# Noninvasive Positive-Pressure Ventilation in Patients With Chronic Obstructive Pulmonary Disease Exacerbation: Not Too Late But Not Too Soon?

Noninvasive positive-pressure ventilation (NPPV) is now the first-line treatment to manage acute hypercapnic respiratory failure during exacerbation of chronic obstructive pulmonary disease (COPD). As compared to standard treatment alone, NPPV is associated with a quicker improvement in pH, $P_{aCO_2}$, and respiratory rate, resulting in a 28% reduction of endotracheal intubation rate, a 10% reduction of mortality rate, and a 4–6 days shorter hospital stay.[1–4] However, most of all previous studies have included highly selected COPD patients and have consistently revealed a 20–30% failure rate, as judged by death or intubation requirement.[1,2,5–8] In an observational, nonselected cohort study, Girault et al[9] found that NPPV failure rates during acute hypercapnic respiratory failure range between 35 and 49%.

Such discrepancies may be explained by several factors, such as the severity at admission,[10] some technical considerations to deliver NPPV (eg, masks, ventilatory modes), the experience of the involved personnel, and some intrinsic limits of NPPV versus invasive endotracheal ventilation. In parallel, high failure rates should be expected if more heterogeneous groups of patients with COPD exacerbation situated in less severe situations are considered for NPPV, as less than half of them may be successfully managed without mechanical ventilation.[8] Indeed, the real need for NPPV was 16% in a recent British study,[11] as NPPV could evidently be inappropriate in less severe patients, even explaining one negative study[12] where no intubation was required in the control arm.

In the present issue of RESPIRATORY CARE, Keenan et al[13] have addressed that controversy through a prospective randomized study in COPD patients presenting with "mild" exacerbations, defined as a worsening of dyspnea associated with pH $>$ 7.30. Assuming that the diminution of the work of breathing is one of the main mechanisms by which NPPV achieves clinical benefit in such patients, the authors suggested that an early intervention (within the first 3 days) might significantly decrease the hospital length of stay, this criteria being utilized as the primary outcome. They recruited 52 patients out of 355 admissions for COPD exacerbation, who were randomly allocated to receive either standard therapy with NPPV (according to a decreasing NPPV duration during the first 3 days) or standard therapy alone in a respiratory ward. Even if the study was not sufficiently powerful to demonstrate a significant reduction of hospitalization duration in the NPPV arm, it provides interesting information about NPPV in these specific patients. For instance, tolerance appeared rather low, since more than 50% of patients did not use NPPV as recommended by the medical staff. However, dyspnea improved more rapidly with NPPV, with a significant improvement as soon as the first hour and at the second day of application. This study also provides a "real life" observation of 355 unselected COPD patients presenting at the emergency unit with COPD exacerbation. Indeed, 7% of them had to be immediately intubated, and 23% were managed by NPPV in the emergency unit because of criteria of immediate severity. Two hundred forty-seven patients (70%) met the inclusion criteria for the present study, but 195 of them were excluded for some reasons, including a denied informed consent or technical impossibility to apply NPPV.

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This study emphasizes 3 major points that should be now considered in the future studies:

1. The need to refine the definition of COPD exacerbation, which remains controversial,[14] as the 20–30% of NPPV failures concern a subset of threatening exacerbations (where ventilatory assistance is mandatory) and not "common" exacerbations.

2. The need to quantify the interval of time between the beginning of the exacerbation and the occurrence of acute hypercapnic respiratory failure. This information is rarely available but may influence NPPV failure rates either in the acute setting or after discharge, as recently showed by Plant et al.[11]

3. The need to consider that in "real life," the immediate prognosis of a mild COPD exacerbation is not always easy to predict in the emergency unit and may explain why NPPV is sometimes over-used in this context.

If NPPV is indicated in the most severe COPD patients (ie, with pH at admission $<$ 7.30), the impossibility of predicting the immediate prognosis of a milder exacerba-

tion may justify enlarging NPPV indications in patients with pH between 7.30 and 7.35, in order to reduce the hospital duration and to prevent a potential pejorative evolution on a short-term basis. However, a poor compliance and a poor NPPV acceptability should be expected in these patients. Because NPPV is feasible in respiratory wards, even when performed by recently trained personnel,[2] prospective studies including a large number of patients with pH between 7.30 and 7.35 are now warranted, in order to define the immediate outcome of these milder exacerbations, the characteristics of the NPPV responders, and to precisely assess the NPPV cost-effectiveness in this setting.

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