

High Flow Nasal Catheter (HFNC) for Sepsis Induced Respiratory Failure after Extubation Meta Analysis of Clinical Control Studies on Reintubation Rate and Mortality¹

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Abstract:

Objective: To analyze the reintubation rate and mortality of patients with sepsis complicated (or induced) respiratory failure after extubation, and to seek evidence-based basis for the efficacy of HFNC in the re intubation rate and mortality of sepsis induced respiratory failure after extubation.

Methods: The databases of PubMed, EMBASE, Ovid, CNKI, CBM, VIP and Wanfang were searched to find the clinical studies of patients with sepsis and respiratory failure, and meta-analysis was carried out by Stata software.

Results: Meta analysis showed that there was no significant difference between HFNC and noninvasive positive pressure ventilation (NPPV) in 72 hour reintubation rate, mortality during ICU and 28-day in hospital.

Conclusion: The reintubation rate and mortality of HFNC after extubation in sepsis induced respiratory failure are equivalent to that of NPPV.

Keywords: Sepsis; Respiratory failure; High flow nasal catheter; Noninvasive positive pressure ventilation

Sepsis is a syndrome caused by a series of inflammatory reactions in the host and accompanied by organ failure, with critical condition and high mortality. A large number of studies have shown that sepsis can cause changes in respiratory muscles and respiratory patterns^[1], and most sepsis can induce respiratory failure^[2]; respiratory failure is also closely associated with increased sepsis mortality^[3]. Necessary mechanical ventilation support for patients with sepsis complicated with respiratory failure is the main measure to improve a series of symptoms of insufficient ventilation, such as hypoxemia and respiratory distress. When the respiratory condition improves, it is necessary to take off-line extubation. After extubation, it is usually given sequential treatment of noninvasive positive pressure ventilation (NPPV), which can effectively reduce the rate of re intubation and mortality. In recent years, high flow nasal catheter (HFNC) has been widely used in respiratory support because of its comfort, convenience and providing high flow, high concentration, heated and humidified oxygen^[4]. It has also been used in sequential treatment of sepsis induced respiratory failure after extubation. This study aims to provide evidence-based evidence

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for the clinical efficacy of HFNC in the treatment of sepsis induced respiratory failure after weaning from mechanical ventilation and extubation by meta-analysis of clinical control studies on the reintubation rate and mortality rate after weaning from mechanical ventilation and extubation.

1. Method

1.1 Literature inclusion criteria

We assessed studies including randomized controlled trials, clinical controlled trials, cohort studies, case-control studies, case series studies, and case reports about high flow nasal catheter and noninvasive positive pressure. The subjects met the diagnostic criteria of sepsis, and there was no significant difference in basic characteristics. The treatment group was high flow nasal catheter and the control group was noninvasive positive pressure ventilation. The routine treatment methods were the same. The outcome indicators included the rate of re intubation within 72 hours, ICU mortality, 28-day hospitalization mortality, adverse reactions, etc. There are no language restrictions.

1.2 Exclusion criteria

Other literatures that did not meet the inclusion criteria were excluded, such as no clinical reports, reviews, inconsistent research objectives, inconsistent interventions and repeated literatures.

1.3 Data extraction

According to the pre-established data extraction table, literature data were extracted and a unified data table was established using Excel 2013 (Microsoft, Redmond, Washington, USA), including author, year of publication, sample size, gender, age, underlying diseases, intervention measures, observation indicators, clinical results, etc.

1.4 Data processing

The re-intubation rate within 72 hours, ICU mortality and 28-day mortality were meta analyzed by Stata 13. 0.

2. Result

2.1 Literature screening

The search scheme of nasal catheter / high flow nasal catheter + noninvasive positive pressure ventilation + sepsis is adopted. The search words include similar phrases expressing the same meaning, such as "sepsis" [title / Abstract] and "nasal" [title / Abstract] and "noninvasive" [title / Abstract] and "ventilation" [title / Abstract] in PubMed. The retrieval time is from the establishment of the database to January 3, 2022. We searched the literature and read the title and abstract. The literatures that did not meet the inclusion criteria were excluded, the full text of the remaining literatures was read, and the retrospective studies, repeated studies, studies with inconsistent intervention measures, non controlled studies and other literatures were excluded. Finally, two studies were included^[5-6] (Figure 1)

