Noninvasive ventilation for acute respiratory failure

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Purpose of review
This article reviews the use of noninvasive ventilation (NIV) in patients with acute respiratory failure (ARF), with a critical review of the most recent literature in this setting.

Recent findings
The efficacy of NIV is variable depending on the cause of the episode of ARF. In community-acquired pneumonia, NIV is often associated with poor response, with better response in patients with preexisting cardiac or respiratory disease. In patients with pandemic influenza H1N1 and severe ARF, NIV has been associated with high failure rates but relatively favorable mortality. In acute respiratory distress syndrome, NIV should be used very cautiously and restricted to patients with mild–moderate acute respiratory distress syndrome without shock or metabolic acidosis due to the high failure rate observed in several reports. Despite limited evidence, NIV may improve the outcomes of patients with chest trauma and severe ARF. In postoperative ARF, both continuous positive airway pressure and NIV are effective to improve clinical outcomes, particularly in those with abdominal, cardiac, and thoracic surgery.

Summary
Although patients with severe hypoxemic ARF are, in general, less likely to be intubated when NIV is used, the efficacy is different among these heterogeneous populations. Therefore, NIV is not routinely recommended in all patients with severe hypoxemic ARF.

Keywords
acute respiratory failure, invasive mechanical ventilation, noninvasive ventilation

INTRODUCTION

Noninvasive ventilation (NIV) is widely used in patients with severe acute respiratory failure (ARF) of different causes [1]. The main objective of NIV in this setting is to help in overcoming the acute episode without the need for invasive mechanical ventilation (IMV), hence decreasing the morbidity and mortality associated with this technique. The best established indications for NIV in ARF are severe acute exacerbations of chronic obstructive pulmonary disease (COPD) [2] and severe cardiogenic pulmonary edema [3].

The efficacy of NIV in patients with different types of hypoxemic ARF is, however, less evident from randomized clinical trials (RCTs) [4], with controversial results, when all these trials are analyzed together. Robust RCTs in these patients are scarce, explaining why the absence of specific recommendations often predominates in the evidence-based guidelines [5]. One of the major confounders of these studies was the marked variability of the case mix; patients with different underlying disorders and pathophysiologic pathways were included under the same generic definition of having hypoxemic ARF. Studies assessing the outcome of patients with hypoxemic ARF treated with NIV in the ICU identified up to nine different groups of patients, with substantial differences among them in the outcomes [6]. Moreover, a majority of clinical trials that assessed the efficacy of NIV in patients with hypoxemic ARF studied mixed populations.

The first RCT conducted in hypoxemic patients compared NIV with tracheal intubation in 64 patients with severe hypoxemic ARF and predefined criteria for initiating ventilatory support [7]. Among patients who received NIV, only 31% required intubation. Similarly, the improvement in arterial oxygenation after the protocol was implemented was similar in both the groups, the incidence of severe infectious complications was lower in patients who received NIV compared with those

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Curr Opin Crit Care 2015, 21:1–6
DOI:10.1097/MCC.0000000000000173

KEY POINTS

- Evidence for the benefit in using NIV in severe ARF has been described in patients with CAP, particularly in those with preexisting cardiac or respiratory disease, thoracic trauma, and postoperative ARF, particularly in those with abdominal, cardiac, and thoracic surgery.
- In ARDS, NIV should be used very cautiously and restricted to patients with mild–moderate ARDS without shock or metabolic acidosis due to the high failure rate observed in several reports.
- Although patients with severe hypoxemic ARF are, in general, less likely to be intubated when NIV is used, the efficacy is different among these heterogeneous populations. Therefore, NIV is not routinely recommended in all patients with severe hypoxemic ARF.

who were initially intubated, and the ICU mortality and length of stay tended to be lower in this group [7].

A physiologic study in patients with acute lung injury showed that NIV combined with positive end-expiratory failure is needed to unload the respiratory muscles and reduce inspiratory muscle effort, with a higher reduction of dyspnea when higher levels of pressure support were applied [8]. In this setting, continuous positive airway pressure (CPAP) improves oxygenation but fails to unload the respiratory muscles.

The use of NIV in different settings of patients with ARF will be revised.

NONINVASIVE VENTILATION IN PNEUMONIA

Severe community-acquired pneumonia (CAP) is defined as those cases that require ICU admission. Direct ICU admission is required for patients with septic shock or ARF requiring IMV, defined as major severity criteria in current guidelines used to define severe CAP [9].

