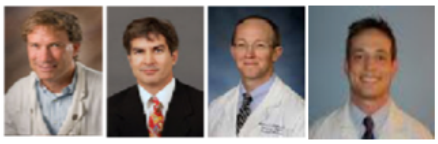
critical care perspectives in emergency medicine



How Much Supplemental Oxygen Should We Use in COVID-19 Infection?

Key Article

- *Nielsen FM, Klitgaard TL, Siegemund M, et al. Lower vs higher oxygenation target and days alive without live support in COVID-19. The HOT-COVID Randomized Clinical Trial. JAMA. 2024; 331:1185-1194.*

Background

- COVID-19 pneumonia may result in hypoxemic respiratory failure and require high levels of supplemental O2.
- Current SSC guidelines recommend targeting an SpO2 between 90-96% for COVID-19 patients.
- In recent years, we have reviewed several trials that have evaluated oxygenation targets in critically ill ICU patients. At present, there continues to be uncertainty on the effects of lower vs higher oxygenation strategies in critically ill patients.
- Establishing a safe oxygenation strategy for COVID-19 patients can ensure that supplemental O2 is optimally dosed with minimal harm and that oxygen supplies, ICU beds, and ventilators are used efficiently.

Objective

- The Handling Oxygenation Targets in COVID-19 (HOT-COVID) study was planned to test the hypothesis that targeting a PaO2 of 60 mm Hg would increase the number of days alive without life support compared to a PaO2 target of 90 mm Hg in ICU patients with COVID-19 and severe hypoxemia.

Methods

- Investigator-initiated, multicenter, parallel-group, randomized trial
- 13 ICUs in Denmark, Switzerland, Norway, Iceland, and Wales
- Patients
    - Included:
        - Adults $\geq$ 18 years
        - Admitted to the ICU with confirmed COVID-19
        - Severe hypoxemia
            - Defined as receiving O2 with a flow of at least 10L/min in an open system or receiving NIV, CPAP, or mechanical ventilation irrespective of the FiO2.
        - Expected to receive supplemental O2 for at least 24 hrs in the ICU.
        - Had an arterial line to monitor PaO2.
    - Excluded
        - Age < 18 years
        - Were unable to undergo randomization within 12 hrs of admission.
- Trial procedures
    - Randomized in 1:1 ratio.

        - Lower oxygenation target: PaO2 of 60 mm Hg
        - Higher oxygenation target: PaO2 of 90 mm Hg
    - Patients monitored with continuous SpO2 measurements and correlated with associated PaO2 measurements.
    - Ventilator settings and choice of O2 delivery device were at the discretion of the clinician.
    - Patients treated with supplemental O2 in an open system were not allowed to be intubated just to reach the O2 target if no other criteria for invasive mechanical ventilation were present.
    - Frequency of PaO2 measurements was not protocolized.
    - All ICUs in the study were experienced in intubation and extubation in the 2 oxygenation target groups.
    - Intervention was implemented for the entire ICU stay up to a max of 90 days.
- Primary outcome
    - Absolute number of days alive without life support in 90 days
    - Life support defined as:
        - Respiratory – mechanical ventilation, NIV, CPAP
        - Circulatory support – inotropes or vasopressors
        - RRT
    - ECMO not included as life support.
- Secondary outcomes
    - 90-day all-cause mortality
    - Number of patients with 1 or more serious adverse events in the ICU – new episode of shock, cerebral ischemia, MI, mesenteric ischemia
    - Absolute number of days alive and out of the hospital at 90 days

Results

- A total of 726 patients were enrolled in the trial.
    - Lower oxygenation group: 365 patients
    - Higher oxygenation group: 361 patients
    - No patients enrolled in Iceland or Wales
- Characteristics
    - Median age 65 years
    - Approximately 73% had pneumonia.
    - Approximately 40% with ARDS
    - Approximately 23-24% were receiving mechanical ventilation and approximately 63% were receiving supplemental O2 via an open system.
- Primary Outcome – median number of days alive without life support
    - Lower oxygenation group: 80.0 days
    - Higher oxygenation group: 72.0 days
    - P=0.009
    - Difference in number of days alive without life support mainly driven by use of mechanical ventilation.
    - Subgroup analysis showed a significant interaction for patients with shock at baseline with an increased number of days alive without life support in the lower oxygenation group.
- Secondary outcome

- 90-day all-cause mortality
  - Lower oxygenation group: 30.2%
  - Higher oxygenation group: 34.7%
  - Risk ratio 0.86 (CI 0.66 to 1.13; p=0.18)
- Serious adverse events in the ICU did not differ between groups.
- Number of days alive and out of the hospital at 90 days did not differ.

Limitations Identified by Authors

- Trial stopped early due to slow enrollment – number of patients with severe hypoxemia from COVID-19 not as common toward the end of the pandemic.
- Clinicians not blinded to the interventions.
- No specific protocols for intubation or weaning from mechanical ventilation.
- Overall mortality lower in patients in this trial compared to others that included COVID-19 patients from the first wave of the pandemic.
- Investigators did not have information about the devices used for supplemental oxygen therapy in open systems.
- Investigators did not have information on the specific COVID-19 variants or other treatments specific to COVID-19.

Take Home

- Targeting a PaO2 of 60 mm Hg resulted in more days alive without life support compared to a PaO2 of 90 mm Hg in adult ICU patients with COVID-19 and severe hypoxemia.