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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.

Once intubated, the right ventilation regimen in COVID-19 patients has to be decided on. The earlier stated concept of the COVID-19 phenotypes led to the assumption that the L-Type representing an early stage of the disease is significantly different to “classic” ARDS with respect to a variety of lung characteristics, which was supposed to be found at least in a part of the COVID-19 cases.^{8,4}

Subsequently, quite a few larger studies from various countries looking at a total number of about 7,000 patients, however, did not confirm these findings and postulated the compliance as more or less in the range of patients with non-COVID-ARDS. This challenged the idea of the “different” ARDS.

Currently it seems to be consensus that type L and type H phenotypes should not be used to guide clinical practice.¹⁴

As large randomized studies on the invasive ventilation of COVID-19 patients are still lacking, most recommendations for ventilation therapy of patients with CARDS are derived from the known recommendation for the ventilation non-COVID-19 ARDS as published in current guidelines.

The following measures are recommended by at least one of the reviewed guidelines. Differences in guidelines will be stated accordingly.

Tidal Volume. Use V_t of approx. 6ml/kg/IBW.

Only 2 of the reviewed guidelines provide specific guidance on tidal volume: Whereas the Germany S3 guideline recommends a V_t of ≤ 6 ml/kg/IBW, the guideline of the ‘Survive Sepsis Campaign’ (SSC) recommends 4-8ml/kg/PBW.

Endinspiratory airway pressure. Use < 30 cmH₂O.

Only 2 of the reviewed guidelines provide specific guidance on end-inspiratory airway pressure. Both the German S3 guidelines as well as the SSC guideline provide the same recommendation.

PEEP. High-FiO₂/PEEP table to be used in moderate to severe ARDS. This seems to be the consensus across the reviewed guidelines. The German S3³⁴ guideline provides a slightly more practical guidance, see more below.

Electrical Impedance Tomography (EIT) may be helpful when titrating the PEEP to the need of an individual patient by

identifying PEEP values at which both overdistension and collapse are minimized.²⁷ Various care reports have stated the usefulness of EIT in the individualization of ventilatory management.⁵⁵

Prone position. Proning is recommended by all reviewed guidelines. The German S3 guidelines is the only reviewed guideline to provide $\text{PaO}_2/\text{FiO}_2$ of $<150\text{mmHg}$ as a threshold for consequent proning. Regarding the duration of prone positioning, recommendations range from 12-16 hours (GS3 16h, SSC 12-16h, NCCET $>12\text{h}$ per day)

Even though not mentioned in the guidelines, the use of EIT to measure of success of prone position has been described in various reports. Recently, Zhao and colleagues mention the use of EIT in identifying unilateral worsening of the lung in their positioning strategy.⁵⁶ Taenaka and colleagues presented two COVID-19 cases with different responses to PEEP and positioning. Distribution of ventilation was monitored with EIT. They concluded that the careful evaluation of respiratory system mechanics and visualization of ventilation with EIT was useful in individualizing ventilatory management.⁵⁵

Recruitment Maneuvers. Recruitment maneuvers are only recommended as a rescue maneuver in severe cases if hypoxemia persists despite optimized ventilation. SSC and NCCET specifically recommend against stepwise recruitment maneuvers. Recruitment maneuvers should only be applied on responders, as in non-responders both measures seem to have rather a

detrimental effect.²⁹ Monitoring patients with EIT reveals if a patient responds positively by a more homogenous distribution of ventilation. During a decremental PEEP trial, EIT can show where and to what extent lung overdistension and lung collapse take place. This information can be used to find the best compromise.³⁰

Neuromuscular Blocking Agents. Recommendations differ: The SSC recommends continuous infusion of NMBA for up to 48 hours as rescue maneuver in patients with persistent ventilator dyssynchrony, the need for ongoing deep sedation, prone ventilation or persistently high plateau pressures. NCCET recommends against continuous infusion, except for patients in which protecting ventilation cannot be achieved.

Nitric Oxide. The application of nitric oxide seems to be controversial. Only 2 of the reviewed guidelines provide guidance. While the German S3 guideline would consider NO as a rescue medication in severe cases, the SSC guideline recommends against the use of NO.