Although the key aspect in the management of patients with pneumonia is an early and appropriate initial empirical antimicrobial treatment, the supportive measures (respiratory failure, shock, renal failure, protection of the airways, among others) are also essential in patients with severe CAP. The background for the use of NIV in severe CAP is to support patients with severe ARF in order to overcome the acute episode with the need for IMV and the associated morbidity and mortality.

Pneumonia in patients treated with NIV is persistently associated with poor outcome in the literature. The first study that found this association was conducted in patients with COPD exacerbations. Among others, pneumonia as the cause of exacerbation was associated with higher failure of NIV compared with other causes of exacerbation [10]. A multinational study in eight ICUs analyzed the evolution of 356 patients who received NIV for an episode of severe hypoxemic ARF in relation with the etiology of the episode [6]. Among the different causes of hypoxemic ARF, the highest rates of tracheal intubation corresponded to patients with acute respiratory distress syndrome (ARDS, 51%) and CAP (50%); both diseases independently predicted NIV failure. Other studies confirmed high failure rates in patients with pneumonia and severe ARF [11–14].

More recent prospective studies, however, have reported better outcomes related with the use of NIV in patients with CAP. The outcome of patients with CAP and severe ARF treated with NIV was prospectively assessed in 184 patients [15]. This study showed that patients with 'de-novo' ARF failed NIV more frequently than patients with previous cardiac or respiratory disease (46 vs. 26%). Among intubated patients with 'de-novo' ARF, longer duration of NIV before intubation was associated with decreased hospital survival, adjusted for confounders; this association was not observed in patients with previous cardiac or respiratory disease. The authors concluded that, in the presence of predictors for NIV failure, avoiding delayed intubation of patients with 'de-novo' ARF would potentially minimize mortality [15]. A more recent series of 127 patients with severe CAP and ARF treated with NIV has reported a 25% failure rate with the use of NIV, with a strong relationship between successful treatment and less-severe illness as well as a good initial and sustained response to medical therapy and NIV [16▪].

The only prospective RCT in CAP included 56 patients who were allocated to receive conventional treatment with or without NIV [17]. This study demonstrated that patients who had received NIV together with conventional treatment had lower rate of tracheal intubation and a shorter stay in the intermediate care unit than those who received conventional treatment only, although the hospital mortality was similar between both the groups. In a subset analysis, this study also showed that the significant benefits of NIV occurred in patients with COPD and hypercapnic respiratory failure only; this subset of patients had also a lower mortality after 2 months. By contrast, patients without COPD nor hypercapnic respiratory failure did not benefit from NIV.

A more recent prospective RCT in patients with severe hypoxemic ARF demonstrated that NIV

decreased the need for tracheal intubation and ICU mortality, with a faster improvement of arterial hypoxemia and tachypnea, compared with high-concentration oxygen therapy [18]. However, a subgroup analysis observed that the benefits in decreasing tracheal intubation and ICU mortality were restricted in patients with pneumonia as the cause of the episode of ARF.

Although these results were promising, the routine use of NIV in patients with CAP and without COPD has not been clearly established. Patients with severe CAP who receive NIV as a support for severe hypoxemic ARF should be managed in settings with appropriate resources in staff and equipment for a correct monitoring in order to early detect NIV failure and therefore avoid unnecessary delay in the intubation of patients.

NONINVASIVE VENTILATION IN SEVERE ACUTE RESPIRATORY FAILURE SECONDARY TO INFLUENZA A H1N1 INFECTION

Since the 2009 influenza A H1N1 pandemic, a large number of patients with severe ARF have been managed in ICUs. The use of NIV in patients with H1N1 infection and severe ARF is particularly controversial since several reports found that the use of NIV in these patients was associated with high failure rates but relatively favorable mortality [19,20,21▪]. In addition, there was a concern about risk of viral transmission that could be associated with NIV that has emerged after the severe acute respiratory syndrome experience [22,23].

A recent multicenter study assessed the efficacy of NIV and identified predictors of outcome in these patients [20]. Among 98 patients with H1N1 virus infection, 38 (39%) required immediate intubation and 60 received NIV as first-line therapy. The failure rate of NIV was 13 (22%) in these patients, and intubation was associated with higher number of infectious complications and death than successful treatment with NIV. The early application of NIV during the H1N1 pandemics was associated with an overall success rate in 47 out of 98 (48%). Patients presenting at admission with high severity scores and low oxygenation, or those unable to promptly correct gas exchange, are at high risk of intubation and mortality in this study [20]. Another recent multicenter study assessed 685 patients with confirmed influenza A (H1N1) viral pneumonia admitted to ICUs; 177 (26%) of them were treated with NIV, with a 41% success rate [21▪]. Success of NIV was independently associated with less radiograph extension and no vasopressor requirement in this study. NIV success resulted in shorter hospital stay and mortality similar to nonventilated patients. NIV failure was associated with mortality similar to those who were intubated from the start [21▪].

