Lessons Learned in Mechanical Ventilation/ Oxygen Support in Coronavirus Disease 2019

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KEYWORDS

• COVID-19 • SARS-CoV-2 • ARDS • Mechanical ventilation

KEY POINTS

- Evidence-based treatment principles for patients with non-COVID ARDS apply to patients with COVID-19 ARDS as well.
- A trial of HFNC or NIPPV can be offered.
- Once intubated, provide lung protective ventilation. Prone positioning should be considered in patients with persistent hypoxemia or when lung protective ventilation targets cannot be achieved.
- Rescue therapies such as recruitment maneuvers, inhaled pulmonary vasodilators and ECMO should be considered on a case-by-case basis.

BACKGROUND

After its first description in Wuhan, China, in December 2019, the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spread worldwide at a rapid pace, causing the WHO to declare a pandemic on March 11, 2020.[1] Two years later, there have been more than 480 million confirmed cases and more than 6 million confirmed deaths.[2] The spectrum of the disease ranges from asymptomatic infection or mild respiratory symptoms to pneumonia, with severe cases leading to the acute respiratory distress syndrome (ARDS) with multiorgan involvement. Data from the first months of the pandemic reported that approximately 14% of infected individuals required hospitalization and 5% intensive care unit (ICU) admission.[3]

Faced with a global health crisis caused by a previously unknown disease entity, the medical and scientific community felt the imperative to disseminate even preliminary observations and data. Information emerged in real time and clinical management was adjusted as more evidence became available, thus creating certain trends that changed over the course of the pandemic.

This article will review how the ventilatory management of patients with COVID-19 evolved during the course of the pandemic and review the data that are currently available. We will conclude with current evidence-based recommendations.

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SEARCH STRATEGY

To inform our review, we searched MEDLINE/PubMed from inception to February 24, 2022, using a combination of the terms COVID-19, SARS-CoV-2, ARDS, acute respiratory distress syndrome, critical care, mechanical ventilation, and oxygen supplementation. We reviewed relevant references cited in selected articles and added relevant publications.

DISCUSSION

COVID-19 Phenotypes

It became evident early on during the pandemic that respiratory failure is one of the main features of severe COVID-19 disease, with a large number of patients with COVID-19 requiring oxygen supplementation and mechanical ventilation. Although clinical features of this new entity typically met the Berlin definition criteria for ARDS,[4] there was initial concern that lung involvement in COVID-19 might represent a specific disease with distinctive phenotypes, potentially requiring a unique approach to ventilatory support. In a small case series, Gattinoni and colleagues[5] described profound hypoxemia associated with near normal compliance of the respiratory system (Crs), which is rarely seen in cases of ARDS. The authors made a distinction between this non-ARDS, type 1 presentation as opposed to "typical" ARDS, which they called type 2 presentation.[6] These 2 subtypes were soon renamed to Phenotype L—characterized by low elastance, low VA/Q ratio, low lung weight, and low recruitability—and Phenotype H characterized by high elastance, high right-to-left shunt, high lung weight, and high recruitability.[7] Although recognized as being time-dependent manifestations on the same disease spectrum, postulating different phenotypes raised the question of a tailored, different therapeutic approach. Recommendations were made to favor noninvasive approaches or—once intubated—lower positive end-expiratory pressure (PEEP) and more liberal tidal volumes (8–9 mL/kg predicted body weight [PBW]) in type L.[7] Once transitioned to type H, the patient would be treated as a "typical" ARDS patient with low tidal volumes and prone positioning.[7,8]

ARDS is a heterogenous syndrome, and efforts are continuously made to identify subtypes based on biological, clinical, or radiological characteristics—both in non-COVID[9–12] and COVID patients with ARDS.[13,14] Different phenotypic patterns based on the compliance of the respiratory system (Crs) as observed by Gattinoni and colleagues[5] seem to be present in non-COVID-19 ARDS[15] as well, and represent most likely progression of the disease entity. The postulation of the distinct phenotypes L and H requiring different approaches to ventilation has led to discussions in the published literature[16–19]; however, with little additional data to support a dichotomous phenotypic distribution, or the need for a tailored approach to ventilation as suggested by these phenotypes, this concept has been largely deemphasized in the later phases of the pandemic.

