Noninvasive ventilation for acute respiratory distress syndrome: the importance of ventilator settings

Mauro R. Tucci¹, Eduardo L. V. Costa^{1,2}, Maria A. M. Nakamura¹, Caio C. A. Morais¹

¹Respiratory ICU, Pulmonary Division, Heart Institute (INCOR), Hospital das Clínicas, University of São Paulo, São Paulo, Brazil; ²Research and Education Institute, Hospital Sírio-Libanês, São Paulo, Brazil

Correspondence to: Mauro R. Tucci, MD, PhD. Laboratório de Investigação Médica 09 (LIM-09), University of São Paulo School of Medicine, Av. Dr. Arnaldo 455, 2° andar, sala 2144, CEP 01246-903, São Paulo, SP, Brazil. Email: mrotucci@gmail.com.

Abstract: Noninvasive ventilation (NIV) is commonly used to prevent endotracheal intubation in patients with acute respiratory distress syndrome (ARDS). Patients with hypoxemic acute respiratory failure who fail an NIV trial carry a worse prognosis as compared to those who succeed. Additional factors are also knowingly associated with worse outcomes: higher values of ICU severity score, presence of severe sepsis, and lower ratio of arterial oxygen tension to fraction of inspired oxygen. However, it is still unclear whether NIV failure is responsible for the worse prognosis or if it is merely a marker of the underlying disease severity. There is therefore an ongoing debate as to whether and which ARDS patients are good candidates to an NIV trial. In a recent paper published in $\mathcal{J}AMA$, "Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients with Acute Respiratory Distress Syndrome: A Randomized Clinical Trial", Patel *et al.* evaluated ARDS patients submitted to NIV and drew attention to the importance of the NIV interface. We discussed their interesting findings focusing also on the ventilator settings and on the current barriers to lung protective ventilation in ARDS patients during NIV.

Keywords: Noninvasive ventilation (NIV); respiratory distress syndrome; adult; respiratory insufficiency

Submitted Jul 23, 2016. Accepted for publication Aug 02, 2016. doi: 10.21037/jtd.2016.09.29 View this article at: http://dx.doi.org/10.21037/jtd.2016.09.29

Noninvasive ventilation (NIV) is a well-established treatment for acute respiratory failure (1), especially in patients with hypercapnia (2) and cardiogenic pulmonary edema (3). Conversely, the use of NIV for hypoxemic respiratory failure, including the acute respiratory distress syndrome (ARDS), is still controversial (4-12). Avoidance of NIV in these patients is often justified by the association between a failed NIV attempt with worse prognosis (8,11-13). In these studies, however, it is unclear whether NIV failure was responsible for the worse prognosis (a causal association, likely by delaying intubation) or if it was merely a marker of the underlying disease severity, such as severe sepsis, higher SAPS-II score, and lower arterial partial pressure of oxygen to inspired fraction ratio (PF-ratio) (8,14,15). A recent study showed similar adjusted outcomes in patients who failed a trial of NIV as compared to patients primarily intubated, supporting the non-causal association hypothesis (14).

Despite the debatable recommendation, NIV is regularly used for hypoxemic respiratory failure (13). Specifically for ARDS patients, a recent study (16) showed that NIV was used in 14.4% of patients (436 of 3,022), with 69% of them (300 of 436) being exclusively managed with NIV. These numbers highlight the importance of the topic, on which there is scarce literature.

In a recent study, Patel *et al.* (17) brought to attention the importance of the NIV interface in the outcome of ARDS patients. In this single-center trial, interrupted early for efficacy, 83 ARDS patients requiring NIV by face mask for at least 8 hours were randomized to NIV by helmet or to continue with the face mask. In the helmet group, intubation rate (the primary endpoint) was less than a third that in the face-mask group (18.2% *vs.* 61.5%). The lower intubation rate was associated with more ventilator-free days and lower mortality.