NONINVASIVE VENTILATION IN ACUTE RESPIRATORY DISTRESS SYNDROME

Most observational studies and subgroup analyses of RCT showed that patients with ARDS are among those with the worst outcome when they receive NIV as a support measure for severe ARF, with high rates of NIV failure [6,11,18,24–26] and limited efficacy of NIV. The severity of arterial hypoxemia and the frequent impairment of pulmonary mechanics in these patients may explain the high intubation rate regardless of NIV use or not.

A recent small prospective, multicenter RCT in 40 patients with mild ARDS compared treatment with NIV or high-concentration oxygen therapy [27]. Patients with NIV required less intubation and developed less organ system failure, with a trend to lower hospital mortality.

NIV failure in patients with ARDS seems to be strongly predictable in case of shock, metabolic acidosis, high severity scores of illness, and marked hypoxemia [11]. Because the observed mortality of patients who failed NIV was higher than that predicted by severity scores in this study, NIV should be tried very cautiously, or not at all, in patients with predictors of NIV failure, and particularly discouraged in those patients presenting with shock and metabolic acidosis.

Another prospective cohort study in three European ICUs investigated the application of NIV as a first-line intervention in early ARDS [28]. Among 479 patients admitted with ARDS, 147 of them could be treated with NIV as a first-line intervention. In this study, NIV improved hypoxemia and avoided intubation in 54% patients, and avoidance of intubation was associated with less ventilator-associated pneumonia and a lower mortality. NIV failure was independently associated with higher severity scores and failure to improve hypoxemia after 1 hour of NIV. Overall, only 16.5% of the patients admitted with ARDS were successfully treated with this technique. This study suggested that, in absence of criteria for immediate intubation, NIV could be tried in expert centers for patients with ARDS, avoiding the use in patients with predicted high mortality. However, the observational design of this study precludes any inference with respect to outcomes and it should be noted that the study centers had extensive experience with NIV. Even in these selected patients, the high mortality rate (54%) observed in patients intubated after NIV failure suggests the possibility that delaying intubation

might have contributed to mortality. Conversely, it is not possible to determine whether the low mortality rate (19%) of patients who succeeded NIV truly represents a beneficial effect or simply denotes less-sick patients [28]. A recent observational study in 64 patients with ARDS following esophagectomy for esophageal cancer showed a similar success rate (48%) of NIV [29▪].

Overall, the risk-benefit ratio of NIV is still not defined in ARDS and current evidence does not support the routine use of NIV in these patients, except, perhaps, for mild ARDS without other major organ failures.

NONINVASIVE VENTILATION IN CHEST TRAUMA

Patients with chest trauma present a high risk of pulmonary dysfunction with consecutive hypoxemic ARF. In selected patients, both CPAP and NIV may have a good clinical tolerance [30,31]. In patients with chest trauma, remaining hypoxic despite regional anesthesia showed that NIV reduced intubation compared to oxygen therapy in severe thoracic trauma-related hypoxemia, with reduced length of hospital stay. However, mortality in this study was the same in both the groups [32]. In addition to improving hypoxemia with NIV, adequate analgesia remains essential in these patients. However, the current evidence on the use of NIV in this indication is limited, as recently highlighted by a systematic review [33▪▪].

NONINVASIVE VENTILATION IN THE POSTOPERATIVE PERIOD

The respiratory function may be substantially modified during the postoperative period. Anesthesia, postoperative pain, and surgery, particularly when the site of the surgery approaches the diaphragm, often induce hypoxemia, pulmonary volume decrease, and atelectasis associated with a restrictive syndrome and a diaphragm dysfunction [34,35]. These modifications of the respiratory function occur early after surgery, and diaphragm dysfunction may last up to 7 days, with important deterioration in arterial oxygenation [36,37]. Moreover, swallowing disorders and vomiting may cause aspiration during the postoperative period. Maintenance of adequate oxygenation in this period is of major importance, especially when pulmonary complications such as ARF occur [38].

