Noninvasive Positive-Pressure Ventilation: A Silver Bullet for Extubation Failure?

Extubation failure, or the need for reintubation within 24–72 hours of extubation, occurs in up to 25% of critically ill patients. Extubation failure is associated with a markedly increased morbidity and mortality, including duration of mechanical ventilation, intensive care unit (ICU) and hospital stay, the need for post-acute-care hospitalization, and the need for tracheostomy.[1,2] The most common cause of extubation failure is respiratory failure secondary to respiratory, cardiac, or neuromuscular disease. In this case, it seems plausible to consider the use of noninvasive positive-pressure ventilation (NPPV), given the extensive evidence that supports the use of NPPV to prevent intubation. The use of NPPV in the post-extubation period might be considered in 3 different clinical scenarios: (1) to allow earlier extubation, (2) to prevent extubation failure, and (3) to prevent reintubation in the setting of extubation failure.

Use of NPPV to Allow Earlier Extubation

The use of NPPV to allow extubation of mechanically ventilated patients with weaning failure was first reported by Udwadia et al[3] in 1992 and has subsequently been evaluated in both uncontrolled prospective studies[4–7] and randomized controlled trials (RCTs).[8–12] A meta-analysis of 5 RCTs that evaluated extubation of patients directly to NPPV who do not meet standard extubation criteria,[13] and which included 171 patients, demonstrated that NPPV, compared to invasive mechanical ventilation, resulted in a decrease in mortality (relative risk [RR] 0.41, 95% confidence interval [CI] 0.22 to 0.76), ventilator-associated pneumonia (RR 0.28. 95% CI 0.09 to 0.85), and total duration of mechanical ventilation (weighted mean difference −7.33 d, 95% CI −11.45 to −3.22 d). Weaning failures (ie, reintubation or resumption of NPPV) occurred at a similar rate in patients who were extubated to NPPV or who remained intubated. It is important to note that 2 of these studies included only patients with COPD,[8,9] in 2 others COPD was present in 75% of the patients,[10,11] and COPD was present in a third of the patients in the remaining study.[12] This suggests that NPPV might be considered to allow earlier extubation in a selected patient population, particularly those with COPD.

The Use of NPPV to Prevent Extubation Failure in Patients at Risk

In this issue of Respiratory Care, Agarwal et al[14] focus on the use of NPPV to prevent reintubation. They present a meta-analysis on the only 2 published RCTs and report a decreased reintubation rate (RR 0.46, 95% CI 0.28 to 0.76) and ICU mortality (RR 0.26, 95% CI 0.1 to 0.66). The number-needed-to-treat was 9 (95% CI 5 to 29) for reintubation and 9 (95% CI 6 to 21) for ICU mortality.

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Hospital mortality, however, was unchanged (RR 0.71, 95% CI 0.42 to 1.20). These 2 multicenter RCTs included 259 patients with risk factors that predisposed them to respiratory failure after extubation, who were randomized to extubation with immediate initiation of NPPV or to remain intubated. Both studies included patients who required > 48 hrs of mechanical ventilation, tolerated a spontaneous breathing trial, and were at risk of post-extubation respiratory failure. This risk was defined in one study[15] as hypercapnia, congestive heart failure, ineffective cough and excessive airway secretions, > 1 failure of a weaning trial, > 1 comorbid condition, and upper-airway stridor that did not require immediate reintubation. In the other study,[16] risk was defined as age > 65 years, cardiac failure as the cause of intubation, or Acute Physiology and Chronic Health Evaluation score > 12 on the day of extubation.

Additional studies[17,18] that addressed this question were not included in the meta-analysis by Agarwal et al,[14] because of their methodology. Jiang et al[17] used NPPV in the post-extubation setting for patients who were not at high risk for post-extubation respiratory failure, and reported no benefit from NPPV. In an observational study that compared historical controls, El Solh et al[18] reported that NPPV was beneficial in preventing post-extubation respiratory failure in obese patients.