Use of Noninvasive Respiratory Support

The COVID-19 pandemic saw a renewed interest in noninvasive forms of respiratory support—including high-flow nasal cannula (HFNC) and noninvasive ventilation (NIV) for the treatment of COVID-19-associated respiratory failure. This was due in part to the initial reports of high mortality in patients on invasive mechanical ventilation[20] and in part to the limited availability of ventilators in some jurisdictions. The early observation of preserved lung compliance and increased shunt fraction in patients with COVID-19[5] also seemed to favor maintaining spontaneous breathing. Using a helmet interface for NIV, rather than more typical mask interfaces, was suggested to reduce risk of airborne transmission[21,22] because NIV and HFNC were initially considered aerosolizing procedures. Evidence that their use did not produce additional viral contamination emerged in later phases of the pandemic.[23] Early observational studies with considerable limitations reported safe usage of HFNC[24] and NIV,[25] both in the ICU and outside the ICU setting, and variable rates of escalation to intubation.[26–28] The Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients with COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure (HENIVOT) randomized clinical trial[29] compared helmet NIV followed by HFNC versus HFNC alone in 109 patients with COVID-19 induced moderate-to-severe respiratory failure ($PaO_2/FiO_2 < 200$ mm Hg and $PaCO_2 \leq 45$). This trial failed to show a difference in respiratory support-free days at 28 days (mean difference, 2 days [95% CI, −2 to 6]); however, the incidence of intubation was significantly lower in the helmet NIV group compared with the HFNC group (30% vs 51%; difference −21% [95% CI -38% to −3%], $p = 0.03$).

The use of noninvasive respiratory support continued through the course of the pandemic, with both HFNC and NIV being used. A recent parallel group, adaptative, randomized clinical trial of 1273 hospitalized patients with COVID-19-associated hypoxemic respiratory failure (RECOVERY-RS) compared the use of either

continuous positive airway pressure (CPAP), HFNC, or conventional oxygen therapy with the primary composite outcome of tracheal intubation or mortality within 30 days.[30] The trial was discontinued early due to declining numbers of patients with COVID-19 and termination of the funded recruitment period. The primary outcome was significantly lower in the group randomized to CPAP as compared with conventional oxygen therapy (36.3% vs 44.4%, absolute difference, −8% [95% CI, −15% to −1%]). This was mainly driven by the reduction in the need for intubation (33.4% vs 41.3%). There was no statistically significant difference in the primary outcome between the HFNC group versus the conventional oxygen therapy group (44.3% vs 45.1%, absolute difference, −1% [95% CI, −8% to 6%]). Safety events were more common in the CPAP arm (130/380–34.2%) compared with the HFNC arm (86/418–20.6%) and the conventional oxygen therapy arm (66/475 or 13.9%). In a post hoc analysis, CPAP was compared with HFNC in 570 participants randomized across all 3 groups, with the primary outcome occurring in 34.6% (91/263) of participants in the CPAP group and in 44.3% (136/307) of participants in the HFNO group (absolute difference 10% [95%CI, −18% to −2%]). This is the largest study of NIV in COVID-19-induced respiratory failure to date. The main limitation of the trial consists in its early termination, which could lead to an overestimation of the results. Additionally, patients, clinicians, and outcome assessors were unblinded and the clinical criteria for intubation were left to provider discretion.

