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Noninvasive ventilation for weaning in hypoxemic respiratory failure: not ready for prime time

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Once patients have been intubated during an episode of acute respiratory failure, physicians must work diligently to extubate them successfully as soon as possible [1]. Ignoring this fundamental tenet exposes patients to unnecessary morbidity and mortality [1–3]. The three components of management include treatment of the cause of respiratory failure, measurement of weaning predictors, and trials of unassisted breathing [4] (Fig. 1).

What should intensivists do when the episode of respiratory failure is resolving—or has resolved—and weaning predictors suggest that a patient is not ready for a weaning trial? What should physicians do if weaning predictors suggest that a patient is ready for a weaning trial but the patient fails the trial?

In patients recovering from hypercapnic respiratory failure, intensivists have two choices. They may continue invasive mechanical ventilation until patients can be extubated [5]. In selected cases, intensivists may extubate patients straight away and immediately institute noninvasive mechanical ventilation (NIV) [6, 7]. In contrast, for patients recovering from hypoxemic respiratory failure intensivists have one choice: continue invasive mechanical ventilation until extubation [8]. In the current issue of *Intensive Care Medicine*, Vaschetto et al. [9] raise the possibility that intensivists may have a second choice: the use of NIV to facilitate discontinuation of invasive mechanical ventilation.

The pilot study by Vaschetto et al. [9] was designed to test the feasibility of using NIV to facilitate weaning in patients with resolving acute hypoxemic respiratory failure. Ten patients were randomized to invasive pressure support (PS, control group) and ten were randomized to noninvasive PS (NIV group). In either case, patients underwent a trial of weaning when positive end expiratory pressure (PEEP) was 8 cmH₂O, PS was 10 cmH₂O, and partial pressure of oxygen (PaO₂) to fractional inspiratory oxygen (FiO₂) ratio was greater than 250 mmHg. In the NIV group, weaning trials consisted of 30 min of patients breathing on their own while solely receiving supplemental O₂. In the control group, trials consisted of 30 min of PS set at 5 cmH₂O plus 5 cmH₂O of PEEP. At the conclusion of the investigation, the two groups were equivalent in terms of arterial blood gas, success of extubation, septic complications, ICU length of stay, and mortality. Twenty-eight days after randomization, the mean (SD) number of days of invasive ventilation were less in the NIV group (10 ± 9 days) than in the control group (20 ± 8 days). The number of days of any ventilator support, however, was not different in the two groups.

What should we make of these results? Should we start using NIV in patients recovering from hypoxemic

Fig. 1 Schematic representation of the clinical course of patients affected by acute respiratory failure (ARF) receiving invasive mechanical ventilation. Early in the clinical course the etiology responsible for ARF is dynamic (*left circle*). The partial pressure of oxygen to fractional inspiratory oxygen ratio (PaO₂/FiO₂) is low and pulmonary mechanics are severely restricted. Most of these patients would die unless invasive mechanical ventilation is

not promptly instituted. Patients who survive the initial insult can experience various degrees of recovery (*large right circle*). In some of these patients, weaning parameters are satisfactory, and most of them are successfully extubated. Whether noninvasive mechanical ventilation should be used in patients recovering from an episode of ARF who have satisfactory or unsatisfactory weaning parameters remains to be determined

respiratory failure? At this time, the answer is no. First, as recognized by the investigators, this pilot study was not designed to provide outcome data. Second, and more importantly, the heterogeneity in the patients and the different weaning strategies used in the intervention and control groups make it impossible to state whether NIV can facilitate weaning in patients with resolving hypoxemic respiratory failure.

Acute hypoxemic respiratory failure can be caused by a diverse group of diseases [8]. In the current investigation [9], 40 % of patients randomized to NIV (and 50 % of controls) had respiratory failure caused by trauma. It is known that trauma patients can respond favorably to NIV [8, 10]. In most of the remaining patients, respiratory failure was caused by pneumonia, acute lung injury, or acute respiratory distress syndrome. Respiratory failure caused by any of these three etiologies usually responds poorly to NIV [8]. Unfortunately, Vaschetto et al. [9] do not specify whether the positive results with NIV were driven by their trauma patients or not.

In the Italian study [9], the time for successful discontinuation of invasive and noninvasive ventilation after randomization ranged from zero to 25 days. That is, some patients were ready for unsupported breathing on study enrolment. Including these patients in the study cannot

clarify whether NIV may facilitate discontinuation of mechanical ventilation in hypoxemic respiratory failure.

In the investigation by Vaschetto et al. [9], once a target PS was reached, patients in the control group underwent PS weaning. When the same target PS was reached in the NIV group, however, PS was discontinued and patients did breathe on their own while solely receiving supplemental O₂. These choices could have prolonged the duration of weaning in the control group for two reasons. First, PS wean can lengthen the weaning period compared to T tube trials [11]. Second, the study was not blinded: investigators were responsible for titration of PS and for starting PS wean as well. This could have introduced a bias towards a more conservative weaning approach in the control group.

Where does all this leave us? We first need to determine whether NIV helps when weaning patients who have satisfactory weaning parameters but fail a trial of unassisted respiration (Fig. 1). If NIV is not inferior to usual care—as the Italian study [9] seems to suggest—we should move to more challenging patients: those with poor weaning parameters and a reasonably high PaO₂/FiO₂ ratio (Fig. 1). (The pilot data reported by Vaschetto et al. [9] suggest that a ratio of 200–250 mmHg on an FiO₂ less than 0.6 could be such a reasonably high ratio.)

In summary, the investigation by Vaschetto et al. [9] is a challenge to intensivists interested in research on weaning. The economic onus and, more importantly, the human suffering associated with protracted invasive ventilation of patients recovering from an episode of acute hypoxemic respiratory failure demand that we take on this challenge. Our patients deserve no less.

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