



HAL
open science

Pre-Emptive Noninvasive Ventilation to Facilitate Weaning from Mechanical Ventilation in Obese Patients at High Risk of Re-Intubation

Domenico Luca Grieco, Samir Jaber

► **To cite this version:**

Domenico Luca Grieco, Samir Jaber. Pre-Emptive Noninvasive Ventilation to Facilitate Weaning from Mechanical Ventilation in Obese Patients at High Risk of Re-Intubation. *American Journal of Respiratory and Critical Care Medicine*, In press, 10.1164/rccm.202111-2649ED . hal-03485796

HAL Id: hal-03485796

<https://hal.science/hal-03485796>

Submitted on 17 Dec 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Pre-Emptive Noninvasive Ventilation to Facilitate Weaning from Mechanical Ventilation in Obese Patients at High Risk of Re-Intubation

Domenico Luca Grieco MD^{1,2}, Samir Jaber MD, PhD³

1. Department of Emergency, Intensive Care Medicine and Anesthesia, Fondazione Policlinico Universitario A. Gemelli IRCCS; Rome, Italy.
2. Istituto di Anestesiologia e Rianimazione, Università Cattolica del Sacro Cuore Rome, Italy.
3. Department of Anesthesia and Intensive Care Unit, Regional University Hospital of Montpellier, St-Eloi Hospital, University of Montpellier, PhyMedExp, INSERM U1046, CNRS UMR, 9214, Montpellier Cedex 5, France

Correspondence to

Domenico Luca Grieco, MD

Email: dlgrieco@outlook.it

Department of Anesthesiology and Intensive Care Medicine, Catholic University of the Sacred Heart. Fondazione 'Policlinico Universitario A. Gemelli' IRCCS.

L.go F. Vito, 00168, Rome, Italy. Tel. +39 06 3015 4507

Author contribution

DLG and SJ drafted the editorial and agreed on submitting it to The American Journal of Respiratory and Critical Care Medicine.

Conflict of interests

DLG has received payments for travel expenses by Maquet, Getinge and Air Liquide, and disclose a research grant by General Electric Healthcare.

Funding

Not applicable.

Word count:

Weaning from mechanical ventilation and extubation are critical procedures in mechanically ventilated patients, as weaning failure and re-intubation occur in up to 10-30% of cases and are associated with increased mortality (1). Different tools have been proposed to prevent and treat post-extubation respiratory failure, but there is a substantial lack of final evidence regarding the optimal tool for the management of patients undergoing scheduled extubation in the intensive care unit.

While the uncontrolled use of pre-emptive noninvasive ventilation (NIV) using pressure support ventilation (PSV) with positive end-expiratory pressure (PEEP) in unselected cohorts of critically ill patients may lead to delayed re-intubation and worsen mortality (1), it may be of benefit as a bridge to full spontaneous breathing in hypercapnic patients and in selected cohorts of hypoxemic subjects at high risk of weaning failure (2).

Heated and humidified high-flow nasal oxygen (HFNC) appears as the optimal tool to administer oxygen to hypoxemic patients in the weaning phase (3, 4): HFNC allows accurate delivery of the set fraction of inspired oxygen, provides a low PEEP level (less than 5 cmH₂O) and reduces work of breathing by favouring CO₂ clearance from upper airways (5, 6). Pre-emptive HFNC has been shown to reduce the need for re-intubation in a large randomized trial when compared to low-flow oxygen after extubation critically ill patients at low risk of weaning failure (7), and seemed as effective as NIV in patients at high risk of weaning failure (8).

These data indicate that, in patients who have high risk of extubation failure, both HFNC and NIV are promising techniques and may finally improve clinically outcome (9). Further evidence regarding the best balance between these two techniques came from a recently published multicentre clinical trial, in which 641 critically ill patients showing at least one risk factor for extubation failure (i.e. age > 65 years, underlying chronic cardiac or lung disease - 50% of patients were recovering from respiratory failure) were randomly assigned to receive NIV alternating with HFNC or HFNC alone as pre-emptive treatments after scheduled extubation in the intensive care unit (8). NIV was delivered for sessions of at least 4 hours, with a minimal treatment duration of 12 hours per day in the initial 48 hours, and was applied through a face mask and specific settings: pressure support titrated to obtain an expiratory tidal volume between 6 and 8 ml/kg of predicted body weight and PEEP ranging between 5 and 10 cmH₂O.

