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Focus on noninvasive respiratory support before and after mechanical ventilation in patients with acute respiratory failure

Audrey De Jong[1,2], Jonathan D. Casey[3] and Sheila Nainan Myatra[4*]

The recent literature provides new insights into the potential of noninvasive respiratory support to prevent tracheal intubation (TI), improve the safety of TI, and support patients following extubation. In this article, we discuss how such data can be used to improve patient care (Fig. 1).

Oxygen therapy in patients with acute respiratory failure

High flow nasal oxygen (HFNO) devices are capable of providing up to 100% oxygen at flow rates up to 70 L per minute (exceeding inspiratory flow rates). In addition to noninvasively providing a high fraction of inspired oxygen, HFNO has been shown to have physiologic benefits including provision of a low level of continuous positive airway pressure, decreased work of breathing and dead space washout [1, 2]. Prior studies have suggested that HFNO may be superior to conventional oxygen therapy (COT) and noninvasive ventilation (NIV) in treating acute hypoxemic respiratory failure [3] while other trials have shown no difference in outcomes [4]. This question was further explored in a recent systematic review and meta-analysis [5]. Across nine RCTs and 2,093 patients, Rochwerg et al. demonstrated that HFNO, compared to COT, reduced the need for TI and escalation of respiratory support but did not appear to affect mortality. However, the meta-analysis included a very heterogeneous population, some studies were at a high risk of bias and accurate subgroup analyses could not be performed, suggesting a need for further research.

Optimizing oxygenation and ventilation during tracheal intubation

Hypoxemia is the most common complication during TI of critically ill patients [6].Oxygenation and ventilation can be provided at three distinct phases of the TI: preoxygenation, induction to laryngoscopy, and laryngoscopy to TI. Studies conducted in 2019 evaluated the use of HFNO and NIV in all the three phases of TI [7]. Following up on the PREOXYFLOW study from 2015 [8], which evaluated HFNO during the TI of patients with acute hypoxemic respiratory failure, Guitton et al. conducted the PROTRACH study [9] among patients without pre-existing hypoxemia undergoing TI in the ICU (PaO2/FiO2 ratio $\geq$ 200 mmHg).The study randomized 192 patients to HFNO (which was continued throughout the procedure) or to oxygen by face mask (which was removed for laryngoscopy). HFNO failed to increase the lowest oxygen saturation during intubation (the primary outcome), but several secondary outcomes including mild hypoxemia (oxygen saturation < 90%) favored HFNO. While the results favored HFNO over COT during TI, the trial failed to meet its primary outcome and must be interpreted in the context of the PREOXYFLOW trial which failed to show benefit among hypoxemic patients who would have been expected to have a larger benefit [10–12].

The failure of HFNO to provide more robust improvements in oxygen saturation during TI may be explained by a recent physiologic study [13], which demonstrated a significantly higher end-tidal oxygen following pre-oxygenation with face mask, compared to HFNO, suggesting

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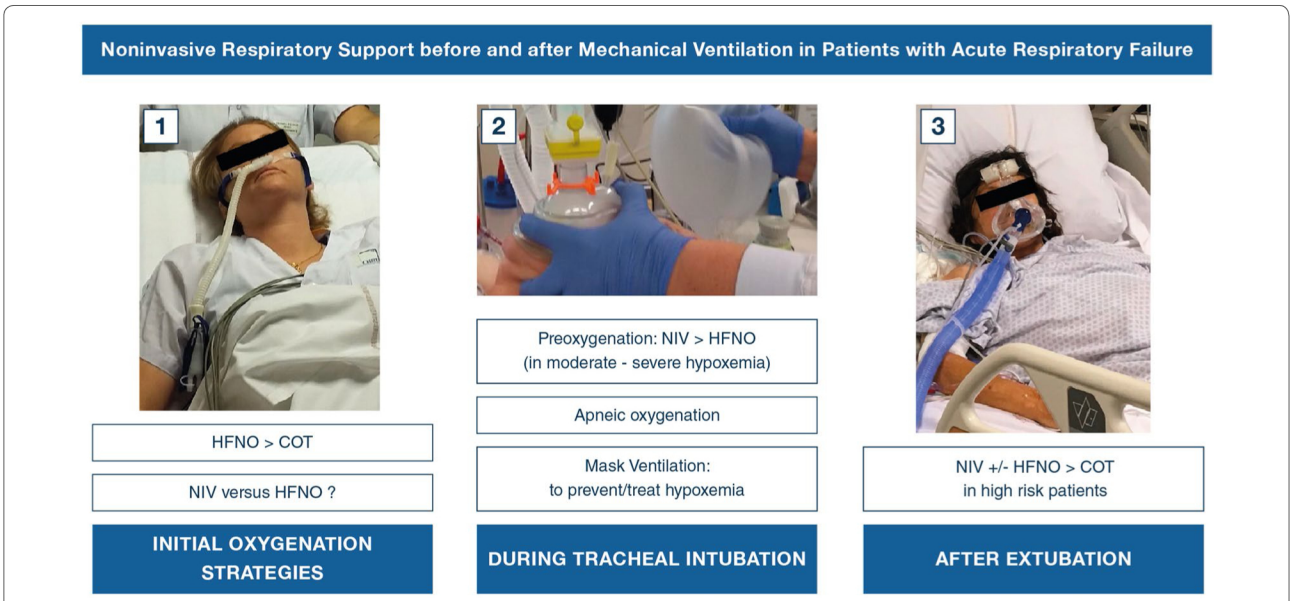

