

# Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization

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**Disclaimer:** This is an updated guideline from the Extracorporeal Life Support Organization (ELSO) for the role of extracorporeal membrane oxygenation (ECMO) for patients with severe cardiopulmonary failure due to coronavirus disease 2019 (COVID-19). The great majority of COVID-19 patients (>90%) requiring ECMO have been supported using venovenous (V-V) ECMO for acute respiratory distress syndrome (ARDS). While COVID-19 ECMO run duration may be longer than in non-COVID-19 ECMO patients, published mortality appears to be similar between the two groups. However, data collection is ongoing, and there is a signal that overall mortality may be increasing. Conventional selection criteria for COVID-19-related ECMO should be used; however, when resources become more constrained during a pandemic, more stringent contraindications should be implemented. Formation of regional ECMO referral networks may

facilitate communication, resource sharing, expedited patient referral, and mobile ECMO retrieval. There are no data to suggest deviation from conventional ECMO device or patient management when applying ECMO for COVID-19 patients. Rarely, children may require ECMO support for COVID-19-related ARDS, myocarditis, or multisystem inflammatory syndrome in children (MIS-C); conventional selection criteria and management practices should be the standard. We strongly encourage participation in data submission to investigate the optimal use of ECMO for COVID-19.

**Key Words:** acute respiratory distress syndrome, coronavirus disease 2019, extracorporeal life support organization, extracorporeal life support program, extracorporeal membrane oxygenation, multisystem inflammatory syndrome in children, pandemic

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Submitted for consideration February 2021; accepted for publication in revised form February 2021.

Disclosure: Dr. Stead is a chief executive officer of the Extracorporeal Life Support Organization (ELSO). Dr. Paden is a president of the ELSO. Multiple patents and intellectual property regarding a novel renal replacement device to be used with extracorporeal membrane oxygenation (device not discussed in this article). Dr. Bartlett serves on ELSO's board of directors. Dr. Barrett received grants from Getinge and ALUNG. Dr. Combes received grants from Getinge and personal fees from Getinge, Baxter, and Xenios outside the submitted work. Dr. Lorusso is a consultant for Medtronic, LivaNova, and Eurosets (all honoraria paid to the University). Dr. Ogino is a past-president of the ELSO; he serves on ELSO board of directors. Dr. Schmidt receives lecture fees from Getinge, Xenios, and Dräger outside the submitted work. Dr. Shekar acknowledges research support from Metro North Hospital and Health Service. Dr. MacLaren serves on ELSO's board of directors. Dr. Brodie receives research support from ALUNG Technologies. He has been on the medical advisory boards for Baxter, Abiomed, Xenios, and Hemovent. He is the President-elect of the ELSO. The remaining authors have no conflicts of interest to report.

Drs. MacLaren and Brodie are co-senior authors.

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DOI: 10.1097/MAT.0000000000001422

The role of extracorporeal membrane oxygenation (ECMO) support for patients with cardiopulmonary failure due to coronavirus disease 2019 (COVID-19) is evolving. A prominent feature of COVID-19 in critically ill patients is acute respiratory distress syndrome (ARDS). Early in the pandemic, data on ECMO use was limited, and guidance was offered based on best practices at the time.<sup>1-4</sup> Very limited case series available at the onset of the pandemic seemed to indicate poor survival for patients with ARDS placed on ECMO.<sup>5</sup> However, the role of ECMO for COVID-19-related ARDS and other indications has become more apparent as the pandemic unfolds and evidence is generated.

A multicenter French study of 83 patients with COVID-19-related ARDS managed with ECMO revealed an estimated 60 day mortality of 31%.<sup>6</sup> Subsequently, data from the Extracorporeal Life Support Organization (ELSO) Registry reported an estimated cumulative incidence of in-hospital mortality 90 days after ECMO initiation of 37.4%. This report included 1,035 patients with COVID-19 who received ECMO in 36 countries.<sup>7</sup> An additional observational study reported 45% mortality for 1,531 patients from 177 centers in Europe and Israel.<sup>8</sup>

According to prepandemic historical data from the ELSO registry, venovenous (V-V) ECMO results in an approximate mortality of 40%, venoarterial (V-A) 55%, and extracorporeal cardiopulmonary resuscitation (ECPR) 71%. Mean V-V run duration is generally longer (12 days) than V-A (7 days).<sup>9</sup> For patients with COVID-19, mortality is similar to historical V-V ECMO mortality; however, mortality is still being determined with ongoing data collection and may be increasing.<sup>10</sup> Median (14 days<sup>7</sup> and 20 days<sup>6</sup>) and mean (18 days<sup>8</sup>) run duration appears to be longer.

