

Red, yellow or green for non-invasive mechanical ventilation

Mechanical ventilation (MV) can be classified as a supportive treatment modality for hypoxemic respiratory failure/ARDS, as we do not have any data to support MV as a curative treatment modality for ARDS.

The question here is how to manage the supportive treatment period in ARDS. For this aim, we have the possibility of increasing the FiO_2 level by several methods (such as high flow nasal O_2 therapy 'HFNOT' and non-rebreathing masks) or the application of invasive/non-invasive MV for a period to allow time for curative treatments. These supportive treatment modalities may be alternated during the application of curative treatment agents (such as antibiotics). For example, we may start supportive therapy by applying HFNOT and switch to non-invasive ventilation according to patient needs. Later on, we may institute invasive MV if the patients condition deteriorates. We may also use adjunctive treatment options such as positioning the patient during these supportive treatment modalities. The problem is choosing the correct modality of support for the individual patient.

Noninvasive ventilation may be used in the initial period of supportive treatment, following a period of HFNOT or invasive MV. It may also be used as a weaning modality of invasive MV. The application rules of NIN ventilation are the same for its application in the case of several diseases. It may have some indications (green), relative contraindications (yellow) or contraindications (red).

To clarify, non-invasive MV may be contraindicated in a patient with pneumonia caused by gram positive bacteria due to high amount of secretions (red). However, it may be used for a patient with pneumocystis carinii pneumonia (green). While choosing the correct patient to administer MV; mild ARDS can be considered green, moderate ARDS may be considered yellow, and severe ARDS may be deemed red.

During application of non-invasive MV, the most important issue is to monitorize the patient. If goals such as decreasing FiO_2 levels are reached, it may be continued. However, if the patients response is not sufficient, invasive ventilation should be instituted without delay.

A recent study in 50 countries has shown that approximately 15% of 3022 ARDS patients were ventilated with non-invasive MV, whereas 10% of them were ventilated exclusively with non-invasive MV (1). This 10% highlights cases in which non-invasive MV was the sole supportive treatment modality in ARDS. To clarify its usage, we have to study or find the answer to the following questions:

Which ARDS patients should receive non-invasive MV?

When should non-invasive MV be used in ARDS?

Which mode and interface should be used during non-invasive MV in ARDS?

How can we prevent intubation delay in patients with ARDS during usage of non-invasive MV?

By answering these questions, we will be able to decide if the use of non-invasive MV is green, yellow or red for the individual patient.

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Noninvasive Ventilation in Hypoxemic Patients: an Ongoing Soccer Game or a Lost One?

Cesare Gregoretti, Andrea Cortegiani, Santi Maurizio Raineri, Antonino Giarrjato

Department of Biopathology and Medical Biotechnologies (DIBIMED), Section of Anesthesia, Analgesia, Intensive Care and Emergency, Policlinico P. Giaccone, University of Palermo, Palermo, Italy

Noninvasive ventilation (NIV) is nowadays a medical intervention used worldwide in daily practice in many clinical settings (1). Almost 35 years have been passed by since the first clinical studies on the use of NIV in the critical area (2, 3). NIV has been increasingly used to avoid or to serve as an alternative to invasive mechanical ventilation (IMV) (4). Compared with standard medical therapy (STM), and in some cases with IMV, NIV has been found to improve survival and reduce complications in selected patients with acute respiratory failure (ARF). The main indications are exacerbation of chronic obstructive pulmonary disease (COPD), cardiogenic pulmonary oedema, pulmonary infiltrates in immunocompromised patients, weaning of previously intubated stable patients with chronic obstructive pulmonary disease, postoperative patients, terminally ill patients, or as ventilatory assistance during invasive procedure as bronchoscopy (4). NIV has also been used in the so labelled "de novo" acute hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS). Nevertheless, after many years from NIV institution in ICU (3) its use in hypoxemic patient not only need to be better "tuned" but it also seems to be decreasing compared to the last ten years (5, 6). In this patient population despite a satisfactory initial response (7), late failure may occur leading to increases in mortality rate (5). The possible causes of immediate failure may be due to excessive secretions, interface intolerance and agitation, and severe patient-ventilator asynchrony. However beyond these risk factors there are possibly some differences between failing in a hypercapnic or in hypoxemic ARF. In patients with hypoxemic ARF delayed intubation may lead to an increase mortality while it does not occur in COPD patients (8). In addition, in hypoxemic patients keep using NIV and delaying intubation may expose the deleterious effects on an increased transpulmonary pressure. The major determinant of lung stress, the transpulmonary pressure, is the result from the sum of the pressure applied to the airway by the ventilator and the pleural pressure generated by the patient's spontaneous effort (9). The pressure generated by the respiratory muscle (respiratory effort) added to the level of patient-synchronized pressure support level (10) may generate high

