COVID-19 related ARDS – Timing of intubation

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The development of clinical data on COVID-19 has been very rapid, resulting in a large amount of data being generated in a very short time. However, hard evidence still appears to be scarce. This article has been written to the best of our knowledge based on selected literature and opinions of clinical experts. It does not represent a summary of all available literature and therefore does not claim to be exhaustive. As COVID-19 is a very complex disease, you should always refer to the original literature mentioned in this article, other relevant literature and the circumstances of the individual case when deciding on the right ventilation strategy for your patients. It is also strongly advised to follow your national/local guidelines and standards.

The timing of intubation is a contentious issue: It is clearly critical, as delayed intubation is associated with a worse prognosis; at the same time, controversy exists regarding the role of early intubation vs. use of non-invasive respiratory support (NRS) to avoid intubation.[41] However, one current review of twelve studies on close to 9,000 patients came to the conclusion that the timing of intubation may actually have no effect on mortality and morbidity of critically ill COVID-19 patients ('early': intubation within 24h from ICU admission, 'late'= intubation any time after 24h of ICU admission); the conclusion was that these findings might well justify a "wait and see" approach, which in turn could lead to fewer intubations.[42]

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IMPORTANT:

All reviewed Guidelines recommend closely monitoring patients treated with HFNC or CPAP/NIV in order to not miss the right point for intubation. So possibly, it is once again not a matter of "early" vs. "late" as timing starting with admission to ICU, but rather a question of the right time for the individual patient.

However, only one of the reviewed guidelines provide specific information for the decision on when to perform endotracheal intubation.

Reviewed Guidelines:

- German S3 Guideline – Recommendations for the therapy of hospitalised patients with COVID-19, Version 4.1, February 2021 [referred to as **GS3**)[34]
- Surviving Sepsis Guidelines on the Management of Adults with Coronavirus Disease 2019 (COVID-19) in the ICU: First Update; March 2021 [referred to as **SSC**)[35]
- ERS Guideline for the Management of hospitalized adults with coronavirus disease 2019 (COVID-19): A European Respiratory Society living guideline, January 2021 [referred to as **ERS**][36]
- Australian guideline for clinical care of people with COVID-19, National COVID-19 Clinical Evidence Taskforce [referred to as **NCCET**][37]

GS3:

- Recommends considering intubation and mechanical ventilation of patients with severe hypoxemia (P/F <150) and respiratory rate (RR) >30/min. In patients with P/F <100mmHg, intubation and mechanical ventilation is generally recommended.

Going through the existing literature, the monitoring of respiratory drive and effort along with other parameters seems to be in the foreground in order not to miss the right point in time for intubation.

What seems clear is that intubation should be patient-led, based not only on PaO_2/FiO_2, but also on respiratory drive and specifically effort and risk of P-SILI. Patients who show signs of clinical deterioration or high respiratory distress that is not alleviated by non-invasive respiratory should promptly be intubated and treated with a lung-protective ventilation strategy.[41]

When to consider intubation?

- Worsening or unbearable dyspnea
- Lack of improvement in oxygenation
- Hemodynamic instability
- Persistent respiratory muscle fatigue
- Persistent tachypnea
- Neurologic deterioration

Parameters to monitor[43]:

- Every 1-3 hours
  PaO_2/FiO_2 ratio
  Respiratory Rate
  Signs of respiratory muscle fatique
  $PaCO_2$
  Dyspnea
- Continuous monitoring
  SaO_2
  Blood Pressure
  Heart Rate

Also, monitoring esophageal pressure (Pes) swings to identify excessive respiratory effort during NIV, as previously described above, may provide an indication of excessive respiratory effort.

Carteaux and colleagues studied the role of tidal volume in the failure of noninvasively ventilated patients with acute hypoxemic failure and conclude that “in patients with moderate-to-severe hypoxemia, the expired tidal volume above 9.5 mL/kg predicted body weight accurately predicts noninvasive ventilation failure.”[44]

In an editorial, Pisano and colleagues state that most guidelines fail to provide concrete parameters for the decision for intubation and invasive ventilation, which we can confirm with regards to the guidelines reviewed for this article.[45] They discuss the reliability of common criteria for intubation, such as PaO_2/FiO_2 ratio, absolute PaO_2, SaO_2, and state that these might not be sufficiently precise as they are impacted by various variables. Therefore they suggest the following criteria:

1. Need for airway protection (alteration of consciousness)
2. Severe decompensated acidosis (e.g. pH <7.2-7.25)
3. Severe absolute hypoxemia (PaO_2 <50mmHg or SaO_2 <90%-92%) despite maximal non-invasive respiratory support
4. Signs and symptoms of significant respiratory distress or tissue hypoxia despite max. non-invasive respiratory support
5. Decision for ECMO in patients refractory (PaO_2/FiO_2 ratio <100mmHg, arterial partial pressure of carbon dioxide above 60mmHg, pH <7.2) to standard treatment.