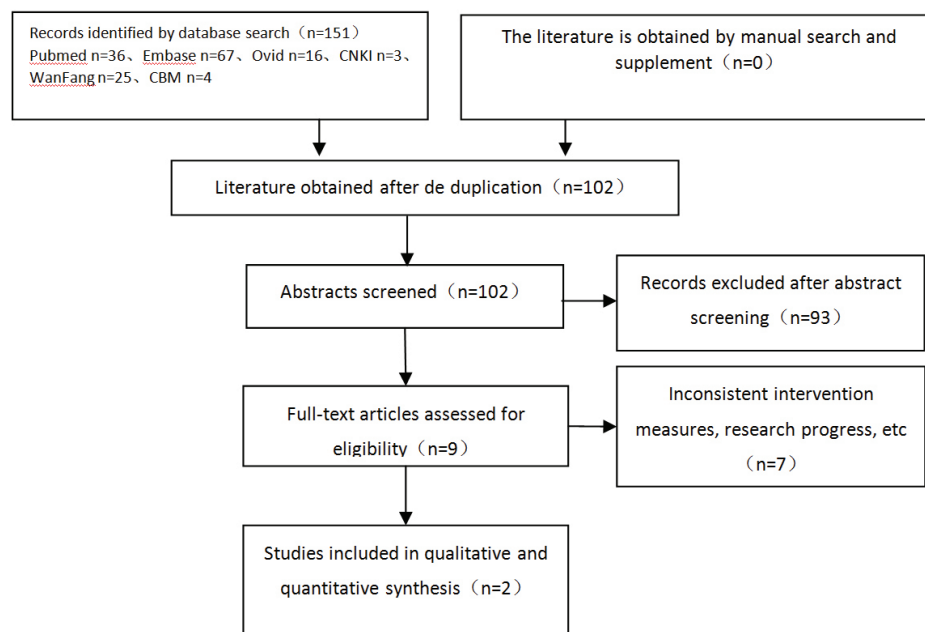


Figure 1 PRISMA flow chart of study selection

2.2 Effectiveness evaluation of high flow nasal catheter and noninvasive positive pressure ventilation

Two controlled studies on the clinical efficacy of HFNC and NPPV after extubation in patients with purulent respiratory failure were included (Xuan LZ et al. , 2021; Surat et al. , 2021), one from China and the other from Thailand. A total of 505 people were included in the study population, 279 in HFNC group and 226 in NPPV group. There was no significant difference between the two groups in demographic characteristics (age, gender, BMI, etc.), general clinical status at ICU admission, arterial blood gas index at extubation and before sequential treatment, APACHE II score, SOFA score or invasive MV time before extubation.

Both studies reported 72 hour reintubation rate, mortality during ICU and 28-day mortality in hospital. Meta analysis of 72 hour reintubation rate showed that there was no significant difference between high flow nasal catheter and noninvasive positive pressure ventilation[OR = 0. 94, 95% CI (0. 53, 1. 69), P > 0. 05]. (Figure 2)

