

COMMENTARY

Non-invasive mechanical ventilation in hematology patients: let's agree on several things first

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See related research by Molina *et al.*, <http://ccforum.com/content/16/4/R133>

Abstract

Acute respiratory failure is a dreaded and life-threatening event that represents the main reason for ICU admission. Respiratory events occur in up to 50% of hematology patients, including one-half of those admitted to the ICU. Mortality from acute respiratory failure in hematology patients depends on the patient's general status, acute respiratory failure etiology, need for mechanical ventilation and associated organ dysfunction. Non-invasive mechanical ventilation is clearly beneficial for chronic obstructive pulmonary disease exacerbation and cardiogenic pulmonary edema. These benefits are based mainly on the avoidance of invasive mechanical ventilation complications. Non-invasive mechanical has also been recommended in hematology patients with acute respiratory failure but its real benefits remain unclear in these settings. There is growing concern about the safety of non-invasive mechanical ventilation to treat hypoxemic acute respiratory failure overall, but also in hematology patients. Prophylactic non-invasive mechanical ventilation in patients with acute respiratory failure but not respiratory distress seems to be effective in hematology patients with a reduced rate of intubation. However, curative non-invasive mechanical ventilation should be restricted to those patients with isolated respiratory failure, with fast improvement of respiratory distress under non-invasive mechanical ventilation, and with rapid switch to intubation to avoid deleterious delays in optimal invasive mechanical ventilation.

In a previous issue of *Critical Care*, Molina and colleagues provide the results of a large multicenter Spanish observational cohort study of hematology patients with acute respiratory failure (ARF) [1]. Their main findings are that non-invasive mechanical ventilation (NIV) failure is an independent risk factor for ICU mortality. Indeed, NIV patients exhibited higher mortality rates compared with patients who were intubated early. Not surprisingly, cardiogenic pulmonary edema was associated with reduced proportion of NIV failure.

The observational design does not actually allow any firm conclusion about NIV efficacy in hematology patients. The poorer prognosis associated with NIV failure could simply result from patient selection, clinicians being less keen to intubate patients without lifespan-expanding therapy or those who were older or sickest. Late intubation would thus only be a surrogate marker of poor prognosis. Nevertheless, this study is along the line of other studies in the literature that show early intubation to be associated with lower mortality [2,3]. In hematology patients with hypoxemic ARF, therefore, the questionable benefit from NIV supports the dilemma of intubation timing faced by clinicians managing these patients.

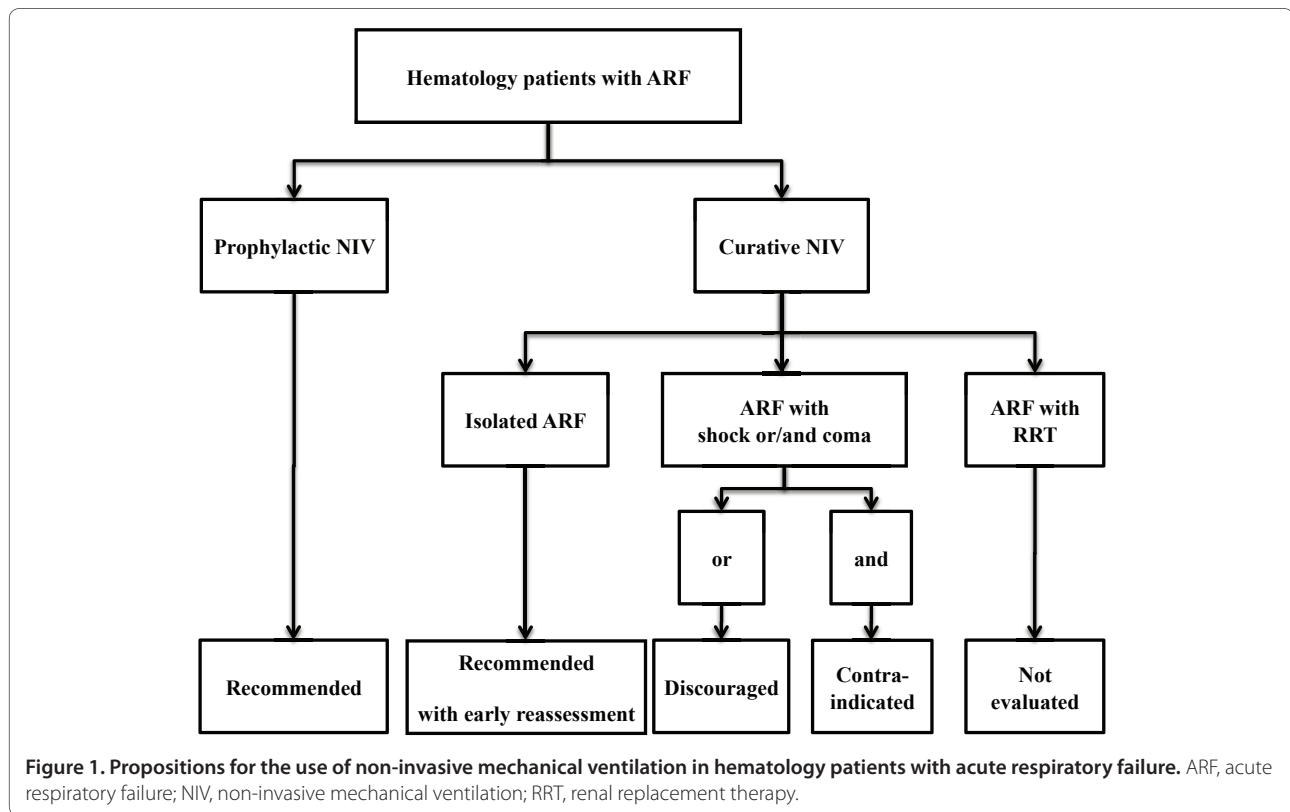
ARF occurs in up to 50% of hematology patients and is the leading reason for ICU admission in this population. Despite significant improvement in the last years [4,5], ARF still carries a high mortality rate of 50% overall, with even higher rates in patients needing mechanical ventilation [4,6,7]. The high incidence of cancer together with the use of a highly intensive curative regimen will increase the number of patients at risk of respiratory complications, and physicians will be asked to manage these patients more and more.