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Address for Correspondence:

Cesare Gregoretti, E-mail: c.gregoretti@gmail.com

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tidal volumes that are far from the suggested “safe” level of tidal volume suggested to protect the lung (11). In addition the level of PEEP may be insufficient to recruit consolidated lung areas (12, 13). This in turn may cause a “self induced ventilation lung injury (14). Last but not least, it has been recently found that to improve the outcome in ARDS patients, one needs to identify potentially modifiable factors associated with mortality. Higher positive end expiratory pressure (PEEP), lower peak, plateau, and driving pressures, and lower respiratory rate seem to be associated with improved survival from ARDS (15). Carreaux et al. (16) found that expired tidal volume was one of the factors determining NIV failure. In their study they found that patients with a tidal volume above 9.5 mL kg⁻¹ of predicted bodyweight had increased risk of NIV failure. Interestingly, the relationship between NIV success or failure and expired tidal volume was observed only among patients with moderate-to-severe hypoxaemia (PaO₂/FiO₂ ≤ 200), and was not found in patients with milder (PaO₂/FiO₂ > 200) degrees of hypoxaemia (17). Frat et al. (18) found that the use high-flow nasal cannula (HFNC) reduced ICU and 90-day mortality as compared to standard oxygen and NIV. The authors speculated that the greater mortality with NIV might have been related to the use of tidal volumes greater than 9 mL kg⁻¹, predisposing to ventilator-induced lung injury (VILI). However, NIV was used intermittently and not continuously. The level of noninvasive pressure-support was only of 8±3 cmH₂O of water, a PEEP only of 5±1 cmH₂O. In addition it can be hypothesized that the use of other interfaces as helmets could have increase patient tolerability and time on NIV (19). Patel et al. (19) found that among patients with ARDS, treatment with helmet NIV resulted in a significant reduction of intubation rates. There was also a statistically significant reduction in 90-day mortality with helmet NIV. Nevertheless, although NIV failure seemed not to longer associated with higher mortality rate suggesting improved patient selection (13). Bellani et al. (20) found that NIV failure occurred in 22.2% of mild, 42.3% of moderate and 47.1% of patients with severe ARDS. Hospital mortality in patients with NIV success and failure was 16.1% and 45.4%, respectively. NIV use was independently associated with increased ICU (HR 1.446-95% CI 1.159-1.805), but not hospital mortality. In a propensity-matched analysis, ICU mortality was higher in NIV than invasively ventilated patients with a PaO₂/FiO₂ lower than 150 mmHg. Among immunocompromised patients admitted to the ICU with hypoxemic ARF, early NIV compared with oxygen therapy alone did not reduce 28-day mortality (21). However the median durations of NIV were 8 hours (interquartile range [IQR], 4-11) in the first 24 hours, 6 hours (IQR, 4-8) on day 2, and 5 hours (IQR, 3-7) on day 3. Overall, in the first 72 hours the patients received NIV for a median time of 19 hours only, potentially too few for NIV to be effective in reducing the intubation rate (9). The results of the post-hoc analysis study of Frat et al. (22) indicates that oxygen delivery through HFNC was associated with lower mortality and a lower risk of IMV compared with NIV in immunocompromised patients. However, although

the patients were ventilated with 7-10 mL kg⁻¹ of expired tidal volume, the amount of tidal volume that reached the lungs was probably not more than 5-8 mL kg⁻¹ of bodyweight because of dead space thus making unlikely to lead to substantial likelihood of developing VILI (17). In conclusion, NIV in in hypoxemic patients still remain a hot topic. Although clinicians should be aware of the possible harmful effects of using NIV in hypoxemic patients there are still many issues to discuss. Among them the experience and familiarity to NIV use, which hypoxemic patient do we have to prefer to undergo NIV (i.e. ARDS vs non ARDS), which patients should need immediate IMV, inspiratory synchronization especially when high VT is undesirable. Maybe, we can reason in another way starting a new soccer game: late vs early extubation (using NIV as tool to early extubate our patients) in hypoxemic patients to prevent IMV complications (23-25).

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