Study results showed that the pre-emptive combined use of NIV and HFNC resulted in a lower rate of re-intubation at 7 days and in a lower incidence of post-extubation respiratory failure, as compared to HFNC alone.

Here, the authors report the results of a post-hoc analysis of the trial, in which inter-group differences in study outcomes were analyzed after classifying patients according to whether they were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$ - 206 patients), overweight ($25 \leq \text{BMI} < 30$ - 204 patients) or normal/underweight ($\text{BMI} < 25$ -213 patients)(10). The research question addressing the potential heterogeneity in NIV effects according to different BMI is sound, as obesity significantly interferes with the physiology of respiratory system: this may affect the effect of applied interventions (11, 12).

Study results showed that, in the subgroup of obese or overweight patients, the rate of re-intubation rate at day 7 was significantly lower in patients treated with NIV alternating with HFNC than in those who received HFNC alone: 7% (15/204) vs. 20% (41/206), with an absolute risk reduction of 13% and a number needed-to-treat of 8. This result was accompanied by significantly lower in-intensive care unit and 90-day mortality in patients treated with NIV alternating with HFNC.

Conversely, no intergroup difference in study outcomes were found in patients who had $\text{BMI} < 25 \text{ kg/m}^2$.

These results have a robust physiological rationale. Obesity is associated to increased absolute values of pleural pressure, which favours the development of atelectasis: atelectasis yield intrapulmonary shunt and consequent hypoxemia (11), which is the most frequent cause of extubation failure. Atelectasis may also cause reduction in lung and respiratory system compliance, which increases the muscle workload to generate an adequate tidal volume. PEEP, by counterbalancing pleural pressure, maintains positive transpulmonary pressure, prevents atelectasis due to alveolar collapse, and favours a more homogenous ventilation (11). Also, airway closure and expiratory flow limitation are magnified in obese patients (13, 14). Application of PEEP may reduce work of breathing by preventing airway closure and limiting the isometric muscle workload needed to generate inspiratory flow: this, together with the inspiratory assistance provided by pressure support, may reduce the occurrence muscle exhaustion, which is a frequent causes of weaning failure (15). From study results, it would be reasonable to suggest that,

contrarily to PSV that delivers an adequate sufficient positive insufflation pressure, HFNC generated a PEEP-effect which was insufficient to reopen collapsed alveoli and relieve respiratory muscles workload.

Finally, obese patients may show a lower risk of alveolar overdistension due to high alveolar pressure (11), which is major concern when NIV in the pressure support mode is applied in hypoxemic patients (16). This may have mitigated the risk of self-inflicted lung injury during NIV.

The authors must be commended for their effort in better understanding the results of their trial. The results of this study indicate the clinical benefit of an approach including pre-emptive NIV alternating with HFNC over HFNC alone after extubation in critically ill patients with at least one risk factor for re-intubation is magnified in and limited to patients who are overweight or obese.

Despite the non-prespecified post-hoc nature of the analysis, which makes the results hypothesis-generating rather than conclusive, we believe these results provide novel and relevant insights on the management of weaning from mechanical ventilation and represent an important step ahead towards the individualization of care in patients receiving mechanical ventilation. Further randomized controlled studies are needed to confirm these promising findings.