Scores and scales to help making decision on intubation

Scores and Scales

A few scoring systems may provide support in the decision for ETI and invasive ventilation. To the best of our knowledge, there is no data available demonstrating superiority of one score over the other. Also, these scores for COVID-19 have not been fully validated, even though some data may be available.

Work of breathing scale. The above mentioned clinical scale for work of breathing described by Apigo et al. may be a simple clinical tool in this phase in addition to the available technical measurements also mentioned above.

ROX Index for patients receiving HNFC. The ROX-Index was introduced by Roca and colleagues in 2019 to provide support in the identification of patients with acute respiratory failure treated with HFNC running at low or high risk for intubation (HFNC failure).[46]

ROX-Index:

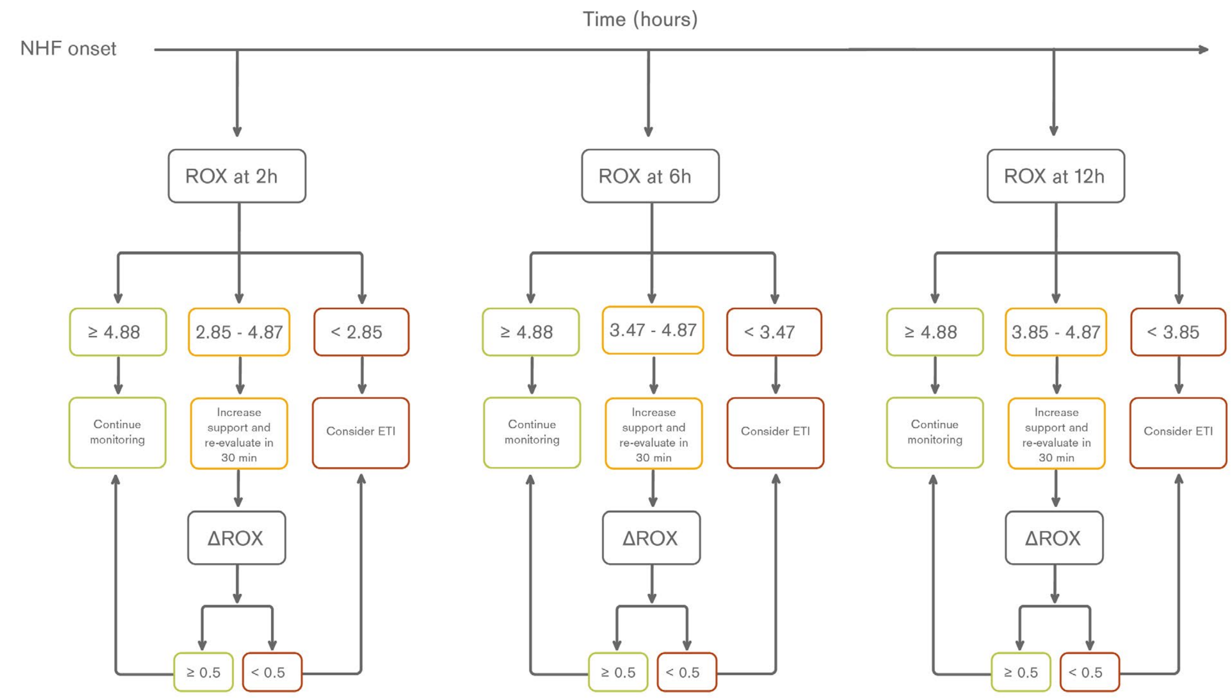
$$\textbf{ROX index} = \frac{SpO_2/FiO_2}{\text{Respiratory Rate}}$$

A ROX Index >4.88 at 2, 6 or 12 hours after HFNC onset was consistently associated with a lower risk of mechanical ventilation, even after adjusting for potential confounding.

Thresholds described: 2h: <2.85; 6h: <3,47;
12h: <3,85.

ROX-Index for prediction of HFNC treatment failure

Ricard and colleagues suggested an algorithm for the systematic application of the ROX index in the decision making process for ETI[47].

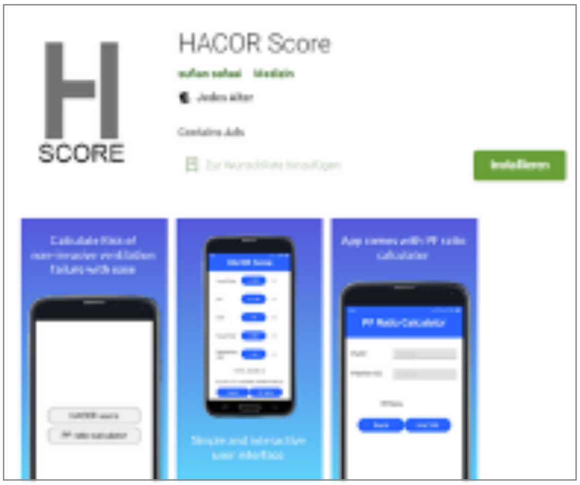


Leasa D et al., Knowledge translation tools to guide care of non-intubated patients with acute respiratory illness during the COVID-19 Pandemic, Crit Care. 2021 Jan 8;25(1):22. doi: 10.1186/s13054-020-03415-2