In the great majority (>90%) of reported cases, V-V ECMO was utilized for COVID-19.<sup>6-8</sup> Some patients with COVID-19 develop myocarditis, massive pulmonary embolism, stress cardiomyopathy, arrhythmias, and acute coronary syndrome,<sup>11-13</sup> which may require mechanical circulatory support such as V-A ECMO. Data on V-A ECMO for COVID-19 are limited in the ELSO Registry study and may be found in small case series, making the utility of V-A ECMO for COVID-19-related cardiogenic shock less clear.<sup>6-8,14</sup> As a general guide to practice, we recommend the use of ECMO for patients with COVID-19 and severe cardiopulmonary failure who meet traditional criteria and when appropriate resources are available.<sup>15</sup>

Given the paucity of available data when prior ECMO guidelines were published,<sup>1,4</sup> this guideline has been created to summarize currently available literature and offer recommendations to update select areas within the previous guidelines.<sup>4</sup> This document will focus on care specific to COVID-19 patients receiving ECMO and recommended alterations in the utilization of ECMO during a pandemic. We recommend referral to existing guidelines for general ECMO practices.<sup>2</sup>

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#### Key Recommendations

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V-V ECMO may be utilized for patients with COVID-19 and severe respiratory failure with expected outcomes comparable to patients supported with V-V ECMO prepandemic.

V-A ECMO may be utilized for patients with COVID-19 and severe cardiac failure; however, the experience is more limited.

Mobile ECMO is feasible and may be conducted safely for patients with COVID-19.

Organize ECMO centers within geographic regions to coordinate patient referrals, where feasible.

Unify patient selection criteria across a geographic region, where feasible.

Contraindications for ECMO use should become more stringent as ECMO capacity diminishes.

Data submission to facilitate research is essential for our evolving understanding of optimal ECMO care for patients with COVID-19.

While some centers have increased their anticoagulation targets, bleeding remains a concern, and there is no data to recommend deviation from conventional anticoagulation goals.

There is no data to recommend deviation from conventional ECMO practices, e.g., blood product transfusion thresholds, tracheostomy, endotracheal extubation, rehabilitation, cannulation configuration, or ventilator management.

Potential discontinuation of ECMO in the setting of perceived futility should be clearly discussed with patients and their surrogate decision-makers.

Rarely, children can require ECMO support for severe ARDS, myocarditis, or multisystem inflammatory disease in children; ECMO patient selection and management should follow conventional guidelines.

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### ECMO Program Organization<sup>3</sup>

#### International

- Centers providing ECMO that are not ELSO member centers are encouraged to join ELSO and contribute to COVID-19-related ECMO cases in the international registry.
- We also recommend participation in other key international efforts related to COVID-19 data collection, such as the EuroELSO survey<sup>8</sup> and COVID-19 Critical Care Consortium,<sup>16,17</sup> to enable a real-time understanding of COVID-19 ECMO practices and to help facilitate crucial research and quality assurance in this area.<sup>15</sup>

#### National/Regional

- Creating or utilizing existing national and regional ECMO networks is encouraged to coordinate referrals within given geographic areas in which patient transport is possible.<sup>18-21</sup>
- If a patient is referred to an ECMO center that lacks capacity, efforts should be made to redirect the referral to another ECMO center in the region with available capacity, with consideration of availability of mobile ECMO if indicated.
- Before ECMO capacity becomes saturated within a given region, we recommend these ECMO networks adapt unified patient exclusion criteria (see below: Patient Selection) at a regional level to promote equitable access to ECMO and to avoid the need for transferring centers to make referrals to multiple ECMO centers.
- Mobile ECMO has been safely used to retrieve patients with COVID-19 from referring centers.<sup>22-27</sup>
- Adult and pediatric ECMO centers within a region<sup>28</sup> should consider pooling resources, whenever feasible, such as pumps, disposables, or staff, to optimize ECMO capacity from existing resources.

- When ECMO equipment resources are constrained, ECMO centers may use ELSO's Supply Exchange (supplies.else.org) to improve access to ECMO services when there is a supply disruption, either due to increased demand or an unforeseen limitation in supplies.
- ECMO centers and referring centers may use ELSO's ECMO Availability Map (else.org) for the purposes of regional coordination of ECMO capacity. This tool is publicly available and updated by ELSO member centers.
- Educational webinars and conferences hosted by ELSO and other scientific societies, as well as regional ECMO networks, should be utilized to rapidly disseminate new data to ECMO practitioners as they emerge.

### *Institutional*

- In select cases, where regional resources exist to support the creation of new ECMO centers, and it is felt essential to meet increased demand due to the pandemic, this should be undertaken utilizing guidance from ELSO and in close collaboration with other experienced centers to optimize patient outcomes.<sup>29,30</sup> Telemedicine could be utilized to facilitate this.<sup>31</sup>
- Tracking of available staffing, equipment, and beds should be performed to determine ECMO capacity on a regular basis. Capacity determination should take into consideration other related services that utilize the same resources as ECMO (cardiothoracic surgery, cardiac critical care, medical critical care, transplant, etc.).<sup>32,33</sup>
- Bedside staffing ratios may be altered under contingency and crisis capacity<sup>34</sup> to allow a bedside specialist to care for more patients than usual. This may be facilitated using methods for remote monitoring and co-locating patients who are receiving ECMO (including both COVID-19 and non-COVID-19 ECMO patients, as appropriate for the individual hospital).
- If surgical procedures involving cardiopulmonary bypass are suspended, perfusionists may be deployed to the bedside to relieve ECMO specialists for other duties, where applicable.