Journal of Thoracic Disease, Vol 8, No 9 September 2016

Can we attribute all of this expressive difference in outcome solely to the interface? To be able to address this question, it can be useful to examine the results more closely. The most common reason for intubation was tachypnea and hypoxemia (83.3% for the face mask vs. 37.5% for the helmet). Positive end-expiratory pressure (PEEP), a ventilatory setting used to avert hypoxemia, was set 3 cmH₂O higher in the helmet group [median of 8.0 (5.0-10.0) vs. 5.1 (5.0-8.0) cmH₂O]. This could explain at least in part the significant reduction in the intubation rate in the helmet group. In their discussion, the authors argued that, in the facemask group, patient intolerance and excess air leaks limited the titration of PEEP to higher levels. Curiously, pressure support levels were 3 cmH₂O higher in the face-mask group leading to comparable total inspiratory pressures (~16 cmH₂O) between groups. It is true that the helmet interface has been associated with better tolerance in some studies (18). On the other hand, other authors (19,20) have been able to deliver even higher inspiratory pressures ($\geq 20 \text{ cmH}_2\text{O}$) through face masks with good tolerance (19). Of note, one study showed that the amount of leak was related to the total inspiratory pressure, not the PEEP (19). In that study, either a low PEEP (5 cmH₂O) and high pressure support (15 cmH₂O) or a high PEEP (10 cmH₂O) and low pressure support (10 cmH₂O) were both well tolerated and associated with similar measured leaks (~36%). In Patel's study, subjective decisions regarding patient comfort and excess leaks might have influenced the results. More stringent criteria for the definition of patient tolerance and acceptable leaks would have been welcome.

Several studies (21-23) have shown that using the helmet interface predisposes to CO₂ rebreathing due to its increased internal volume. In fact, the helmet works as a semi-closed system, and the degree of CO₂ rebreathing depends basically on the amount of fresh gas (on top of the patient minute ventilation) and the CO_2 production by the patient (21). For example, in a study by Taccone et al. (21) in normal volunteers with high flow rates of fresh gas (60 L/min), the inspired pressure of CO₂ (PiCO₂) was on average 2.5 mmHg; with a flow rate of fresh gas of 10 L/min, the average PiCO₂ was 13.7 mmHg, an amount of rebreathing similar to that obtained with a critical care ventilator (average PiCO₂ of 12.4 mmHg) such as the one used in the Patel's study (17). Bear in mind that the flow rate of fresh gas has to be on top of the patients' minute volume. This quantity is also known as bias flow and is settable in some mechanical ventilators within a prespecified range. In the mechanical ventilator used in Patel's study, this quantity is limited to 10 L/min and is unrelated

with the peak inspiratory flow displayed by the ventilator. It is the bias flow and not the inspiratory flow the quantity that matters for the rebreathing of CO_2 , what suggests that there was considerable rebreathing in Patel's study.

Having said this, how can we reconcile the likely relevant dead space ventilation in the helmet group with the decreased respiratory rate (24.5 vs. 29.1 bpm in the face mask group) together with lower pressure support levels (8 vs. 11 cmH₂O in the face mask group)? Once more, we believe that the higher PEEP values in the helmet group might have been the key. Higher PEEP levels can promote recruitment of alveolar units leading to both decreased shunt and decreased shunt dead space ventilation. In other words, it is possible that the higher PEEP levels were responsible not only for better oxygenation (and thus lower intubation rate), but also for improved CO₂ elimination.

Perhaps one the most important contributions of Patel's study was to emphasize that protective ventilation is as important during NIV as it is during invasive mechanical ventilation (24,25) in patients with hypoxemic respiratory failure. Lung-protective strategies were an important development in the treatment of patients with ARDS. Such strategies improve survival combining the use of low tidal volumes, low plateau pressures, and high PEEP values (24,25). Unlike patients under invasive mechanical ventilation, for whom there are established protective ventilation protocols, NIV currently lacks ventilation protocols directed to avoid the mechanisms of ventilator-induced lung injury. This is perhaps one of the major difficulties of the use of NIV in patients with ARDS. As a result, non-protective settings are commonly used. For example, tidal volumes greater than 10 mL per kilogram of predicted body weight were used in over half the patients included in a recent European cohort of acutely hypoxemic patients (26). In that study, tidal volume was a strong predictor of NIV failure, suggesting that close monitoring of tidal volume is important. In patients with persistently high tidal volumes, early invasive ventilation might be a reasonable option to avoiding ventilator induced lung injury.

In Patel's study, besides higher PEEP levels in the helmet group, driving pressure was also lower, settings again consistent with a lung-protective strategy. Amato *et al.* (27), analyzing data from previously published trials of protective ventilatory strategies in ARDS, recently demonstrated that driving pressure (plateau pressure minus PEEP) was the variable most closely related to survival. This finding was later confirmed in a large prospective study in patients with ARDS (16) and also in patients (28) undergoing mechanical

E984

ventilation for general anesthesia, in whom lower driving pressures during the intraoperative period were associated with less postoperative pulmonary complications. A word of caution, though, in actively breathing patients, driving pressure is usually underestimated because of the unmeasured force exerted by the respiratory muscles.

