Can we predict failure of HFNC in patients with acute hypoxemic respiratory failure?

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Last change: 06.10.2020, Revision 01, First published 16.07.2020: ROX (values) at 12 hours after HFNC initiation (previously: intubation) were predictors of HFNC failure.

The coronavirus pandemic has stretched many hospitals’ resources to the limit. Patients are requiring respiratory support on an unprecedented scale and a possible – or in some cases very real – shortage of ventilators is forcing institutions to weigh up the risks and benefits of alternative forms of therapy.

Takeaway messages

✔ Delivery of oxygen by high flow nasal cannula has a range of benefits including greater patient comfort, and improved oxygenation and ventilation.

✔ One of the major challenges is identifying those patients in which HFNC is likely to fail, as delayed intubation may result in worse outcomes.

✔ An index defined as the ratio of SpO₂/FiO₂ to the respiratory rate is an easy-to-use bedside tool that can help identify the need for mechanical ventilation in pneumonia patients with AHRF treated with HFNC.

On the one hand, evidence on the use of oxygen delivered by high flow nasal cannula (HFNC) in patients with acute hypoxemic respiratory failure (AHRF) has demonstrated its superiority to standard oxygen therapy by facemask in many respects, including better tolerance, and improved oxygenation and work of breathing (1, 2, 3). It has also been
shown to reduce the need for intubation compared to conventional oxygen (4, 5, 6). A network analysis of 25 randomized controlled trials investigating different noninvasive oxygenation strategies in adult AHRF patients showed that high-flow nasal oxygen was associated with a lower risk of intubation compared with standard oxygen therapy (7). However, in the light of conflicting evidence with respect to both reduced intubation rates and mortality, there are currently no specific recommendations for using high flow nasal cannula devices in COVID-19 patients. This uncertainty is compounded by concerns that use of high flow devices may increase virus dispersion. In this respect too there are many unanswered questions, such as to what extent aerolization translates into a significant infection risk, how that risk compares with risks posed by other forms of treatment and to what extent healthcare workers can protect themselves. Although the available evidence on generation and dispersion of bio-aerosols indicates that HFNC poses no greater risk than standard oxygen masks (8), many clinicians are reluctant to apply this treatment in a COVID-19 setting. Furthermore, guidelines issued by organizations around the world for the treatment of COVID-19 patients with respect to HFNC vary greatly. However, considering the high efficacy of HFNC with respect to oxygenation, the fact that for some patients it may be almost the only viable alternative, and the significance of lower intubation rates in light of limited resources, some are urging for an open-minded approach and a careful look at the risk-benefit profile for both clinicians and patients (8, 9).

Application and benefits in a general setting

There are several mechanisms of action for HFNC that translate into a range of benefits, including greater patient comfort (1, 2, 10), improved airway secretion clearance and less work of breathing (11, 12), improved ventilation and oxygen delivery (13, 14, 15). The high flow rate ensures a stable fraction of inspired oxygen (FiO2) without room air entrainment (16, 17, 18). In comparison with delivery by face mask, HFNC has been shown to result in a higher partial pressure of arterial oxygen (PaO2), lower respiratory rate (RR), more comfort, less mouth dryness, and less dyspnea (1). Lastly, HFNC generates a positive end-expiratory pressure (PEEP) effect (19) and increases in end-expiratory lung volume (EELV) (20, 21) and tidal volume (21). However, as many of the proven benefits are physiologic, there are not yet absolute indications for the use of HFNC. One of the major challenges is identifying those patients in which HFNC is likely to fail, to ensure intubation is not delayed unnecessarily. In such patients, delayed intubation is associated with worse outcomes (22); therefore, identification of variables that may help clinicians to make a timely decision to intubate would impact positively on clinical practice. A study by Roca et al. (23) looked at the use of an index as an easy-to-use bedside tool for accurately identifying the need for mechanical ventilation in pneumonia patients with AHRF treated with HFNC.

