of our study can be summarized as follows: 1) we found no benefit of using HFNT in comparison to COT in immunocompromised patients with ARF; 2) we found a statistically significant reduction in intubation rate in patients receiving HFNT as compared with COT (with no statistical heterogeneity). To the best of our knowledge, the present meta-analysis is the most updated evidence on the use of HFNT as compared with standard oxygen therapy in immunocompromised patients.

We conducted the present study based on the recent publication of a large and well-conducted randomized trial comparing the use of HFNT *vs.* COT in immunocompromised patients and showing no significant differences in mortality and intubation rate. Conversely, a recently published meta-analysis including six studies suggested benefit from HFNT. Nonetheless, their analysis included considerably heterogeneous studies. Indeed, in one included study HFNT was associated to NIV (which was the primary treatment and HFNT was used between NIV pause) while other two studies compared HFNT with NIV [9,16]. Such studies were not included in our meta-analysis, which remained strictly focused on a more homogeneous comparison between HFNT and COT patients.

We focused on mortality, although this is a particularly complex outcome in immunocompromised patients. A recent multi-centre observational prospective cohort study (EFRAIM) reported data on 1611 immunocompromised patients with ARF [4]. The study had purely descriptive aims and 20% of this cohort received HFNT. After propensity score matching among other factors, the authors found that initial oxygenation strategy did not impact on mortality. Similarly, a post-hoc joint analysis pooling data from three studies concluded that, after adjusting for confounders, the initial ventilator strategy (including NIV) had no impact on intubation rate [10]. Interestingly, the EFRAIM study showed that failure to recognize the cause of ARF was significantly associated with mortality [4]. Contrary to NIV, in this study HFNT resulted in a clear trend towards lower rate of intubation (Hazard Ratio=0.77, 95% CI 0.59-1.00, p=0.05), possibly increasing the lag time between the initial treatment and the eventual patient's deterioration, thus maximizing the chances to timely recognize (and treat) the true cause of ARF. The EFRAIM study also showed that other factors such as age, PaO_2/FiO_2 ratio and non-pulmonary Sequential Organ Failure Assessment (SOFA) score at day 1 were associated with mortality. In line with these findings, a recent post-hoc analysis of the LUNG SAFE study on 584 immunocompromised patients with acute respiratory distress syndrome confirmed that only higher non-pulmonary SOFA score, lower PaO_2/FiO_2 ratio and lower improvement of respiratory failure were associated with greater in-hospital mortality [5]. Importantly, as compared with

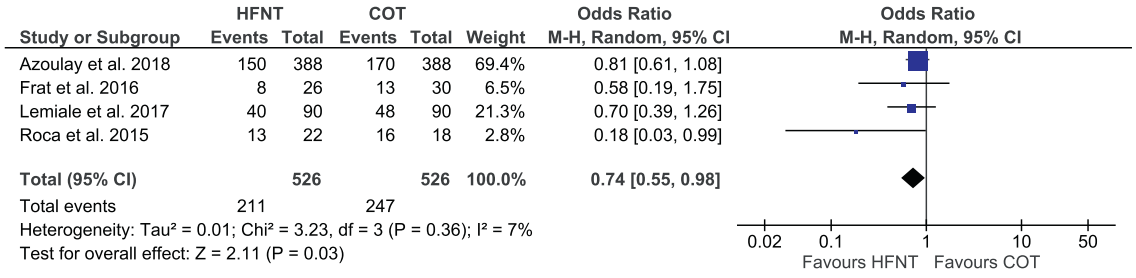

Fig. 4. Forest plot analyzing the risk of intubation in immunocompromised patients with acute respiratory failure treated high flow nasal therapy (HFNT) or conventional oxygen therapy (COT).

immunocompetent patients, immunocompromised subjects presented lower survival rate regardless of disease severity, suggesting that general conditions, underlying pathologies and ARF aetiology may have more importance than oxygenation strategy for the management of immunocompromised patients. Of note, one recent meta-analysis including 18 trials enrolling 3881 adult patients with ARF, demonstrated that HFNT reduced intubation rate in comparison to COT (p=0.01) without affecting mortality [23]. Our main results – no differences in mortality but a significant reduction in intubation rate – point in the same direction, although our meta-analysis suffers from lower number of included studies. Nonetheless, the methodological quality of the included studies was generally high and our result on intubation rate indicated no statistical heterogeneity. In our opinion, such result should be further investigated as the recent RCT [17] was possibly underpowered in this regard (5.1% mean difference with large CI 12.3% to 2.0%, p=0.17).

The ability of HFNT to reduce respiratory rate and decrease respiratory distress, dyspnoea and improve oxygenation [24-26], may postpone or avoid the need to intubate giving more time to clinicians to investigate the ARF aetiology and to deliver appropriate treatment. We believe this is a key endpoint in this population of patients since avoidance of intubation could have clinical (i.e. administration of chemotherapy), ethical (i.e. time for discussing end-of life options and advanced directives) and economical (i.e. reduction of ICU admission and lower costs) implications. Indeed, several studies have found an association between invasive mechanical ventilation and mortality in this patients' population [4,5,10]. However, it should be clearly kept in mind that delaying unavoidable intubation is associated with worse outcomes, even in the immunocompromised population [27].