Both NIV and CPAP are frequently used in this clinical setting. Imaging studies have shown that the use of NIV may increase lung aeration and decrease the amount of atelectasis during the postoperative period of patients undergoing major abdominal surgery [39].

Physiological studies have shown that CPAP is effective in improving arterial oxygenation after extubation without adverse hemodynamic effect during postoperative high-risk patients, particularly after elective cardiac or thoracic surgery [40]. Similarly, the addition of NIV to patients submitted to elective lung resection resulted in improved arterial oxygenation without changes in arterial carbon dioxide levels, dead space, and pleural leaks, compared with standard medical therapy [41]. By contrast, in patients extubated after elective cardiac surgery, NIV improved the cardiac index without changes in systemic and pulmonary artery pressure or in arterial oxygenation [42].

In morbidly obese patients with restrictive ventilatory disorder undergoing gastroplasty, nasal NIV during the postoperative period improved the diaphragm dysfunction and accelerated recovery of patients [43]. In a similar population of morbidly obese patients with known obstructive sleep apnea undergoing laparoscopic bariatric surgery, NIV given immediately after extubation significantly improved spirometric lung function at 1 hour and 1 day postoperatively, compared with nasal CPAP started in the postanesthesia care unit [44].

Several RCTs have assessed the efficacy of NIV and CPAP in the management and prevention of postoperative ARF of different cause. In patients with solid organ transplantation and postoperative ARF, NIV improved arterial oxygenation and decreased the needs for tracheal intubation, compared with conventional treatment [45].

A study in patients who developed ARF during the postoperative period of lung cancer resection demonstrated that NIV was effective in decreasing the needs for tracheal intubation and improving hospital mortality [46]. More recently, a prospective survey confirmed the feasibility and efficacy of NIV in patients with ARF following lung resection [47]. In a small population of 32 patients with preexisting decreased lung function undergoing lung resection surgery, the use of prophylactic NIV during the preoperative and postoperative period resulted in less incidence of postoperative atelectasis, improvement of arterial blood gases, and pulmonary volumes, as well as shorter length of hospital stay [48]. However, in a more recent RCT in a larger population, which consisted of 360 patients with COPD undergoing lung resection surgery, prophylactic postoperative NIV did not reduce the rate of acute respiratory events or ARF and influence other postoperative complications rates, mortality rates, and duration of ICU and hospital stay [49▪▪].

The prophylactic use of nasal CPAP in the postoperative period in patients undergoing elective thoracic–abdominal aortic surgery decreased the incidence of pulmonary complications, such as severe hypoxemia, atelectasis, pneumonia, and reintubation, and the length of hospital stay [50]. The same group obtained similar benefits with the administration of prophylactic nasal CPAP following cardiac surgery, with improved arterial oxygenation, reduced incidence of pulmonary complications including pneumonia and reintubation rate, and reduced readmission rate to the ICU [51]. More recently, a RCT has been conducted in the treatment of patients who developed ARF following cardiac surgery [52▪▪]. Compared with conventional treatment, use of NIV in these patients resulted in decreased rate of reintubation, tracheostomy, ventilator-associated pneumonia, and hospital mortality, with shorter duration of ventilation and ICU stay. Pneumonia and higher severity scores were independent predictors for NIV failure in this population.

Another RCT in patients with ARF after major abdominal surgery compared the use of CPAP and oxygen therapy [53]. This study showed that CPAP reduced the rate of tracheal intubation, compared with oxygen therapy (1 vs. 10%, respectively, $P = 0.005$), as well as other severe complications, although the reduction of hospital mortality was not significant.

In summary, the evidence suggests that CPAP and NIV are effective strategies to improve clinical outcomes in patients with postoperative ARF, particularly those with abdominal, cardiac, and thoracic surgery. This results in reduction of intubation rates, nosocomial infections, length of stay, morbidity, and mortality [38,54]. However, it is recommended that before initiating NIV, any surgical complication must be treated.

CONCLUSION

The RCTs of the literature suggest that patients with severe hypoxemic ARF are, in general, less likely to be intubated when NIV support is added to the standard medical treatment. However, the effects of NIV on mortality are less evident, and the heterogeneity of the different published studies suggests that the efficacy may be different among different populations. Therefore, NIV is not routinely recommended in all patients with severe hypoxemic ARF.

Acknowledgements

None.

Financial support and sponsorship

This work was supported by the Centro de Investigación Biomédica en Red-Enfermedades Respiratorias (CibeRes CB06/06/0028)-Instituto de Salud Carlos III (ISCiii), 2009 SGR 911, and Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS).

Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
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