The ROX index

The ROX index is defined as the ratio of SpO2 (oxygen saturation as measured by pulse
oximetry)/FiO2 (fraction of inspired oxygen) to the respiratory rate. SpO2/FiO2 has been shown to have a positive association with the success of HNFC, while RR has an inverse association. In their results published in 2016, Roca et al. concluded that the ROX index, which combined both parameters, could successfully be used to identify patients who were at low risk of HFNC failure and could therefore continue to receive HFNC after 12 hours (23). Subsequent results published in 2019 (24) showed that while SpO2/FiO2 was almost as good as the ROX index, adding RR further improved the diagnostic accuracy. In this 2-year multicenter prospective observational cohort study including 191 patients with pneumonia-related ARF treated with HFNC, the prediction accuracy of the index was also shown to increase over time, from 2 h to 6 h and then 12 h. ROX index values measured at 12 hours after the start of HFNC demonstrated the best prediction accuracy. At all time points, patients with ROX $\geq$ 4.88 were less likely to be intubated. ROX < 2.85 at 2 hours, < 3.47 at 6 hours, and < 3.85 at 12 hours after HFNC initiation, respectively, were predictors of HFNC failure. The patients in whom therapy failed were those who showed a smaller increase in ROX index values during the 12-hour period. The authors concluded that the ROX index may help physicians predict which patients might need intubation and consequently avoid delaying mechanical ventilation.

**Correlation between ROX index and increase in flow**

Based on previous data from patients with AHRF treated with HFNC, which showed that the set flow rate has a significant effect on oxygenation and RR (25), Mauri et al. (26) subsequently investigated whether an increase in the set flow rate might impact the ROX index values. In addition, they looked at a possible association between a more severe condition at baseline and an improvement in ROX index values at the higher rate. Fifty-seven hypoxemic patients underwent two, 20-minute sessions of HFNC, one with the gas flow at 30 l/min and one at 60 l/min. The ROX index was measured at each flow rate. Results showed that the increase in flow rate from 30 to 60 l/min during a “flow challenge” session correlated with a small but significant increase in the ROX index, with forty patients demonstrating an increase in ROX index values at the higher flow rate. These patients were also shown to be in a more severe condition, with lower SPO2/FiO2, higher RR and lower ROX index at 30 l/min, and as such, responded more positively to the flow increase. In addition, the improvement in the ROX index was shown to correlate with the increase in EELV at the higher flow rate. Therefore, this study showed that the set flow rate may affect the ROX index value. Such a change in the ROX index after a 20-minute “flow challenge” could be a simple and quick means of identifying severe patients in need of closer monitoring. Furthermore, standardizing measurement of the ROX index at the lowest flow rate of 30 l/min may help better predict the success or failure of HFNC.

**What is next?**

On top of the limitations of previous studies, concerns have been expressed about the
relationship between the SpO2/FiO2 ratio and the PaO2 (partial pressure of arterial oxygen)/FiO2 ratio that may not always be so linear (27). However, a study by Chen et al. in 2015 showed that characteristics and outcomes in ARDS diagnosed by the SpO2/FiO2 ratio were very similar to those in patients diagnosed by the PaO2/FiO2 ratio (28).

To date, all evidence documented with respect to the ROX index has been based on observational studies. A randomized controlled trial is currently underway to assess whether use of the ROX index in addition to traditional criteria for determining the need for intubation in AHFR patients is both feasible and associated with earlier intubation.

**Conclusion**

The ROX index is an accurate, simple-to-use tool for any staff member at the bedside. As such, it could potentially be measured routinely in those patients undergoing HFNC. Further research will shed light on the feasibility and usefulness of using the ROX index in combination with traditional criteria for determining whether intubation is necessary.

Ventilators from Hamilton Medical offer high flow oxygen therapy as a standard or optional feature, in addition to continuous SpO2 and SpO2/FiO2 measurement*. No additional device or ventilator is required and the therapy can be alternated with noninvasive ventilation as needed by changing the interface and simply switching modes. The HAMILTON-H900 humidifier now also offers a special high flow oxygen therapy mode with dedicated settings to support high flow oxygen therapy for all patient groups.

* Not all features and ventilators are available in all markets.

**References**

5. Li J, Jing G, Scott JB. Year in review 2019: high-flow nasal cannula oxygen therapy for adult patients. Respir Care 2020; 65: 545–557