The findings of Patel's study highlight the importance to devise an NIV protocol specific for patients with hypoxemic respiratory failure. In hypercapnic respiratory failure, the protocol usually consists of the application of enough pressure support to improve alveolar hypoventilation and to unload the respiratory muscles, usually in combination with low values of PEEP until the underlying condition resolves (29). In hypoxemic respiratory failure, the main goals are to improve oxygenation, to unload the respiratory muscles, and to relieve dyspnea (19). The first goal can usually be achieved by using higher PEEP levels to recruit and stabilize previously collapsed lung tissue. Therefore, PEEP is the main factor to improve oxygenation and we believe that its setting should take precedence as it could reduce the need for high inspiratory pressures. Moreover, optimization of PEEP can result in reduced tidal recruitment, improved dead space, and decreased inspiratory effort leading to lower tidal volumes (30-34). Tidal volumes need to be monitored, and pressure support levels, adjusted accordingly to avoid tidal volumes over 8 mL per kilogram of predicted body weight. Driving pressures should be kept low (note that-in the presence of respiratory muscle effort-driving pressures are underestimated). In the inability to follow these basic protective principles, intubation should be considered.

An additional and potentially valuable resource to improve oxygenation is lung recruitment, a maneuver seldom used during NIV (31,35). For example, Cammarota *et al.* (35) used the helmet to deliver a CPAP of 10 cmH₂O, which was transiently increased to 25 cmH₂O for 8 s to recruit the lungs. This recruitment was associated with a 37% improvement in oxygenation (from a PF-ratio of 225 to 308 mmHg).

In conclusion, the findings of Patel's study suggest that, in patients with ARDS, NIV settings consistent with the principles of a protective ventilatory strategy produced better, clinically relevant outcomes. Use of NIV interfaces less prone to leakage may facilitate the application of lung-protective ventilation protocols for hypoxemic respiratory failure.

Acknowledgements

MA Nakamura is supported by a grant from FAPESP;

CC Morais and MR Tucci are supported by a grant from CAPES (Coordination for the Improvement of Higher Level Personnel).

Footnote

Provenance: This is an invited Perspective commissioned by the Section Editor Zhongheng Zhang (Department of Critical Care Medicine, Jinhua Municipal Central Hospital, Jinhua Hospital of Zhejiang University, Jinhua, China). *Conflicts of Interest:* The authors have no conflicts of interest to declare.

Comment on: Patel BK, Wolfe KS, Pohlman AS, *et al.* Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 2016;315:2435-41.

References

- Cabrini L, Landoni G, Oriani A, et al. Noninvasive ventilation and survival in acute care settings: a comprehensive systematic review and metaanalysis of randomized controlled trials. Crit Care Med 2015;43:880-8.
- Brochard L, Mancebo J, Wysocki M, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med 1995;333:817-22.
- Peter JV, Moran JL, Phillips-Hughes J, et al. Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis. Lancet 2006;367:1155-63.
- Barbas CS, Serpa Neto A. New puzzles for the use of noninvasive ventilation for immunosuppressed patients. J Thorac Dis 2016;8:E100-3.
- Curley GF, Laffy JG, Zhang H, et al. Noninvasive respiratory support for acute respiratory failure-high flow nasal cannula oxygen or non-invasive ventilation? J Thorac Dis 2015;7:1092-7.
- Del Sorbo L, Jerath A, Dres M, et al. Non-invasive ventilation in immunocompromised patients with acute hypoxemic respiratory failure. J Thorac Dis 2016;8:E208-16.
- Beitler JR, Owens RL, Malhotra A. Unmasking a Role for Noninvasive Ventilation in Early Acute Respiratory Distress Syndrome. JAMA 2016;315:2401-3.
- 8. Antonelli M, Conti G, Esquinas A, et al. A multiplecenter survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory

Journal of Thoracic Disease, Vol 8, No 9 September 2016

distress syndrome. Crit Care Med 2007;35:18-25.