The ROX index has been tested in COVID-19 patients by Zucman and colleagues. They conclude that "in this circumstance, the ROX index measured within the first 4 hours after NHF initiation could be an easy-to-use marker of early ventilatory response. Its most accurate cut-off was slightly higher than previously validated in AHRF, probably because of specific ventilatory adaptation observed in COVID-19-related AHRF."[48]

HACOR scale for noninvasively ventilated hypoxemic patients. Duan and colleagues introduced a scale assessing heart rate, acidosis, consciousness, oxygenation and respiratory rate in order to predict failures of noninvasively ventilated non-COVID hypoxemic patients.[49] They conclude: "The HACOR scale variables are easily obtained at the bedside. The scale appears to be an effective way of predicting NIV failure in hypoxemic patients".

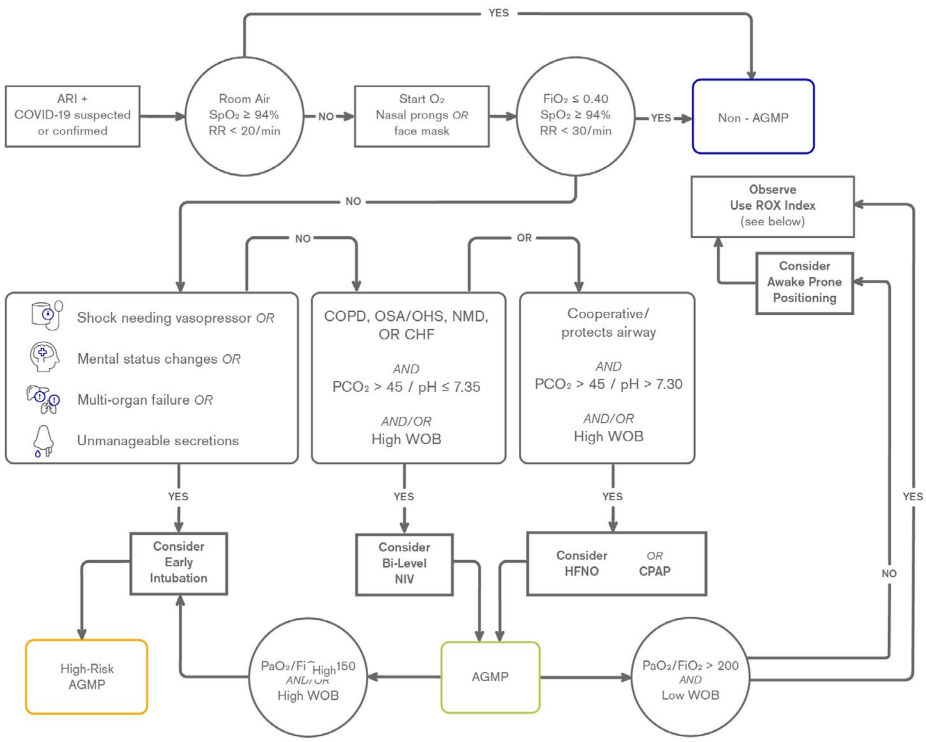
There is even an app for Android devices to calculate the HACOR Score.



Ref: HACOR Score App in Google Play Store

Algorithm from conventional oxygen therapy to intubation. In their article "Knowledge translation tools to guide care of non-intubated patients with acute respiratory illness during the COVID-19 Pandemic", Leasa and colleagues propose an algorithm that may provide guidance from providing conventional oxygen therapy to the decision on ETI and invasive ventilation based on "best knowledge available", and also incorporating indices such as the above mentioned ROX Index.[41]

Algorithm for respirator support in COVID-19 patients



PaO_2/FiO_2	≥ 300	200	150	< 100
SpO_2/FiO_2	315	235	190	150
FiO_2	0.30	0.40	0.50	0.60
SpO_2 (%)	> 94	94	95	< 90

$$\text{ROX Index} = \frac{SpO_2/FiO_2}{RR}$$

Time post intervention	2 hours	6 hours	12 hours	All times
ROX Index	< 2.85	< 3.47	< 3.85	> 4.88
Decision	Intubate	Intubate	Intubate	Observe

Leasa D et al., Knowledge translation tools to guide care of non-intubated patients with acute respiratory illness during the COVID-19 Pandemic, Crit Care. 2021 Jan 8;25(1):22. doi: 10.1186/s13054-020-03415-2

In our article on ventilating patients with COVID-19-associated ARDS, we reviewed relevant literature and four current guidelines to provide a practical overview. For references and details, please visit our website: www.draeger.com/covid-ventilation

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