Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study

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Abstract Context: In patients with hypoxemic acute respiratory failure (ARF), randomized studies have shown noninvasive positive pressure ventilation (NPPV) to be associated with lower rates of endotracheal intubation. In these patients, predictors of NPPV failure are not well characterized.
Objective: To investigate variables predictive of NPPV failure in patients with hypoxemic ARF.
Design: Prospective, multicenter cohort study.
Setting: Eight Intensive Care Units (ICU) in Europe and USA.
Patients: Of 5,847 patients admitted between October 1996 and December 1998, 2,770 met criteria for hypoxemic ARF. Of these, 2,416 were already intubated and 354 were eligible for the study.
Results: NPPV failed in 30% (108/354) of patients. The highest intubation rate was observed in patients with ARDS (51%) or community-acquired pneumonia (50%). The lowest intubation rate was observed in patients with cardiogenic pulmonary edema (10%) and pulmonary contusion (18%). Multivariate analysis identified age > 40 years (OR 1.72, 95% CI 0.92–3.23), a simplified acute physiologic score (SAPS II) ≥55 (OR 1.81, 95% CI 1.07–3.06), the presence of ARDS or community-acquired pneumonia (OR 3.75, 95% CI 2.25–6.24), and a PaO₂/FiO₂ ≤146 after 1 h of NPPV (OR 2.51, 95% CI 1.45–4.35) as factors independently associated with failure of NPPV. Patients requiring intubation had a longer duration of ICU stay (P < 0.001), higher rates of ventilator-associated pneumonia and septic complications (P < 0.001), and a higher ICU mortality (P < 0.001).
Conclusions: In hypoxemic ARF, NPPV can be successful in selected populations. When patients have a higher severity score, an older age, ARDS or pneumonia, or fail to improve after 1 h of treatment, the risk of failure is higher.

Keywords Noninvasive positive pressure ventilation · Acute hypoxemic respiratory failure · Endotracheal intubation · Prospective, multicenter cohort study
**Introduction**

Noninvasive positive pressure ventilation (NPPV) is a safe and effective means to improve gas exchanges in selected patients with acute respiratory failure (ARF) of varied etiology [1]. Randomized studies in homogenous patient populations with ARF have provided supporting evidence for the early application of NPPV in hypercapnic ARF due to acute exacerbation of chronic obstructive pulmonary disease (COPD) [2, 3, 4, 5], and in hypoxic ARF due to cardiogenic pulmonary edema [6, 7, 8, 9], severe community-acquired pneumonia [10], and following solid organ transplantation [11]. In these studies, the early application of NPPV in patients not yet meeting criteria for mechanical ventilation was associated with a significant reduction in the rate of endotracheal intubation. Compelling data indicate that avoidance of intubation reduces morbidity and mortality associated with mechanical ventilation [12]. The effectiveness of noninvasive ventilation was also investigated in patients with severe hypoxic ARF meeting preselected criteria for mechanical ventilation and randomized to receive mechanical ventilation via a face mask or an endotracheal tube [12]. In this randomized study, mechanical ventilation delivered via a face mask was found to be equally effective to conventional ventilation in improving gas exchange, and intubation was avoided in 69% of the patients [12]. A recent randomized study [13] found that hypoxic patients without COPD were less likely to require intubation if randomized to NPPV.

Factors vital to the success of noninvasive ventilation include careful selection of patients, properly timed intervention, a comfortable, well-fitting interface, coaching and encouragement of patients, careful monitoring, and a skilled and motivated team [14]. For patients with hypercapnic ARF, reports of controlled and uncontrolled trials have described variables associated with an increased rate of intubation, including a higher severity of illness score [4, 15, 16] a higher PaCO₂ at study entry [16, 17], and failure to reduce PaCO₂ within 1–2 h of initiating noninvasive ventilation [17, 18]. In two studies, an inability to improve PaCO₂ was related to a leak in the nasal mask [15, 19], a factor that underscores the importance of selecting the proper interface to achieve best results with noninvasive ventilation.

Outcome predictors are important to identify patients who are less likely to improve with noninvasive ventilation, thus requiring closer observation and a readily available means of intubation. This is particularly important for patients with severe hypoxemia, where unnecessary delays in intubation may have serious consequences. Reported outcome predictors for noninvasive ventilation in patients with hypoxic ARF are limited to a few studies with small numbers of patients. Predictors of response in older studies investigating continuous positive airway pressure (CPAP) delivered by face mask in hypoxic ARF caused by a wide variety of lung pathologies, included the degree of hypoxemia at initiation of therapy [20, 21], and improvement in gas exchange and respiratory rate shortly after applying CPAP [22]. In a recent randomized study, Antonelli et al. [12] reported that among patients randomized to noninvasive ventilation those requiring intubation were older ($P = 0.006$), had a higher SAPS I ($P = 0.009$), and were less likely to improve PaO₂:FiO₂ ($P = 0.003$).

The aim of the present multicenter cohort study was to investigate prospectively outcome descriptors for noninvasive ventilation in a large population of patients with acute hypoxic respiratory failure of varied etiologies.

**Methods**

**Study design and patient selection**

Between October 1996 and December 1998, we enrolled consecutive adult patients with hypoxic ARF admitted to eight different intensive care units in Italy (Università Cattolica del Sacro Cuore and Università La Sapienza, Rome, Unità di Terapia Intensiva Respiratoria, Ospedale Maggiore di Crema, Ospedale Universitario Torrette Ancona, Servizio di Anestesia CTO Torino, Istituto ARTA, Trieste), Spain (M. Meseguer Hospital, Murcia), and the United States (University of Tennessee Medical Center, Memphis).

An ad hoc ethics committee approved the protocol, and all patients, or the next of kin, gave written, informed consent. The criteria for eligibility were acute respiratory distress including severe dyspnea at rest and all the following: a respiratory rate greater than 30 breaths/min, a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO₂:FiO₂) less than 200 while the patient was breathing oxygen through a Venturi mask; and active contractions of the accessory muscles of respiration or paradoxical abdominal motion.

Patients with any of the following were not included in the trial: a requirement for emergent intubation for cardiopulmonary resuscitation, respiratory arrest, severe hemodynamic instability, or encephalopathy; respiratory failure caused by neurological disease, acute exacerbation of COPD (on the basis of the clinical history, physical examination and chest radiograph), or status asthmaticus; more than two new organ failures (e.g., the simultaneous presence of renal and cardiovascular failures) [23]; brief ICU admissions (not exceeding 24 h) for post-operative monitoring or monitoring for other reasons; tracheostomy, facial deformities, or recent oral, esophageal, or gastric surgery; and the inclusion in other studies to compare the efficacy of NPPV versus conventional treatments. The simplified acute physiologic score (SAPS II) was calculated 24 h after admission to the ICU [24].

Patients had continuous electrocardiographic and arterial oxygen saturation monitoring (Biox 3700, Ohmeda, Boulder, Colo., USA). We used four types of mechanical ventilators: the Puritan Bennett 7200 (Puritan Bennett, Overland Park, Kan., USA), the Servo 900 C and Servo 300 Siemens (Siemens Elema, Uppsala, Sweden), and the Vision Respironics (Respironics, Pittsburgh, Pa., USA).