- Zhan Q, Sun B, Liang L, et al. Early use of noninvasive positive pressure ventilation for acute lung injury: a multicenter randomized controlled trial. Crit Care Med 2012;40:455-60.
- Hilbert G, Vargas F, Boyer A, et al. Starting point to embark on a widespread use of noninvasive positive pressure ventilation in acute lung injury or early acute respiratory distress syndrome? Crit Care Med 2012;40:669-71.
- Rana S, Jenad H, Gay PC, et al. Failure of non-invasive ventilation in patients with acute lung injury: observational cohort study. Crit Care 2006;10:R79.
- Agarwal R, Aggarwal AN, Gupta D. Role of noninvasive ventilation in acute lung injury/acute respiratory distress syndrome: a proportion meta-analysis. Respir Care 2010;55:1653-60.
- Schnell D, Timsit JF, Darmon M, et al. Noninvasive mechanical ventilation in acute respiratory failure: trends in use and outcomes. Intensive Care Med 2014;40:582-91.
- Meeder AM, Tjan DH, van Zanten AR. Noninvasive and invasive positive pressure ventilation for acute respiratory failure in critically ill patients: a comparative cohort study. J Thorac Dis 2016;8:813-25.
- 15. Thille AW, Contou D, Fragnoli C, et al. Non-invasive ventilation for acute hypoxemic respiratory failure: intubation rate and risk factors. Crit Care 2013;17:R269.
- Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA 2016;315:788-800.
- Patel BK, Wolfe KS, Pohlman AS, et al. Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 2016;315:2435-41.
- Esquinas Rodriguez AM, Papadakos PJ, Carron M, et al. Clinical review: Helmet and non-invasive mechanical ventilation in critically ill patients. Crit Care 2013;17:223.
- L'Her E, Deye N, Lellouche F, et al. Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med 2005;172:1112-8.
- Schettino GP, Tucci MR, Sousa R, et al. Mask mechanics and leak dynamics during noninvasive pressure support ventilation: a bench study. Intensive Care Med 2001;27:1887-91.
- 21. Taccone P, Hess D, Caironi P, et al. Continuous positive airway pressure delivered with a "helmet": effects on carbon

dioxide rebreathing. Crit Care Med 2004;32:2090-6.

- 22. Vargas F, Thille A, Lyazidi A, et al. Helmet with specific settings versus facemask for noninvasive ventilation. Crit Care Med 2009;37:1921-8.
- Costa R, Navalesi P, Spinazzola G, et al. Influence of ventilator settings on patient-ventilator synchrony during pressure support ventilation with different interfaces. Intensive Care Med 2010;36:1363-70.
- Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998;338:347-54.
- 25. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342:1301-8.
- Carteaux G, Millán-Guilarte T, De Prost N, et al. Failure of Noninvasive Ventilation for De Novo Acute Hypoxemic Respiratory Failure: Role of Tidal Volume. Crit Care Med 2016;44:282-90.
- Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372:747-55.
- Neto AS, Hemmes SN, Barbas CS, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. Lancet Respir Med 2016;4:272-80.
- Nava S, Carlucci A. Non-invasive pressure support ventilation in acute hypoxemic respiratory failure: common strategy for different pathologies? Intensive Care Med 2002;28:1205-7.
- Barbas CS, de Matos GF, Pincelli MP, et al. Mechanical ventilation in acute respiratory failure: recruitment and high positive end-expiratory pressure are necessary. Curr Opin Crit Care 2005;11:18-28.
- 31. Pincelli MP, Park M, Jardim C, et al. Which positive end expiratory pressure (PEEP) should be used during noninvasive positive pressure ventilation (NPPV) in acute lung injury/acute respiratory distress syndrome (ALI/ ARDS) patients? Crit Care 2004;8:S5.
- 32. Yoshida T, Roldan R, Beraldo MA, et al. Spontaneous Effort During Mechanical Ventilation: Maximal Injury With Less Positive End-Expiratory Pressure. Crit Care Med 2016;44:e678-88.
- 33. Vovk A, Binks AP. Raising end-expiratory volume relieves

E986

Tucci et al. Ventilator settings during NIV for ARDS

air hunger in mechanically ventilated healthy adults. J Appl Physiol (1985) 2007;103:779-86.

34. Corley A, Caruana LR, Barnett AG, et al. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Br J Anaesth 2011;107:998-1004.

Cite this article as: Tucci MR, Costa EL, Nakamura MA, Morais CC. Noninvasive ventilation for acute respiratory distress syndrome: the importance of ventilator settings. J Thorac Dis 2016;8(9):E982-E986. doi: 10.21037/jtd.2016.09.29 35. Cammarota G, Vaschetto R, Turucz E, et al. Influence of lung collapse distribution on the physiologic response to recruitment maneuvers during noninvasive continuous positive airway pressure. Intensive Care Med 2011;37:1095-102.