Fig. 1 Noninvasive respiratory support before and after mechanical ventilation in patients with acute respiratory failure. (1) Initial oxygenation strategies: Further studies are still needed to compare the three main methods of oxygenation: COT, HFNO and NIV(with different interfaces and in different settings) to avoid intubation in patients with acute respiratory failure. (2) During tracheal intubation: Preoxygenation using NIV remains the more efficient strategy to decrease oxygen desaturation in critically ill patients. Gentle mask ventilation during apnea before tracheal intubation, may help to further reduce the incidence of severe hypoxemia. (3) After extubation: Early extubation followed by NIV application with or without HFNO, may reduce the rate of respiratory failure and re-intubation. Further studies are needed in selected subgroups of patients. HFNO: high-flow nasal cannula oxygen; NIV = noninvasive ventilation; COT = conventional oxygen therapy

that the intake of room air by mouth during HFNO may outweigh its other physiologic benefits during TI. OPTINIV, a proof of concept study [14], showed that during TI adding HFNO for apneic oxygenation to NIV for preoxygenation was more effective in reducing the severity of desaturation compared to NIV alone.

In a study closely related to the PROTRACH study [9], Frat et al. [15] conducted the FLORALI2, which randomized 322 hypoxemic, critically adults undergoing TI to NIV(from induction to laryngoscopy) or HFNO (from induction to TI). The incidence of severe hypoxemia during TI was 23.2% in the NIV group and 27.5% in the HFNO group (absolute difference −4.2%; 95% CI −13.7% to 5.5%; $P = 0.39$). However, subgroup analyses suggested a potential benefit for NIV among patients with a P/F ratio < 200. Taken together with prior trials, the results of the FLORALI 2 trial suggest that NIV may be the best method of preoxygenation to reduce oxygen desaturation during TI of critically ill patients, particularly among patients at high risk [16].

While the PROTRACH [9] and FLORALI 2 [16] trials focused on preoxygenation, management of the period from induction to laryngoscopy has been similarly controversial. Following induction there is a period where the patient may be apneic or hypopneic. Bag-mask ventilation during this period may prevent hypoxemia but has been proposed to increase the risk of gastric insufflation and pulmonary aspiration. In the PREVENT study, Casey et al. [17] randomized 401 patients to receive bag-mask ventilation from induction to laryngoscopy or no ventilation, except as treatment of hypoxemia. Bag-mask ventilation reduced the incidence of severe hypoxemia (oxygen saturation < 80%) by more than half, without increasing the rate of pulmonary aspiration. The trial, however, was not powered to provide a definitive assessment of the relationship between bag-mask ventilation and pulmonary aspiration.

Applying positive pressure seems beneficial not only during apneic periods but also during pre-oxygenation, raising the question of the potential role of NIV applied from pre-oxygenation to laryngoscopy.

Oxygenation and ventilation following extubation

Protocols for daily spontaneous awakening and breathing trials have shortened the average duration of mechanical ventilation and improved outcomes. However, there are still patients who recurrently fail spontaneous breathing trials and require a prolonged wean from ventilation. Vaschetto et al. [18] evaluated the effect of extubation without performing a spontaneous breathing trial followed by NIV application Among 130 non-hypercapnic patients ventilated more than 48 h (after exclusion of

patients with acute respiratory failure secondary to neurologic disorders, status asthmaticus, COPD, and cardiogenic pulmonary edema and obese patients), it appeared that early extubation reduced the duration of invasive mechanical ventilation but did not affect ICU length of stay.

Other studies have explored the role for HFNO and NIV following extubation to prevent recurrent respiratory failure or hypotension [19]. Thille et al. [20] compared post-extubation support with NIV and HFNO to post-extubation with HFNO alone. Among 648 patients at high risk of reintubation (older than 65 years or with an underlying cardiac or respiratory disease), the investigators found that NIV with HFNO reduced reintubation rates. This study adds to a growing consensus that high-risk patients benefit from post-extubation support. However, each study of post-extubation support has used different criteria to define risk status, and further research is needed to validate these risk factors and determine if there are other populations who would benefit from post-extubation support.

Conclusion

Studies in the past year have improved our knowledge about the conditions for which noninvasive respiratory support devices may provide benefit. While further research is needed, it appears that preoxygenation with NIV and gentle bag-mask ventilation after induction reduce the risk of peri-procedural hypoxemia, while the combination of HFNO and NIV may prevent desaturation during TI and respiratory failure and reintubation following extubation.

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Compliance with ethical standards

Conflicts of interest

ADJ, JDC and SNM have no conflict of interest.

Ethics approval and consent to participate

Not applicable.

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