In the HiFLo-Covid trial,[31] 199 patients with suspected or confirmed infection with SARS-CoV-2, acute hypoxemic respiratory failure with a PaO2/FIO2 less than 200 and clinical signs of respiratory distress were randomized to either HFNC or conventional oxygen therapy. Intubation occurred in 34 (34.3%) patients randomized to the high-flow oxygen therapy and in 51 (51%) patients randomized to receive conventional oxygen therapy. In addition, patients treated with HFNC had a median time to recovery of 11 days (IQR, 9–14) vs 14 (IQR 11–19) days in the conventional oxygen therapy group.

Given the lack of evidence demonstrating a mortality benefit in the usage of one noninvasive modality over the other, both HFNC and NIV are acceptable initial therapeutic modalities for patients with COVID-19 with hypoxemic respiratory failure. Further research is needed to confirm the advantage of CPAP over HFNC, as demonstrated in the post hoc analysis of 570 participants of the RECOVERY-RS trial.

Timing of Intubation

Determining the optimal timing for intubation remains challenging and should be done on a case-by-case basis. Intubation is considered a high-risk, aerosol-generating procedure but the magnitude of the infection risk for health-care personnel is difficult to quantify.[32,33] During the beginning of the pandemic, there was a controversy regarding whether “early” intubation is necessary to prevent patient self-inflicted lung injury[8,34] or not.[35,36] This in keeping with data from patients with non-COVID-19 induced moderate-to-severe ARDS and a PO2/FiO2 ratio of less than 150, in which the use of NIV instead of early intubation was associated with higher mortality.[37] In addition, early intubation was thought to minimize the risks of aerosol transmission and infection of health-care workers by avoiding the exposure of NIV and HFNC, which are considered aerosolizing generating medical procedures. However, what exactly constitutes an “early” timing was never defined. In addition, there were concerns around high mortality in intubated patients,[38,39] which led to some practitioners tolerating high oxygen requirements and low saturations and basing the decision of intubation on the patient’s subjective work of breathing.

The literature published during the pandemic around timing of intubation in COVID-19 consists mainly of retrospective observational studies and does not show a significant association between timing of intubation and mortality.[27,40–44] Thus, given the lack of evidence to the contrary, the decision to intubate a patient in respiratory failure due to COVID-19 should be individualized and follow the same decision-making algorithm as the decision to intubate any patient in respiratory failure.

Lung Protective Ventilation

Pressure-limited, low-tidal volume ventilation improves outcomes in patients with ARDS[45] and without ARDS[46]. In the first months of the pandemic, there was a recommendation to consider liberalizing tidal volumes in patients with the L-phenotype who had difficult to control hypercapnia.[7] This increases the potential risk of ventilator-induced lung injury (VILI) through tidal volumes higher than 6 mL/kg PBW, especially considering the possibility that type L and type H phenotypes represent the temporal evolution of the course in severe pneumonia/ARDS. A scoping review published by Grasselli and colleagues[47] showed that settings for mechanical ventilation used in COVID-19 ARDS generally followed recommendations for lung protective ventilation. A cohort study of 1503 patients with ARDS

secondary to COVID-19[48] reported that the use of lung protective settings of mechanical ventilation (defined as a tidal volume less than 8 mL/kg PBW and a plateau pressure less than 30 cm H2O in the first 24 hours after admission to the ICU) was associated with an increased survival at 28 days (HR 0.763, 95%CI 0.605–0.963), and remained associated with increased survival after adjusting for PEEP, compliance, PaO2/FiO2 (P/F) ratio and pH (aHR 0.73, 95% CI 0.57–0.94). The median plateau pressure and driving pressure were higher in nonsurvivors than in survivors (23 vs 22 cmH2O and 13 vs 12 cmH2O). The distribution of static compliance did not suggest the identification of dichotomous phenotypes.