Acknowledgements

none

References

1. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguía C, González M, Epstein SK, Hill NS, Nava S, Soares M-A, D'Empaire G, Alía I, Anzueto A. Noninvasive positive-pressure ventilation for respiratory failure after extubation. *N Engl J Med* 2004;350:2452–60.
2. Vaschetto R, Longhini F, Persona P, Ori C, Stefani G, Liu S, Yi Y, Lu W, Yu T, Luo X, Tang R, Li M, Li J, Cammarota G, Bruni A, Garofalo E, Jin Z, Yan J, Zheng R, Yin J, Guido S, Della Corte F, Fontana T, Gregoretti C, Cortegiani A, Giarratano A, Montagnini C, Cavuto S, Qiu H, *et al.* Early extubation followed by immediate noninvasive ventilation vs. standard extubation in hypoxemic patients: a randomized clinical trial. *Intensive Care Med* 2019;45:62–71.
3. Rochweg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, Goligher EC, Jaber S, Ricard J-D, Rittayamai N, Roca O, Antonelli M, Maggiore SM, Demoule A, Hodgson CL, Mercat A, Wilcox ME, Granton D, Wang D, Azoulay E, Ouanes-Besbes L, Cinnella G, Rauseo M, Carvalho C, Dessap-Mekontso A, Fraser J, Frat J-P, Gomersall C, Grasselli G, *et al.* The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. *Intensive Care Med* 2020;46:2226–2237.
4. 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;190:282–8.
5. Grieco DL, Maggiore SM, Roca O, Spinelli E, Patel BK, Thille AW, Barbas CS V, de Acilu MG, Cutuli SL, Bongiovanni F, Amato M, Frat J-P, Mauri T, Kress JP, Mancebo J, Antonelli M. Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS. *Intensive Care Med* 2021;47:851–866.
6. Pennisi MA, Bello G, Congedo MT, Montini L, Nachira D, Ferretti GM, Meacci E, Gualtieri E, De Pascale G, Grieco DL, Margaritora S, Antonelli M. Early nasal high-flow versus Venturi

mask oxygen therapy after lung resection: a randomized trial. *Crit Care* 2019;23:68.

7. 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;315:1354–61.
8. Hernández G, Vaquero C, Colinas L, Cuenca R, González P, Canabal A, Sanchez S, Rodriguez ML, Villasclaras 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;316:1565–1574.
9. Fernando SM, Tran A, Sadeghirad B, Burns KEA, Fan E, Brodie D, Munshi L, Goligher EC, Cook DJ, Fowler RA, Herridge MS, Cardinal P, Jaber S, Møller MH, Thille AW, Ferguson ND, Slutsky AS, Brochard LJ, Seely AJE, Rochwerg B. Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis. *Intensive Care Med* 2021;doi:10.1007/s00134-021-06581-1.
10. Thille AW, Coudroy R, Nay M-A, Gacouin A, Decavéle M, Sonnevile R, et al. Beneficial Effects of Non-Invasive Ventilation After Extubation in Obese or Overweight Patients: A Post-Hoc Analysis of a Randomized Clinical Trial. *Am J Respir Crit Care Med* [online ahead of print] 23 November 2021; <https://www.atsjournals.org/doi/abs/10.1164/rccm.202106-1452OC>.
11. Teggia Droghi M, De Santis Santiago RR, Pinciroli R, Marrazzo F, Bittner EA, Amato MBPP, Kacmarek RM, Berra L, Droghi MT, De Santis Santiago RR, Pinciroli R, Marrazzo F, Bittner EA, Amato MBPP, Kacmarek RM, Berra L. High Positive End-Expiratory Pressure Allows Extubation of an Obese Patient. *Am J Respir Crit Care Med* 2018;198:524–525.
12. De Jong A, Wrigge H, Hedenstierna G, Gattinoni L, Chiumello D, Frat J-P, Ball L, Schetz M, Pickkers P, Jaber S. How to ventilate obese patients in the ICU. *Intensive Care Med* 2020;46:2423–2435.

13. Volta CA, Dalla Corte F, Ragazzi R, Marangoni E, Fogagnolo A, Scaramuzza G, Grieco DL, Alvisi V, Rizzuto C, Spadaro S. Expiratory flow limitation in intensive care: prevalence and risk factors. *Crit Care* 2019;23:395.
14. Junhasavasdikul D, Telias I, Grieco DL, Chen L, Gutierrez CM, Piraino T, Brochard L. Expiratory Flow Limitation During Mechanical Ventilation. *Chest* 2018;154:948–962.
15. Dres M, Similowski T, Goligher EC, Pham T, Sergenyuk L, Telias I, Grieco DL, Ouechani W, Junhasavasdikul D, Sklar MC, Damiani LF, Melo L, Santis C, Degraivi L, Decavèle M, Brochard L, Demoule A. Dyspnoea and respiratory muscle ultrasound to predict extubation failure. *Eur Respir J* 2021;58(5):2100002.
16. Grieco DL, Menga LS, Eleuteri D, Antonelli M. Patient self-inflicted lung injury: implications for acute hypoxemic respiratory failure and ARDS patients on non-invasive support. *Minerva Anestesiol* 2019;85:1014–1023.