# Predicting Success of High-Flow Nasal Cannula in COVID-19

High-flow nasal cannula (HFNC) therapy has dramatically changed the management of acute hypoxemic respiratory failure. The ongoing COVID pandemic has only increased its use, and it is a key modality in the management of hypoxemic patients with and without COVID. Predicting which patients may fail HFNC remains a challenge, as does identifying when to transition a failing patient to mechanical ventilation.

In this edition of RESPIRATORY CARE, Chandel et al[1] retrospectively describe 272 subjects with COVID-19 managed with HFNC. The previously validated respiratory to oxygenation (ROX) index was used to stratify subjects at risk for HFNC failure who would thus require endotracheal intubation.[2] This index is simply a ratio of oxygenation ($S_{pO_2}/F_{IO_2}$) to breathing frequency, with a lower number indicative of increased respiratory compromise. A cut-off value of 4.88 was previously reported to differentiate patients with pneumonia at increased risk for intubation.[3] In this cohort, a ROX index $> 3$ was 85% specific for subjects who were able to be weaned from HFNC. As expected, those who "failed" HFNC were significantly older (60 vs 54 y, $P < .01$), sicker (SOFA score 4 vs 2, $P < .01$), and possibly more inflamed (neutrophil to lymphocyte ratio 8.1 vs 6.1, $P < .01$).

Strengths of this study include a large sample size, nearly matching the landmark FLORALI trial.[4] The failure group alone contained 108 subjects and allowed for analysis between those who failed HFNC before and after 48 h from initiation of HFNC. Additionally, multivariate analysis was performed, and mortality data were collected and analyzed. Unlike prior ROX studies and many prior ARDS studies, this study looked at a single disease process, namely COVID-19.

Patients were recruited from nearly the beginning of the COVID-19 epidemic in March 2020 through June 2020. While a "COVID-19 management protocol" is described, it is unclear whether this protocol was uniform throughout the study period. Early in the pandemic, many institutions intubated patients with COVID-19 who presented with less severe hypoxemia due to concerns regarding infection control as well as reports of rapid respiratory collapse. A temporal change in practice may have affected which patients were intubated and when.

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The use of therapies such as steroids, remdesivir, and inhaled nitric oxide may have changed over the course of the epidemic, especially as new data were published. For instance, the results of the RECOVERY trial[5] were not made public until June 2020 and likely led to increased corticosteroid use. The increased rates of steroid use, remdesivir, and self-proning in the late failure group suggest that these treatments were used as salvage rather than upfront therapies. More uniform use of steroids and other emerging evidence-based therapies may have affected which patients failed HFNC.

This report suggests that "late," beyond 48 h, HFNC failure is not associated with excess mortality and perhaps delaying intubation is not harmful in this population. A study randomized to early vs late intubation in patients treated with HFNC would be difficult to design and possibly unethical. This is why there are so few studies and no clinical studies on the indications for intubation. As there are no consensus guidelines as to when a patient should be intubated, this decision remains largely clinical and will vary from institution to institution and even within providers at a single institution. The absolute difference in mortality of 13.9% ($P = .18$) raises the question of whether there exists a subgroup of patients who benefit from early intubation.

One has to wonder why a patient fails late during a hospital stay, and perhaps it is less related to self-inflicted lung injury and has more to do with the disease process in that patient and lack of response to the treatments that are being administered. The data presented do not show a difference in complications such as pneumothorax or ventilator-associated pneumonia, though it may be underpowered to do so.

This study again shows the value of the ROX index in predicting failure of HFNC. This information can inform the bedside clinician as to which patients may deteriorate. The ROX index could be used in triage, especially during a pandemic or other situations where ICU services may be

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Correspondence: Robert J Varipapa Jr MD. E-mail: robert.j.varipapa@gunet.georgetown.edu.

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overwhelmed. The fact that 67.7% of subjects in this report were managed in a non-ICU setting supports this notion. Additionally, this study suggests that HFNC may delay intubation without leading to increased mortality.

**Robert J Varipapa Jr**
**Rajiv Sonti**
Division of Pulmonary, Critical Care and Sleep Medicine
Georgetown University Medical Center
Washington, DC

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