The evidence available to date supports providing mechanical ventilation for patients with COVID-19 ARDS in the same way as for non-COVID-19 ARDS, aiming for a pressure-limited low tidal volume ventilation—as is reflected in current guideline recommendations.[49–52] Similar to non-COVID-19 ARDS, the optimal level of PEEP remains elusive in the COVID-19 ARDS population, with observational studies showing a variable range applied in clinical practice.[47,53]

Prone Positioning

Proning, the positioning of a patient face-down for a period of time in a 24-hour cycle, is standard of care in the therapy for intubated patients with moderate-to-severe ARDS, and high-quality evidence has shown that proning has a mortality benefit in these patients.[54–56] During prone positioning, oxygenation improves by decrease of the shunt fraction as a result of more homogenous lung aeration and strain distribution with perfusion patterns remaining relatively constant.[57] The improvement in gas exchange however does not seem to be the sole driver of the survival benefit.[58] In addition, prone positioning is thought to attenuate VILI by recruiting lung parenchyma in dependent regions and reducing hyperinflation in nondependent regions.[57]

Small, observational studies published early in the pandemic[59–62] showed improved oxygenation through prone positioning, and further observational data described reduced mortality in those patients on mechanical ventilation who were proned.[63–65] Proning protocols were developed, and some centers created specific proning teams to provide relief for the core intensive care team.[66–68] Intermittent prone positioning became standard of care for intubated patients with ARDS secondary to COVID-19, mainly based on literature showing reduction in mortality in non-COVID ARDS.[54–56]

Proning had been shown to provide improvement in oxygenation in awake, nonintubated patients even before the COVID-19 pandemic,[69,70] and its use in COVID-19 awake patients has been shown to be feasible and effective in terms of an oxygenation benefit.[71] Ehrmann and colleagues[72] demonstrated additionally that prone positioning in awake patients reduces the incidence of treatment failure and the need for intubation, without increasing adverse events. In the recently published COVID-PRONE trial—prone positioning of patients with moderate hypoxemia due to COVID-19 multicenter pragmatic randomized trial—257 patients were randomized to prone positioning or standard of care.[73] The rate of the primary outcome—a composite of in-hospital death, mechanical ventilation of worsening respiratory failure defined as needing at least 60% FiO2 for more than 24 hours—was similar in both groups. The investigators also report a low adherence to the prone position, with “discomfort” being anecdotally cited as the main reason. The trial was discontinued early for futility.

In a recent systematic review and meta-analysis on awake prone positioning in COVID-19-related acute hypoxemic respiratory failure, aggregate data of 10 RCTs showed that awake prone positioning significantly reduced the need for intubation in patients who received advanced respiratory support (HFNC or NIV) and those in intensive care setting.[74]

Although robust data showing that self-proning in awake patients reduces mortality is still lacking, it is now part of standard of care in many centers for the COVID-19 patient with increased oxygen requirements.

Timing of Tracheostomy

The optimal timing for tracheostomy is a matter of debate even in prolonged mechanical ventilation outside the context of COVID-19. In the early days of the pandemic, tracheostomies were often deferred until the patients were confirmed to be no longer infectious (ie, using polymerase chain reaction), given that tracheostomy was generally considered a high-risk procedure. Emerging data showed that both recommendations and practice vary from institution to institution and transition to tracheostomy is performed anywhere between 3 and 21 days after intubation,[75] similar to the non-COVID-19 population. Some have suggested support for earlier timing due to emerging data on reduction of sedation and analgesia in patients undergoing tracheostomy.[76] Current guidelines recommend performing a tracheostomy in intubated patients with COVID-19 who are anticipated

to require prolonged mechanical ventilation, with no specific recommendation on the timing of the procedure. In order to mitigate the infectious risk for health-care workers, the use of enhanced protective equipment (airborne precautions) is advised.