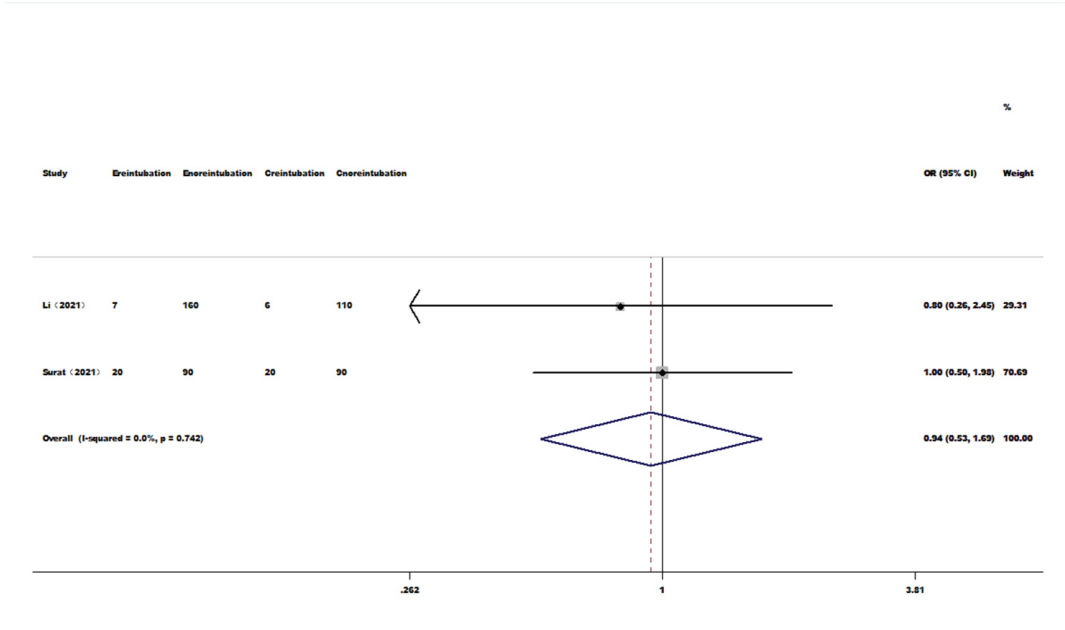


Figure 2 Meta analysis of 72h reintubation rate

Meta analysis of mortality during ICU showed that there was no significant difference between high flow nasal catheter and noninvasive positive pressure ventilation[OR = 1. 21, 95% CI (0. 49, 3. 02), P > 0. 05]. (Figure 3)

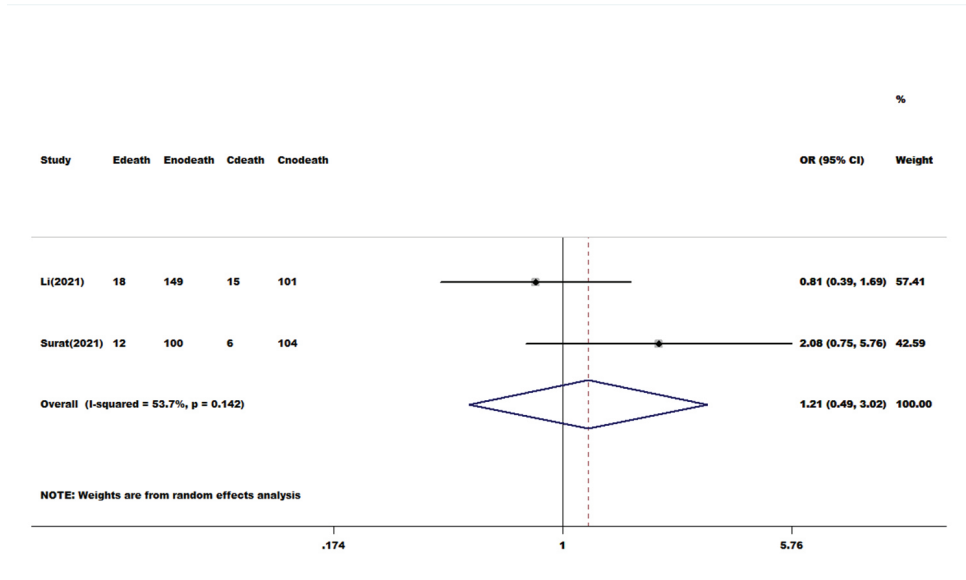


Figure 3 Meta analysis of mortality during ICU

Meta analysis of 28-day mortality in hospital showed that there was no significant difference between high flow nasal catheter and noninvasive positive pressure ventilation [OR = 0.96, 95% CI (0.55, 1.68), $P > 0.05$]. (Figure 4)