ECMO. Two guidelines state ECMO as a rescue therapy. The Germany S3 guidelines provides most concrete guidance recommending ECMO for patients with severe ARDS and refractory hypoxemia ($\text{PaO}_2/\text{FiO}_2$ ratio < 80 and 60 mmHg , respectively). The SSC suggests ECMO in patients with refractory hypoxemia despite optimized ventilation, use of rescue therapies and proning.

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

SUMMARY OF DIRECTIONS OF GUIDELINES FOR INVASIVE VENTILATION OF PATIENTS WITH COVID-19 RELATED ARDS.

GS3:

- **Tidal Volume.** Patients with controlled ventilation and ARDS should receive a tidal volume of $\leq 6\text{ml/kg/IBW}$
- **Endinspiratory Pressure.** Endinspiratory airway pressure should be $\leq 30\text{cmH}_2\text{O}$
- **PEEP.** As a orientation for initial PEEP setting, the FiO_2/PEEP table of the ARDS-Network should be considered. In an early phase without consolidation and with high compliance and expectedly low recruitability, the low- FiO_2/PEEP table might be reasonable. In the classic image of morphological manifestation of ARDS with reduced compliance, the high- FiO_2/PEEP table might be preferable. For patients with more classic ARDS, close monitoring is recommended to adapt PEEP to the individual patient situation.
- **Prone Position.** In case of $\text{PaO}_2/\text{FiO}_2 < 150\text{mmHg}$, consequent prone positioning should be applied at intervals of 16 hours.
- **NO, NMBA, Recruitment Maneuvers.** In individual cases, application of inhaled nitric oxide (NO), NMBA, or a recruitment maneuver may be considered to bridge severe hypoxemia.
- **ECMO.** In patients with severe ARDS and refractory hypoxemia ($\text{PaO}_2/\text{FiO}_2$ ratio < 80 and 60 mmHg , respectively), the use of veno-venous ECMO is a therapeutic option to stabilize gas exchange.

SSC:

- **Tidal Volume.** In mechanically ventilated COVID-19 with ARDS, the use of low-tidal volumes of $4\text{-}8\text{ml/kg/PBW}$ is recommended over high tidal volume of $>8\text{ml/kg/PBW}$. (Strong)
- **Airway pressure.** The guideline recommends to target plateau pressures of $<30\text{cmH}_2\text{O}$ (Strong)
- **PEEP.** For moderate to severe ARDS, a higher PEEP strategy is suggested. If PEEPs $>10\text{cmH}_2\text{O}$ are used, clinicians should monitor patients for barotrauma. (Strong)
- **Prone Position.** Prone positioning is suggested in adults with moderate to severe CARDS for 12-16 hours. (Weak)

- **Recruitment Maneuvers.** Recruitment Maneuvers are suggested for patients with hypoxemia despite optimized ventilation. (Weak) If recruitment is used, the guideline recommends against using a staircase recruitment maneuver. (Strong)
- **NMBA.** Continuous infusion of NMBA for up to 48 hours is recommended in cases of persistent ventilator dyssynchrony, the need for ongoing deep sedation, prone ventilation or persistently high plateau pressures. Otherwise, as-needed intermittent boluses are to be favored over continuous infusion. (Weak)
- **Nitric Oxide.** The guideline recommends against the use of inhaled nitric oxide (NO). (Weak)
- **ECMO.** Veno-venous ECMO is suggested in patients with refractory hypoxemia despite optimized ventilation, use of rescue therapies and proning. If available refer to an ECMO center.

ERS:

- No recommendation for invasive ventilation.

NCCET:

- **PEEP.** For mechanically ventilated adult with moderate to severe CARDS, consider higher PEEP strategy ($>10\text{cmH}_2\text{O}$) over lower PEEP strategy. This recommendation is given in the absence of CARDS-specific evidence. .
- **Prone Position.** Consensus recommendation for prone positioning for more than 12 hours a day in patients with COVID-19 with hypoxemia despite optimized ventilation.
- **Recruitment Maneuvers.** Consensus recommendation to apply recruitment maneuvers for mechanically ventilated patients with hypoxemia despite optimized ventilation. The guideline recommends against stepwise recruitment (incremental PEEP).
- **NMBA.** For mechanically ventilated adults with moderate to severe CARDS, do not routinely use continuous infusion of NMBAs. If protective ventilation cannot be achieved, consider using NMBA for up to 48 hours.



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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