NIV is now recognized as the first-line therapy for patients with ARF due to chronic obstructive pulmonary disease exacerbation or cardiogenic pulmonary edema [8]. The clear benefit of NIV in these patients relies on the reduced rate of complications from invasive mechanical ventilation. NIV has also been recommended for hypoxemic ARF in immunocompromised patients [9]. In the subgroup of hematology patients, invasive mechanical

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ventilation has been associated with the worse prognosis of ARF [4,6,7] and NIV may therefore be particularly beneficial to these patients. However, published studies have inconsistently found a benefit from NIV in these patients [1,4,6,10-12].

Several factors may explain these discordant results. First, studies did not control the timing of NIV implementation and evaluated together prophylactic NIV (in patients with hypoxemia but no respiratory distress) and curative NIV (in patients with established respiratory distress) [10,13]. Second, the unit where NIV was performed – the hematology ward or the ICU – differed between studies [11,12]. Early ICU admission and the opportunity for tight monitoring probably positively impacted the results, whereas delayed ICU admission for patients treated in the hematology ward may have worsened prognosis with delayed intubation and treatment of associated organ failures [13]. Third, studies included patients with ARF from various etiologies, some of which may better respond to NIV. Finally, studies did not take into account associated organ dysfunctions that may have hampered NIV efficacy.

The overall lack of actually proven benefit from NIV in hypoxemic ARF of hematology patients therefore raises safety concerns for its use in patients who may benefit from early intubation and mechanical ventilation [14]. The recent advances in life-sustaining therapies and the

better outcome of hematology patients admitted to the ICU in the last years strengthen these concerns [4,5].

Taken together, studies evaluating NIV in hematology patients highlight the deleterious effects of NIV failure and late intubation, as does the study by Molina and colleagues [1,10,13]. Improving NIV results in these patients will probably derive from tailor-made management based on the lessons we have learned from these studies (Figure 1 and Table 1). In our belief, this relies on the three following points: improved patient selection, careful identification of ARF etiology [7], and early assessment of NIV efficacy. Available evidence supports the use of prophylactic NIV performed in the ICU in hematology patients [10]. These benefits may result from improved oxygenation and reduced work of breathing that alleviate respiratory load. Prophylactic NIV may also help to secure diagnostic procedures such as fiberoptic bronchoscopy and bronchoalveolar lavage [15]. In opposition, we believe the reason why NIV may be effective for hypoxemic ARF in hematology patients and not in other settings is highly questionable. We therefore recommend the cautious use of curative NIV only in patients with isolated ARF and with an early assessment of its efficacy. Curative NIV should be discouraged in patients with an associated extra-respiratory organ failure and should be contraindicated in those with two or more extra-respiratory failures.

Table 1. Situations in which NIV should be encouraged or avoided in hematology patients

Avoid NIV

- Acute respiratory failure-associated septic shock
- Nonhyperbaric deterioration of consciousness
- Deep hypoxemia with criteria for ARDS ($\text{PaO}_2/\text{FiO}_2 < 200$)
- Multiple organ dysfunction
- Persistent tachypnea after the first hour under NIV (respiratory rate > 35)

Encourage NIV

- NIV in patients with isolated respiratory failure and no sign of respiratory distress and no deep hypoxemia
- NIV in hematology patients with chronic respiratory failure
- NIV in hematology patients with pulmonary edema
- NIV in hematology patients to secure fiberoptic bronchoscopy
- NIV in hematology patients who declined tracheal intubation

ARDS, acute respiratory distress syndrome; NIV, non-invasive mechanical ventilation; $\text{PaO}_2/\text{FiO}_2$, ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen.

Ultimately, clinicians must be aware that the identification of a rapidly reversible etiology of ARF probably constitutes the key factor for the success of curative NIV. When no rapid improvement is obtained, invasive mechanical ventilation must be considered early to ensure the highest chance of survival for hematology patients with hypoxemic ARF [13].

Abbreviations

ARF, acute respiratory failure; NIV, non-invasive mechanical ventilation.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed equally to the manuscript.

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