The Use of NPPV to Prevent Reintubation in the Setting of Extubation Failure

Two RCTs[19,20] evaluated the use of NPPV in this setting. Here, NPPV is used only after the onset of respiratory

failure. These studies included 302 patients. Agarwal et al[14] also offer a meta-analysis of these 2 RCTs, and they report no benefit from the use of NPPV in decreasing either reintubation rate (RR 1.03, 95% CI 0.84 to 1.25) or ICU mortality (RR 1.14, 95% CI 0.43 to 3.0). Moreover, although not statistically significant, there was a tendency toward harm with the use of NPPV.

Several observations are important relative to these studies. Very few patients had a diagnosis of COPD.[19,20] This is relevant given the strong evidence that supports the use of NPPV to prevent intubation in this patient population.[21] In the study by Esteban et al,[20] patients could be crossed over to receive NPPV even if they met reintubation criteria. It is of interest that reintubation was avoided in 21 of 28 patients (75%) who were crossed over to NPPV. Moreover, the mortality was low in this group. Unfortunately, Esteban et al[20] did not comment on the apparent success of NPPV in the subgroup of patients who were crossed over. This leaves us to wonder whether physicians selected these patients for a trial of NPPV for some reason that caused them to suspect clinical success.

The higher mortality in the Esteban study[20] among the patients randomized to NPPV was explained by the authors to be the result of delayed reintubation. However, additional analysis does not support this hypothesis. Patients assigned to NPPV had a similarly increased mortality whether they were reintubated (RR 1.77, 95% CI 0.95 to 3.30) or not (RR 1.66, 95% CI 0.51 to 5.37). Multiple regression analysis indicates that both assignment to NPPV and reintubation were independent predictors of mortality, with no evidence of an interaction between NPPV and reintubation ($p = 0.752$). This means that NPPV had the same effect on mortality in patients who were reintubated as those who were not. The bottom line in the Estaban study[20] is that being assigned to NPPV increased the risk of death, but not because of reintubation, and therefore not because of delay to reintubation. The reason for increased mortality in the NPPV group remains unknown.

The Clinician's Dilemma

The evidence that supports NPPV in the post-extubation period is not well-established at this time. For example, the analysis by Agarwal et al[14] in this issue of RESPIRATORY CARE barely qualifies as a meta-analysis, with only 2 studies included in each analysis. Of the 5 studies included in the meta-analysis by Burns et al,[13] one has been published only as an abstract.[12] With such a small evidence base, one cannot strongly recommend for or against the use of NPPV in the post-extubation period. Recommendations for the use of post-extubation NPPV may depend on which of the 3 scenarios described in this editorial best fits the individual patient.

The available evidence is strongest for the use of NPPV to allow early extubation in carefully selected patients who do not successfully complete a spontaneous breathing trial, such as those with COPD. Available evidence also suggests that NPPV may prevent extubation failure in patients who successfully complete a spontaneous breathing trial but are at risk for extubation failure. In both of these scenarios, NPPV is initiated immediately after extubation. However, NPPV for patients who develop post-extubation respiratory failure cannot be recommended on the basis of the current evidence (ie, where NPPV is not initiated immediately after extubation).

A few commonsense recommendations are in order for the use of NPPV to allow earlier extubation or to prevent extubation failure. First, this use should be reserved for settings where the clinical team (physicians, respiratory therapists, and nurses) are experienced with the application of NPPV. Second, the patient should be extubated to NPPV at a time, and in a unit, where personnel are available to carefully monitor the patient's response to NPPV after extubation. Finally, if the patient does not respond well to NPPV, reintubation should not be delayed.

At the present time, we cannot advocate for post-extubation NPPV as a silver bullet for extubation failure. It is neither absolutely right nor absolutely wrong to use NPPV in this setting. Additional high-level studies will be required to better define the role of NPPV after extubation.

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