4.1. Strengths and limitations

As already reported, our meta-analysis was prompted by the discrepancy between the results of the recent RCT published by Azoulay et al. [17] comparing immunocompromised patients treated with HFNT or COT, and the results of a previous heterogeneous meta-analysis [15] that compared HFNT (± NIV) to other respiratory management strategies (COT and/or NIV) and suggested that "*use of HFNC significantly improve outcomes of ARF in immunocompromised patients*".

The main strength of our meta-analysis is the inclusion of studies with homogeneous comparison between respiratory support strategies. Indeed, in all the included studies the difference between the two groups was the use of HFNT *vs*. COT. Such approach decreased the role of the confounders seen in the previous meta-analysis but in turn reduced the number of studies included which remains the main limitation of our study. Moreover, even if our approach allowed a more homogeneous comparison and the statistical heterogeneity was low/moderate (mortality) or absent (intubation rate), it should be clearly highlighted that we included studies with very different methodological design: one RCT [17], two post-hoc analysis of RCTs (one with pair-matching strategy) [11,12] and one retrospective study [13], while a prospective observational cohort study [4] was included only in the sensitivity analysis for its high risk of "selection bias". The overall population consisted of almost 1.000 patients for the 28-day mortality, but the recent RCT [17] accounted for 55% of the analysis weight. Finally, there was also a degree of clinical heterogeneity since one study included patients with lung transplantation, while the others had mixed case mix with an average of oncological patients varying from 44% [11] to 87% [4].

5. Conclusions

We found no benefit in short- and mid-term mortality by the use of HFNT as compared with COT in immunocompromised patients with ARF. However HFNT was associated with lower intubation rate as compared with standard oxygen. Such result warrants further research for its ethical, clinical and economic implications.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

Cesare Gregoretti received fees for consultancies or lectures from Orion Pharma, ResMed, Medtronic, Philips, Air Liquide and EOVE. Giacomo Grasselli received fees for lectures from Getinge, Draeger Medical, Fisher & Paykel, Pfizer and travel accommodation/congress registration from Getinge and Biotest. All other authors declared no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2018.12.015.

References

[1] Azoulay E, Schellongowski P, Darmon M, Bauer PR, Benoit D, Depuydt P, et al. The Intensive Care Medicine research agenda on critically ill oncology and hematology patients. Intensive Care Med 2017. https://doi.org/10.1007/s00134-017-4884-z.
[2] Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J 2017;50. https://doi.org/10.1183/13993003.02426-2016.
[3] Darmon M, Ranzani OT, Azoulay E. Focus on immunocompromised patients. Intensive Care Med 2017;43:1415–7.
[4] Azoulay E, Pickkers P, Soares M, Perner A, Rello J, Bauer PR, et al. Acute hypoxemic respiratory failure in immunocompromised patients: the Efraim multinational prospective cohort study. Intensive Care Med 2017;43:1808–19. https://doi.org/10.1007/s00134-017-4947-1.
[5] Cortegiani A, Madotto F, Gregoretti C, Bellani G, Laffey JG, Pham T, et al. Immunocompromised patients with acute respiratory distress syndrome: secondary analysis of the LUNG SAFE database. Crit Care 2018;22:157. https://doi.org/10.1186/s13054-018-2079-9.
[6] Renda T, Corrado A, Iskandar G, Pelaia G, Abdalla K, Navalesi P. High-flow nasal oxygen therapy in intensive care and anaesthesia. Br J Anaesth 2018;120:18–27. https://doi.org/10.1016/j.bja.2017.11.010.
[7] Carteaux G, Millan-Guilarte T, De Prost N, Razazi K, Abid S, Thille AW, et al. Failure of noninvasive ventilation for De Novo acute hypoxemic respiratory failure: role of tidal volume. Crit Care Med 2016;44:282–90. https://doi.org/10.1097/CCM.0000000000001379.
[8] Cortegiani A, Russotto V, Antonelli M, Azoulay E, Carlucci A, Conti G, et al. Ten important articles on noninvasive ventilation in critically ill patients and insights for the future: a report of expert opinions. BMC Anesthesiol 2017;17:122. https://doi.org/10.1186/s12871-017-0409-0.
[9] Coudroy R, Jamet A, Petua P, Robert R, Frat J-P, Thille AW. High-flow nasal cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients with acute respiratory failure: an observational cohort study. Ann Intensive Care 2016;6:45. https://doi.org/10.1186/s13613-016-0151-7.
[10] Dumas G, Chevret S, Lemiale V, Pene F, Demoule A, Mayaux J, et al. Oxygenation/non-invasive ventilation strategy and risk for intubation in immunocompromised patients with hypoxemic acute respiratory failure. Oncotarget 2018;9:33682–93.
[11] Frat J-P, Ragot S, Girault C, Perbet S, Prat G, Boulain T, et al. Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial. Lancet Respir Med 2016;4:646–52. https://doi.org/10.1016/S2213-2600(16)30093-5.
[12] Lemiale V, Resche-Rigon M, Mokart D, Pene F, Argaud L, Mayaux J, et al. High-flow nasal cannula oxygenation in immunocompromised patients with acute hypoxemic respiratory failure: a Groupe de Recherche Respiratoire en Reanimation Onco-Hematologique Study. Crit Care Med 2017;45:e274–80. https://doi.org/10.1097/CCM.0000000000002085.
[13] Roca O, de Acilu MG, Caralt B, Sacanell J, Masclans JR. Humidified high flow nasal cannula supportive therapy improves outcomes in lung transplant recipients readmitted to the intensive care unit because of acute respiratory failure. Transplantation 2015;99:1092–8. https://doi.org/10.1097/TP.0000000000000460.
[14] Mokart D, Geay C, Chow-Chine L, Brun J-P, Faucher M, Blache J-L, et al. High-flow oxygen therapy in cancer patients with acute respiratory failure. Intensive Care Med 2015;41:2008–10. https://doi.org/10.1007/s00134-015-3994-8.
[15] Huang H-B, Peng J-M, Weng L, Liu G-Y, Du B. High-flow oxygen therapy in immunocompromised patients with acute respiratory failure: a review and meta-analysis. J Crit Care 2018;43:300–5. https://doi.org/10.1016/j.jcrc.2017.09.176.
[16] Tu G, He H, Yin K, Ju M, Zheng Y, Zhu D, et al. High-flow nasal cannula versus non-invasive ventilation for treatment of acute hypoxemic respiratory failure in renal

