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EDITORIAL

Non-invasive ventilation in hypoxemic acute respiratory failure: is it still possible?

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In the past 20 years, the use of non-invasive ventilation (NIV) has dramatically increased for the management of acute respiratory failure (ARF) in critically ill patients [1, 2]. Non-invasive ventilation has been demonstrated to be beneficial for the outcome of patients with acute exacerbation of chronic obstructive pulmonary disease, acute cardiogenic pulmonary oedema, and more recently in the weaning/post-extubation management oe ARF. Non-invasive ventilation can also prevent intubation in selected patients with severe hypoxemic or de novo ARF [3], particularly in the postoperative period [4]. However, its clinical benefit remains controversial for the management of hypoxemic patients [5]. Therefore, NIV is not routinely recommended in this last indication [6], and has also been recently questioned in immunocompromised ARF patients [7].

In fact, several factors (Table 1) may explain the discrepancy of NIV results in hypoxemic ARF, with a failure rate (intubation) ranging from 25 to 60% [3] and an intensive care unit (ICU) mortality rate after intubation reaching up to 60% [8]. Heterogeneity in the underlying aetiology and severity of ARF is probably one of the main confounding factors. All these determinants, therefore, should be considered in the respective interpretation of study results.

In addition, high-flow nasal oxygen (HFNO) has been recently developed in adult ICUs [9, 10]. A multicentre randomized trial conducted in hypoxemic ARF patients has shown that NIV, compared with standard oxygen therapy and HFNO, was related to higher intubation and mortality rates, particularly in more severely hypoxemic patients [11]. Similar results were confirmed whatever the underlying severity of hypoxemia in a post hoc analysis of immunocompromised patients of the previous study [12]. In the same way, another multicentre randomized trial did not show any benefit of NIV compared with oxygen therapy (standard or HFNO) in immunocompromised patients with hypoxemic ARF [13]. These observations have to be interpreted cautiously, since NIV in these trials was used for short median periods of time in patients allocated to this treatment [11, 13]. An additional explanation for these adverse outcomes in hypoxemic ARF could be, as for invasive mechanical ventilation, the potential promotion of ventilator-induced lung injuries, because of a higher expired tidal volume and transpulmonary pressure than expected under NIV [11, 12, 14]. In fact, if not applied in an optimal way, NIV could lead to deleterious effects.

Despite all these concerns, recent epidemiological data show that NIV is routinely used in patients with hypoxemic ARF and can be applied as first-line ventilatory support in 15–30% of them, including ARDS patients [1, 2, 15]. NIV failure is no longer related to increased mortality in daily practice [1]. Moreover, a success rate of more than 50% can be expected in ARDS patients with rapid improvement in oxygenation [15], and helmet interface has been recently found better than facemask for improving outcome with NIV in patients with moderate to severe ARDS [16].

Therefore based on the previous conflicting data, if NIV is attempted in hypoxemic ARF, there is an absolute need for better identification of early predictors of NIV failure to avoid delaying intubation and improve outcome, and even to choose another respiratory support such as HFNO if required.

In a recent article in this journal, Duan and co-workers [17] presented the HACOR score (heart rate, acidosis, consciousness, oxygenation, respiratory rate), based

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Table 1 Main factors to consider in the discrepancy of NIV results applied in hypoxemic ARF

Patient-related factors
Underlying disease
Immunocompetent vs. immunocompromised patient
In immunocompromised patients:
Cause of immunosuppression
Immunosuppressive treatments received
Co-morbidities
Etiology of ARF
Infectious pneumonia
Interstitial pneumonia
Inhalation
ARDS
Atelectasis
Pulmonary embolism
Post-operative ARF
Trauma
Severity of ARF
Clinical features including respiratory rate and respiratory muscles involvement
Degree of hypoxaemia (mild/moderate/severe ARDS)
Severity of the critical illness
SAPS 2, APACHE 2, SOFA score or others
Device and settings-related factors
Ventilators
ICU vs. dedicated NIV ventilators
Bilevel positive airway pressure modes vs. CPAP mode or others
Settings
Level of PEEP
Targeted expired tidal volume (inspiratory pressure)
Interfaces
Facial (oro-nasal) vs. nasal mask or helmet
Timing of NIV initiation in the course of ARF
Early vs. late
Team experience and location
ICU, RICU vs. general wards

ARF acute respiratory failure, *ARDS* acute respiratory distress syndrome, *SAPS* simplified acute physiology score, *APACHE* acute physiologic and chronic health evaluation, *SOFA* sequential organ failure assessment, *ICU* intensive care unit, *RICU* respiratory intensive care unit, *NIV* non-invasive ventilation, *CPAP* continuous positive airway pressure, *PEEP* positive end-expiratory pressure

on five variables easily assessed in the emergency room, to predict, in patients with hypoxemic ARF treated with NIV, the need for intubation. The score was first tested and subsequently validated in two cohorts of patients.

The different influence of these variables in predicting NIV failure is reflected in this score. Decreased consciousness is the most relevant one, with a maximal score of 10 points, followed by decreased oxygenation with 6 points, acidosis and increased respiratory rate with 4 points each. Increased heart rate is less relevant, with a maximal score of 1 point. Overall, the HACOR score can range between 0 and 25 points.

The accuracy of this score in predicting NIV failure is substantially better than any of its single variables. The authors found that 5 points is the optimal cut-off value, with the best balance of sensitivity and specificity. This optimal value and the predictive capacity for this outcome are similar at different time points from NIV initiation to 48 h thereafter. It results in an overall accuracy higher than 80%, particularly after 1 h of treatment. Additionally, the progressive decrease of this score after NIV initiation is associated with successful treatment, while the lack of improvement is strongly associated with NIV failure.

This study found that in patients who fail NIV treatment, the early intubation (after $\leq$12 h of NIV treatment) is associated with nearly 50% reduced risk of death compared with those patients intubated after >12 h of NIV treatment. This association of late NIV failure with higher mortality has already been reported in patients with de novo ARF [8, 18]. Patients who will exhibit early NIV failure can be detected as early as at NIV initiation or after 1 h of treatment, since the HACOR score is significantly higher in patients with early than in those with late NIV failure.

One limitation in using this score alone is that it does not take into account the underlying cause of hypoxemic ARF. Similar to previous reports [19, 20], ARDS or cancer patients were associated with more frequent NIV failure, while heart failure was associated with less frequent treatment failure and pneumonia with an intermediate failure rate.

The HACOR score is not expected to reduce the rate of NIV failure of patients with hypoxemic ARF. However, higher values at NIV initiation and the lack of improvement of this score after 1 h of treatment constitute a strong indicator to proceed early to intubation of these patients in order to avoid the excess mortality associated with late intubation. If clinicians combine the assessment of this score with the underlying cause of hypoxemic ARF, the HACOR score may help to improve the clinical management of these patients.

Finally, applying NIV in hypoxemic ARF is probably still possible in well-selected patients and experienced centres [18], provided ICU clinicians pay particular attention to the ventilator settings (expired tidal volume) [9, 10, 12] or, if experienced, possibly use a helmet as interface [15]. Under these conditions, the new HACOR score could be very useful to avoid unduly delaying the intubation time and increasing mortality, particularly in more severe patients. For the future, whether the diagnostic accuracy of this simple bedside score could perform as well with HFNO remains to be demonstrated.

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