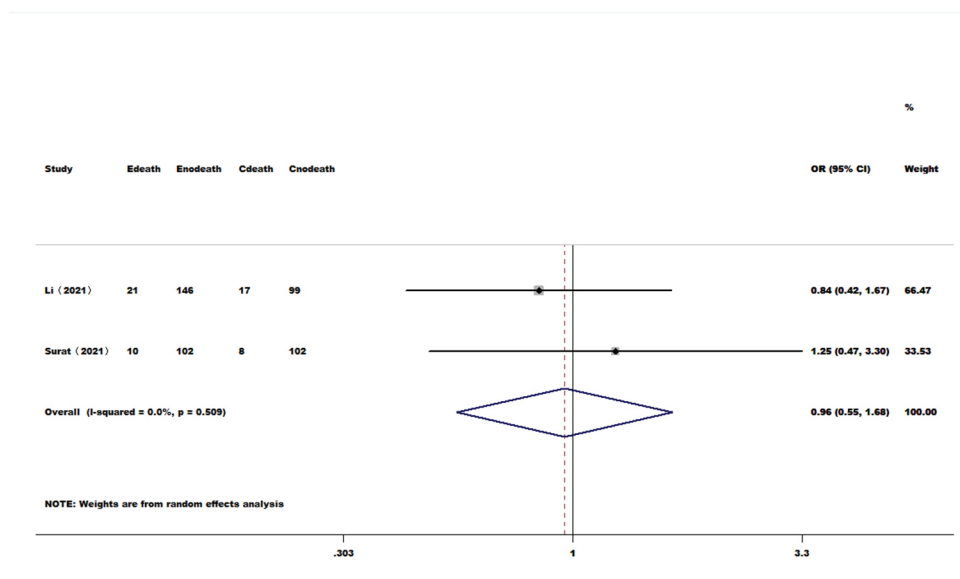


Figure 4 Meta analysis of mortality during ICU

So, there was no significant difference between HFNC and NPPV in the rate of reintubation 72 hours after extubation and the mortality 28-day after hospitalization in the treatment of sepsis induced respiratory failure.

3. Discussion

Respiratory support therapy is very important for the treatment of the patient who have sepsis induced respiratory failure after mechanical ventilation extubation. It can effectively reduce the rate of re intubation and mortality. The commonly used sequential respiratory support mode is NPPV. The research results of Stefano Nava^[7] et al. in 2005, Miquel Ferrer^[8] et al. in 2006 and Alexandre demoule^[9] et al. in 2015 show that the use of NPPV can avoid respiratory failure after extubation and reduce mortality. However, due to the poor comfort of NPPV, the use is limited. In recent years, HFNC has been widely used because of its comfort, convenience and effectiveness. Salvatore Maurizio Maggiore^[10] in 2014, Jean Pierre frat^[11-12] in 2015 and Gonzalo Hern á ndez^[13-14] in 2016 found that HFNC and NPPV can improve patients' shortness of breath and oxygenation index. HFNC is more comfortable than mask and patients have better tolerance. The expert consensus on the clinical standardized application of high flow nasal intubation oxygen therapy in adults published in 2020^[15] recommended that after weaning from mechanical ventilation and extubation, patients with a low risk of reintubation in the ICU, HFNC, patients with a high risk of reintubation in the ICU and weaning from mechanical ventilation after surgery, HFNC or NPPV. The campaign to save sepsis: international guidelines for sepsis and septic shock 2021^[16], jointly released by the American Society of critical care medicine and the European Society of critical care medicine, suggests that for adults with hypoxic respiratory failure caused by sepsis, we recommend using high fow nasal oxygen on the basis of noninvasive ventilation. However, there is no recommendation on the application of weaning extubation in the follow-up treatment of sepsis induced respiratory failure.

Through meta-analysis, this study found that there was no significant difference between HFNC and NPPV in the rate of re intubation 72 hours after extubation, mortality and 28-day mortality after hospitalization in the treatment of sepsis induced respiratory failure, which provided evidence-based basis for the application of HFNC in the follow-up treatment of sepsis induced respiratory failure. Due to the influence of the number of included studies, randomized control and the etiology of sepsis, the accuracy of the results of this study needs to be further confirmed by more high-quality clinical studies.

References

- [1] Xie J, Wang H, Kang Y, Zhou L, Liu Z, Qin B, Ma X, Cao X, Chen D, Lu W, Yao C, Yu K, Yao X, Shang H, Qiu H, Yang Y; CHinese Epidemiological Study of Sepsis (CHESS) Study Investigators. The Epidemiology of Sepsis in Chinese ICUs: A National Cross-Sectional Survey. Crit Care Med. 2020 Mar;48(3): e209-e218. doi: 10.1097/CCM.0000000000004155. PMID: 31804299.