transplant recipients. Transplant Proc 2017;49:1325–30. https://doi.org/10.1016/j.transproceed.2017.03.088.
[17] Azoulay E, Lemiale V, Mokart D, Nseir S, Argaud L, Pene F, et al. Effect of high-flow nasal oxygen vs standard oxygen on 28-day mortality in immunocompromised patients with acute respiratory failure: the high randomized clinical trial. JAMA 2018. https://doi.org/10.1001/jama.2018.14282.
[18] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100. https://doi.org/10.1371/journal.pmed.1000100.
[19] Higgins JPT, Altman DG, Gotzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343. https://doi.org/10.1136/bmj.d5928.
[20] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603–5. https://doi.org/10.1007/s10654-010-9491-z.
[21] Lemiale V, Mokart D, Mayaux J, Lambert J, Rabbat A, Demoule A, et al. The effects of a 2-h trial of high-flow oxygen by nasal cannula versus Venturi mask in immunocompromised patients with hypoxemic acute respiratory failure: a multicenter randomized trial. Crit Care 2015;19:380. https://doi.org/10.1186/s13054-015-1097-0.
[22] Gupta S, Govil D, Srinivasan SJ, Patel SJ, JK N, Gupta A, et al. A406 high flow nasal cannula (HFNC) as an alternative to noninvasive ventilation (NIV) in acute respiratory failure (ARF) in immunosuppressed patients - an Indian post liver transplant experience. ESICM LIVES; 2016.
[23] Ni Y-N, Luo J, Yu H, Liu D, Ni Z, Cheng J, et al. Can high-flow nasal cannula reduce the rate of endotracheal intubation in adult patients with Acute respiratory failure compared with conventional oxygen therapy and noninvasive positive pressure ventilation?: a systematic review and meta-analysis. Chest 2017;151:764–75. https://doi.org/10.1016/j.chest.2017.01.004.
[24] Papazian L, Corley A, Hess D, Fraser JF, Frat J-P, Guitton C, et al. Use of high-flow nasal cannula oxygenation in ICU adults: a narrative review. Intensive Care Med 2016;42:1336–49. https://doi.org/10.1007/s00134-016-4277-8.
[25] Cortegiani A, Accurso G, Mercadante S, Giarratano A, Gregoretti C. High flow nasal therapy in perioperative medicine: from operating room to general ward. BMC Anesthesiol 2018;18:166. https://doi.org/10.1186/s12871-018-0623-4.
[26] Russotto V, Cortegiani A, Raineri SM, Gregoretti C, Giarratano A. Respiratory support techniques to avoid desaturation in critically ill patients requiring endotracheal intubation: a systematic review and meta-analysis. J Crit Care 2017;41:98–106. https://doi.org/10.1016/j.jcrc.2017.05.003.
[27] Kang BJ, Koh Y, Lim C-M, Huh JW, Baek S, Han M, et al. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. Intensive Care Med 2015;41:623–32. https://doi.org/10.1007/s00134-015-3693-5.