Noninvasive positive-pressure ventilation increased risk for death in respiratory failure after extubation


**Question**
In patients in the intensive care unit (ICU) with respiratory failure within 48 hours after extubation, how does noninvasive positive-pressure ventilation (NIPPV) compare with standard medical therapy for mortality?

**Methods**
Design: Randomized controlled trial.
Allocation: Concealed.*
Blinding: Blinded [patients, data analysts, and monitoring committee]†.*
Follow-up period: To discharge from the ICU.
Setting: ICUs of 37 centers in 8 countries.
Patients: 221 from among 980 eligible patients > 18 years of age (mean age 60 y, 57% men) who had been mechanically ventilated > 48 hours and successfully extubated after completing a trial of spontaneous breathing, but who subsequently developed ≥ 2 predefined risk factors for requiring reintubation (respiratory acidosis, respiratory fatigue or effort, tachypnea, or hypoxemia).

**Intervention:** NIPPV (n = 114) or standard medical therapy (n = 107). Patients in the NIPPV group had their bed at a 45-degree angle and received ventilation (initially in a pressure-support mode) through a full facial mask initially set to achieve tidal volume > 5 mL/kg of bodyweight and respiratory rate < 25 breaths/min. NIPPV was preferably used continuously for 4-hour periods. Patients in the standard medical therapy group received supplemental oxygen, respiratory physiotherapy, bronchodilators, and any other therapy directed by the attending physician.

**Outcomes:** All-cause mortality in the ICU. The secondary outcome was need for reintubation according to prespecified criteria. The final decision to reintubate was made by the treating physician.

**Patient follow-up:** 100% (intention-to-treat analysis).

**Main results**
At the preplanned interim analysis, more patients who received NIPPV died than did patients who received standard medical therapy (Table), and the trial was stopped according to prespecified rules. The NIPPV and standard medical therapy groups did not differ for rate of reintubation (Table). Patients in the NIPPV group had a longer interval between the onset of respiratory failure and requiring reintubation than patients in the standard medical therapy group (median 12 vs 2.5 h, P = 0.02). Groups did not differ for length of stay in the ICU (median 18 vs 18 d, P = 0.59).

**Conclusion**
In patients in the intensive care unit who developed respiratory failure within 48 hours of extubation, noninvasive positive-pressure ventilation delayed the time to reintubation and increased all-cause mortality compared with standard medical therapy.

**Sources of funding:** Fondo de Investigación Sanitaria; Instituto de Salud Carlos III; Canadian Institutes of Health Research; Canadian Lung Association.

*For correspondence: Dr. A. Esteban, Hospital Universitario de Getafe, Madrid, Spain. E-mail aesteban@ucigetafe.com.

*See Glossary.
†Information provided by author.

---

It is important to note that unselected patients treated with NIPPV who required reintubation were found to have a 2-fold greater mortality risk. The higher mortality rate in this subgroup of patients suggests that the duration of the NIPPV trial requires close monitoring and patients who do not respond to NIPPV should be reintubated early, because the mortality risk increases with delays. Although the optimal duration of the initial NIPPV trial remains uncertain, a response within 2 hours of initiation is a reasonable expectation (5). Ultimately, this study substantiates the fact that any benefits of NIPPV may be offset by risks to patients and caution is necessary with any such practice.

**Commentary**

The addition of NIPPV to standard medical therapy for acute respiratory failure (ARF) may reduce endotracheal intubation and mortality rates. Current evidence supports the use of NIPPV as adjunctive therapy in patients with ARF caused by severe exacerbations of chronic obstructive pulmonary disease (COPD) as the standard of care, reducing both endotracheal intubation and mortality (1). Although the use of NIPPV in such other clinical situations as pulmonary edema and pneumonia in an immunocompromised host seems promising (2), the results are less conclusive.

The large, multicenter study by Esteban and colleagues showed that the addition of NIPPV to standard medical therapy did not reduce mortality or the need for reintubation in unselected patients with postextubation ARF. It confirms the results of a single-center, randomized, controlled trial of 81 patients (3) and is consistent with evidence that the benefit of NIPPV in unselected patients with hypoxemic respiratory failure remains unclear (4).

Esteban and colleagues did a post hoc subgroup analysis that suggested a role for NIPPV in patients with COPD and postextubation ARF. On its own, this evidence would be hypothesis-generating at best. However, previous studies support NIPPV use in such patients (1) and warrant a judicious trial of NIPPV in patients with COPD and postextubation ARF.

**References**