POTENTIAL RESCUE THERAPIES AND OTHER CONSIDERATIONS

Recruitment Maneuvers

Previous experience from non-COVID-19 ARDS has shown that the effect of recruitment maneuvers varies from patient to patient, often improving oxygenation but with conflicting results on mortality. Recruitment maneuvers are most likely to be beneficial in patients who have a high potential for recruitment.[77] The assessment of recruitability at the bedside can be determined with the recruitment to inflation (R/I) ratio—the ratio between the compliance of the recruited lung and ventilated lung at low PEEP,[78] which can be calculated using an online calculator (https://crec.coemv.ca/).[79] The R/I ratio has only been evaluated in small studies in the COVID-19 population, although with promising results.[59,80,81] Should a recruitment maneuver be performed, most guidelines are currently recommending against the use of a staircase (incremental PEEP increase) maneuver.[50,82]

Airway Pressure Release Ventilation

Airway pressure release ventilation (APRV) has the theoretical physiologic benefit of optimizing alveolar recruitment and allowing for spontaneous breathing at the same time. However, studies failed to show a consistent benefit in non-COVID-19 hypoxemic respiratory failure and ARDS. In a recent RCT, Ibarra-Estrada and colleagues[83] randomized 90 patients with COVID-19 ARDS to receive either low tidal volume ventilation or APRV. There was no difference in ventilator-free days, sedation or analgesia requirements, or barotrauma between the 2 groups. Further evidence is needed before APRV can have an established role in the treatment of COVID-19 ARDS.

Pulmonary Vasodilators

The role of pulmonary vasodilators as a rescue therapy has been established in the non-COVID-19 ARDS population, with improvement in physiologic parameters but no mortality benefit.[84] The current evidence regarding the use of inhaled pulmonary vasodilators as a rescue therapy in refractory hypoxic respiratory failure secondary to COVID-19 ARDS is limited[85–88] and does not allow for definitive conclusions. Current guidelines recommend against the routine use of inhaled nitric oxide and for the use of a trial of inhaled pulmonary vasodilators as a rescue therapy.[50,82]

Extracorporeal Membrane Oxygenation

The indication to use extracorporeal membrane oxygenation (ECMO) as a rescue therapy for refractory hypoxemic respiratory failure secondary to COVID-19 ARDS follows traditional selection criteria while considering availability of resources, as discussed in detail in a separate article of this series.

Resource Shortages Affecting Approach to Respiratory Support

Shortage and need can often lead to bold, new solutions. In August 1952, the Blegdam Hospital in Copenhagen faced a polio epidemic, and there was only one iron lung to treat a large number of patients who required negative pressure ventilation. It was in this context that the anesthesiologist Bjorn Ibsen brought forward and implemented the idea of ventilation with positive pressure through a tracheostomy. It soon became the lifesaving treatment during the polio epidemic, thanks to the coordinated efforts of the University of Copenhagen's medical and dental students, who provided ventilation by hand—around the clock.[89]

The COVID-19 pandemic underscored a fear of lack of sufficient resources to provide ventilatory support. The anticipated shortage of ventilators in the beginning of the pandemic led to a discussion around the use of shared ventilation, with one ventilator supporting 2 patients. A review published by Branson and Rodriguez in 2021 summarizes the proposed technical solution, the limited evidence in human trials as well as neglected ethical aspects, concluding that shared ventilation should be seen as a last resort procedure.[90] Shared ventilation appeared to be safe in a small case series and for a limited time (48 hours) but generalizability is yet untested.[91] Another proposed approach was the use of anaesthesia ventilators for prolonged mechanical ventilation.[92]

These technical aspects of increasing the number of available ventilators can only be one part of a complex response to increased demand for acute and critical care services. During the course of the pandemic, most countries and/or administrative divisions developed protocols to give legal and ethical guidance under a crisis standard of care, with the aim to direct resource allocation for the individual institutions aiming at maximizing resources, discussing how to efficiently redeploy health-care professionals to areas of need and

Table 1
Overview of recommendations made by different societies regarding mechanical ventilation in coronavirus disease 2019 acute respiratory distress syndrome