- [2] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016 Feb 23;315(8):801-10. doi: 10. 1001/jama. 2016. 0287. PMID: 26903338; PMCID: PMC4968574.
- [3] Genga KR, Russell JA. Update of Sepsis in the Intensive Care Unit. *J Innate Immun*. 2017;9(5):441-455. doi: 10. 1159/000477419. Epub 2017 Jul 12. PMID: 28697503; PMCID: PMC6738902.
- [4] Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001 Jul;29(7):1303-10. doi: 10. 1097/00003246-200107000-00002. PMID: 11445675.
- [5] Xuan Lizhen, Ma Jiefei, Tao Jiale et al. Comparative study of high flow nasal catheter device and noninvasive positive pressure ventilation for sequential treatment in sepsis patients after weaning from mechanical ventilation in intensive care unit. [J]. *Ann Palliat Med*, 2021, 10: 6270-6278.
- [6] Tongyoo Surat, Tantibundit Porntipa, Daorattanachai Kiattichai et al. High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial. [J]. *Ann Intensive Care*, 2021, 11: 135.
- [7] Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A, Beltrame F, Navalesi P. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med*. 2005 Nov;33(11):2465-70. doi: 10. 1097/01. ccm. 0000186416. 44752. 72. PMID: 16276167.
- [8] Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med*. 2006 Jan 15;173(2):164-70. doi: 10. 1164/rccm. 200505-718OC. Epub 2005 Oct 13. PMID: 16224108.
- [9] Demoule A, Chevret S, Carlucci A, Kouatchet A, Jaber S, Meziani F, Schmidt M, Schnell D, Clergue C, Aboab J, Rabbat A, Eon B, Guérin C, Georges H, Zuber B, Dellamonica J, Das V, Cousson J, Perez D, Brochard L, Azoulay E; oVNI Study Group; REVA Network (Research Network in Mechanical Ventilation). Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. *Intensive Care Med*. 2016 Jan;42(1):82-92. doi: 10. 1007/s00134-015-4087-4. Epub 2015 Oct 13. PMID: 26464393.
- [10] Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, Montini L, De Gaetano A, Navalesi P, Antonelli M. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med*. 2014 Aug 1;190(3):282-8. doi: 10. 1164/rccm. 201402-0364OC. PMID: 25003980.
- [11] Frat JP, Brugiere B, Ragot S, Chatellier D, Veinstein A, Goudet V, Coudroy R, Petitpas F, Robert R, Thille AW, Girault C. Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation in acute respiratory failure: an observational pilot study. *Respir Care*. 2015 Feb;60(2):170-8. doi: 10. 4187/respcare. 03075. Epub 2014 Oct 7. PMID: 25294935.
- [12] Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottureau A, Devaquet J, Nseir S, Razazi K, Mira JP, Argaud L, Chakarian JC, Ricard JD, Wittebole X, Chevalier S, Herbland A, Fartoukh M, Constantin JM, Tonnelier JM, Pierrot M, Mathonnet A, Béduneau G, Delétage-Métreau C, Richard JC, Brochard L, Robert R; FLORALI Study Group; REVA Network. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015 Jun 4;372(23):2185-96. doi: 10. 1056/NEJMoa1503326. Epub 2015 May 17. PMID: 25981908.
- [13] Hernández G, Vaquero C, Colinas L, Cuenca R, González P, Canabal A, Sanchez S, Rodriguez ML, Villascargas A, Fernández R. Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial. *JAMA*. 2016 Oct 18;316(15):1565-1574. doi: 10. 1001/jama. 2016. 14194. Erratum in: *JAMA*. 2016 Nov 15;316(19):2047-2048. Erratum in: *JAMA*. 2017 Feb 28;317(8):858. PMID: 27706464.
- [14] Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, Laborda C, Colinas L, Cuenca R, Fernández R. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. *JAMA*. 2016 Apr 5;315(13):1354-61. doi: 10. 1001/jama. 2016. 2711. PMID: 26975498.
- [15] Xu JQ, Su LX, Yan P, Hu XS, Wen RX, Xiao K, Gu HJ, Xia JG, Sun B, Zhou QT, Dong YC, Liu JL, Pan PH, Luo H, Li Q, Song LQ, Xu SC, Li YM, Wang DX, Li D, Zhan QY, Xie LX; Pulmonary & Critical Care Medicine Group of Chinese

Thoracic Society/Pulmonary & Critical Care Medicine Committee of Chinese Association of Chest Physician. Expert consensus on clinical standardized application of high-flow nasal cannula oxygen therapy in adults. *Chin Med J (Engl)*. 2020 Jun 5;133(11):1322-1324. doi: 10. 1097/CM9. 0000000000000769. PMID: 32515918; PMCID: PMC7289301.

- [16] Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, McIntyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Wiersinga WJ, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Coz Yataco A, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Hylander Møller M, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, McGloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papatheanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J, Levy M. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med*. 2021 Nov 1;49(11): e1063-e1143. doi: 10. 1097/CCM. 0000000000005337. PMID: 34605781.