	Surviving Sepsis Campaign	NIH COVID-19 Treatment Guideline	WHO: Clinical Management of Patients with COVID-19: Living Guideline	Australian Guidelines for the Clinical Care of People with Covid-19 v62.
Supplemental oxygen	Suggestion to start supplemental oxygen if SpO2 <92% Recommendation to start supplemental oxygen if SpO2 <90%	Target an SpO2 of 92% to 96%	Target SpO2 >90%	Target SpO2 of 92%–96% in most patients Target SpO2 of 88%–92% in patients at risk of hypercapnia
HFNC, NIPPV	HFNC over conventional oxygen therapy HFNC over NIPPV	HFNC oxygen over NIV (NIPPV)	HFNC over standard oxygen therapy HFNC, CPAP, or NIV—no recommendation to chose one device over another	Consider using CPAP. If CPAP is not available or not tolerated, consider HFNC as an alternative to conventional oxygen delivery
Awake proning	No recommendation	Trial of awake proning recommended Awake proning should not be used as a rescue therapy	Awake proning suggested in severely ill hospitalized patients	Consider awake prone positioning
Mechanical Ventilation				
Tidal volumes	Low Vt ventilation (4-8 mL/kg PBW) over higher tidal volumes (>8 mL/kg PBW)	Low Vt ventilation (4-8 mL/kg PBW) over higher tidal volumes (>8 mL/kg PBW)	Lower tidal volumes (4-8 mL/kg PBW)	
Plateau pressure	Target plateau pressure <30 cm H2O	Target plateau pressure <30 cm H2O	Target plateau pressure <30 cm H2O	
PEEP	Higher PEEP strategy over lower PEEP strategy	Higher PEEP strategy over lower PEEP strategy	Trial of higher PEEP instead of lower PEEP is suggested	Higher PEEP strategy over lower PEEP strategy

Rescue therapies			
Recruitment maneuvers	If using recruitment maneuvers, strong recommendation against staircase (incremental PEEP) maneuvers	If using recruitment maneuvers, recommends against using staircase (incremental PEEP) maneuvers	If recruitment maneuvers are used, recommendation to not use staircase (incremental PEEP) recruitment
Inhaled pulmonary vasodilators	Recommendation against the routine use of inhaled nitric oxide Suggestion for a trial of inhaled pulmonary vasodilators as a rescue therapy	Reasonable to attempt an inhaled pulmonary vasodilator as a rescue therapy	

Table 2
Overview of recommendations for ventilation in coronavirus disease 2019 acute respiratory distress syndrome

	Recommendation	Available Evidence
Oxygen supplementation and noninvasive ventilation	Trial of HFNC or noninvasive positive pressure ventilation The use of CPAP possibly reduces the need for intubation	No evidence demonstrating a mortality benefit in usage of one noninvasive modality over the other RECOVERY-RS[30]: CPAP seems to reduce the need for intubation when compared with the use of conventional oxygen therapy Strength of the trial: • Large, multicenter RCT of NIV in respiratory failure secondary to COVID-19 • Allocation concealment Limitations of the trial: • Stopped early—results might be overestimated • No criteria for when to intubate patients • Unblinded
Timing of intubation	No recommendation, individualized decision requiring clinical judgment	No high-quality evidence available
Lung protective ventilation	Tidal volumes limited to 4–6 cc/kg Plateau pressures limited to <30 cmH2O Driving pressures <15 cmH2O	Evidence for pressure limited low tidal volumes as well as limitation of driving pressures in non-COVID ARDS[45] No high-quality evidence available in the COVID-19 population
Prone positioning	In nonintubated patients: trial of awake self proning In intubate patients with moderate to severe ARDS: proning recommended	Awake self proning reduces the incidence of treatment failure and need for intubation in patients with COVID-19 induced hypoxic respiratory failure[72] Evidence showing that proning improves mortality in intubated patients with non-COVID-19 ARDS[54] No high-quality evidence for the benefit of proning in the COVID-19 ARDS population
Timing of tracheostomy	Tracheostomy recommended in patients anticipated to require prolonged mechanical ventilation No recommendation on timing of tracheostomy	Possible benefit from reduction of analgesia and sedation with early tracheostomy in the COVID-19 ARDS population[76]

providing guidance if triage were to become necessary.

Overview of Recommendation from Current Guidelines

The Surviving Sepsis Campaign Guidelines[50] provided an update on their recommendations on the management of adults with COVID-19 in the ICU in March 2021. There continues to be a strong recommendation for oxygen supplementation to keep SpO2 between 92% and 96%, lung protective ventilation with low tidal volumes and limited plateau pressure, a higher PEEP strategy over a lower PEEP strategy, and a strong recommendation against the use of staircase recruitment maneuvers. As a weak recommendation, HFNC is suggested over NIV. No recommendation was made regarding the use of helmet NIPPV compared with mask NIV. As an addition to the previous guideline, there was no recommendation regarding the use of awake prone positioning due to insufficient evidence. Of note, the update to the Surviving Sepsis Campaign Guidelines was released before evidence becoming available showing that awake self-proning reduced the need for intubation without a signal for harm.[72–74]

The NIH COVID-19 Treatment Guidelines,[82] last updated in December 2021, provide similar recommendations, stating that there is no evidence that ventilator management of patients with ARDS secondary to COVID-19 should differ from ventilator management of patients with ARDS secondary to other causes. The guideline does recommend a trial of awake prone positioning for patients with persistent hypoxia requiring HFNC oxygen and adds a recommendation against using awake proning as a rescue therapy to avoid intubation.

The WHO Living guidance for clinical management of COVID-19[49] does suggest awake prone positioning in severely ill patients with COVID-19 who require supplemental oxygen (including HFNC) or NIV. Their recommendations for mechanical ventilation do not differ from recommendations for ventilation in non-COVID-19 ARDS, emphasizing pressure limited low-tidal volume ventilation.

The Australian National COVID-19 Clinical Evidence Taskforce's continuously updated Living Guideline[51] on Caring for people with COVID-19 provides similar recommendations.

Table 1 provides an overview of these societies' recommendations.

SUMMARY

Nearly 3 years since the beginning of the pandemic, it is clear that COVID-19 ARDS does not differ substantially from non-COVID-19 ARDS and that treatment principles of ARDS based on high-quality prepandemic evidence are applicable to COVID-19 as well.

Patients with increased oxygen requirements should be supported with either HFNC or NIPPV. The generally recommended target of SpO2 is between 92% and 96%. Awake self-proning is recommended for patients awake and still hypoxemic despite oxygen supplementation. The timing of intubation remains a challenging decision that should be individualized, with the aim to avoid delaying a necessary intubation. Once intubated, the mainstay of supportive therapy consists in lung protection with pressure-limited and volume-limited mechanical ventilation. Prone positioning should be considered in patients with persistent low PaO_2/FiO_2 ratios or when parameters of lung protective ventilation cannot be achieved. Rescue therapies such as recruitment maneuvers, inhaled pulmonary vasodilators, and ECMO should be considered on a case-by-case basis. As in non-COVID-19-associated ARDS, tracheostomy should be performed when prolonged mechanical ventilation is anticipated.

Table 2 summarizes these recommendations for ventilation in COVID-19 ARDS.

CLINICS CARE POINTS

- Evidence-based treatment principles for patients with non-COVID ARDS apply to patients with COVID-19 ARDS as well.
- A trial of HFNC or NIPPV can be offered.
- Once intubated, provide lung protective ventilation. Prone positioning should be considered in patients with persistent hypoxemia or when lung protective ventilation targets cannot be achieved.
- Rescue therapies such as recruitment maneuvers, inhaled pulmonary vasodilators and ECMO should be considered on a case-by-case basis.

DISCLOSURE

Dr E. Fan reports personal fees from ALung Technologies, Aerogen, Baxter, GE Healthcare, Inspira, and Vasomune outside the submitted work. All other authors declare that they have no conflict of interest.

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