### **Patient Selection**

ECMO is a finite resource and requires the utilization of other finite resources, such as intensive care unit (ICU) beds and staffing. Patient selection must be judicious and equitable and should become more stringent as capacity diminishes.<sup>32,35,36</sup>

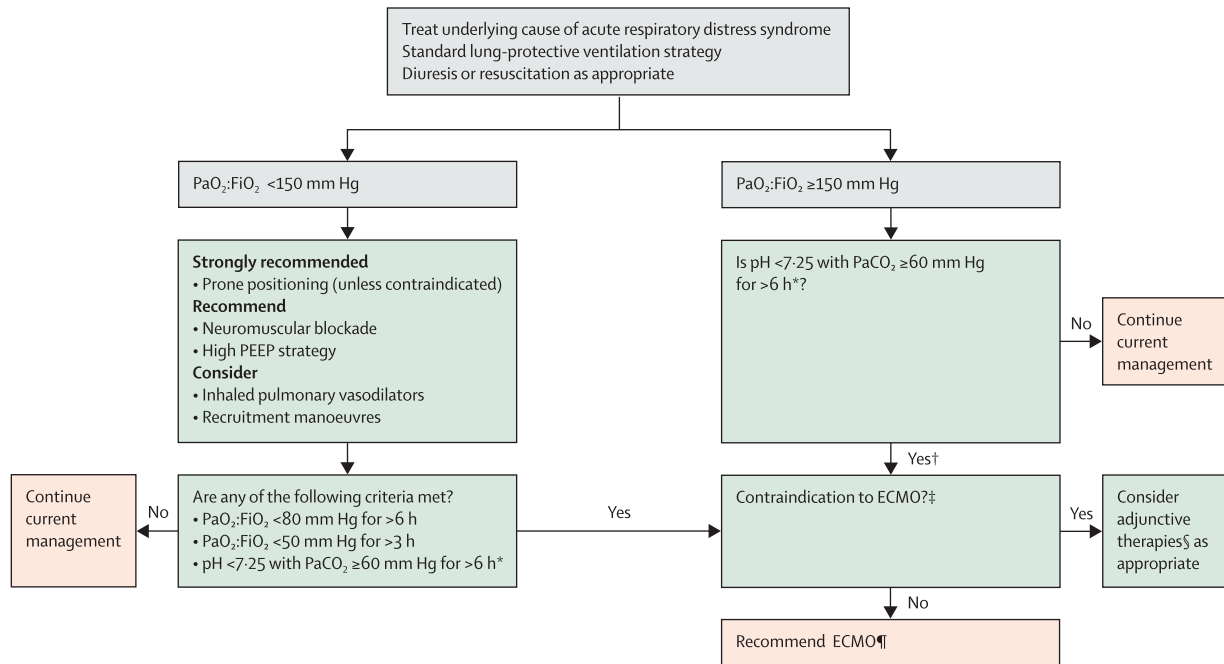
### *Indications*

- Indications for ECMO initiation should remain unchanged during a pandemic, and we refer to ELSO guidelines and established literature outlining these indications.<sup>1,2,4,15,37–40</sup>
- Conventional therapies for ARDS should be applied according to the standard algorithm, leading to the use of ECMO after other measures have been attempted, especially prone positioning, unless contraindicated (Figure 1).<sup>41</sup> It should be emphasized that low-pressure and low-volume ventilation should be adhered to, with consideration of ECMO if unable to safely mechanically ventilate the patient, even if oxygenation is relatively intact.

- While it may be tempting to stretch the use of conventional therapy to avoid placing patients on ECMO due to resource constraints, there is no evidence to support delaying ECMO initiation when it is indicated. We recommend ECMO patient selection as in Figure 1. Outcomes with delayed ECMO initiation may be worse and run duration may be longer, offsetting any potential benefit from attempted conservation of resources.<sup>42–44</sup>
- Patients who are deteriorating in non-ECMO centers should be referred early for ECMO consideration to allow for safe transport or time to organize mobile ECMO rescue in appropriate patients.<sup>22</sup>
- Survival with V-V ECMO for COVID-19–related pneumonia and ARDS<sup>6–8</sup> is similar to historical survival data for other causes of acute severe respiratory failure meeting V-V indications in the ELSO Registry.<sup>9</sup> This suggests that COVID-19 could be considered similarly to other causes of reversible infectious pulmonary disease, with awareness that COVID-19 patients may require longer run times.<sup>6–8,45–47</sup> However, mortality in this population may be increasing over time and updated data should be considered in decision-making (else.org).
- It is currently unknown if COVID-19 patients requiring V-A ECMO have similar survival compared with historical data.

### *Contraindications*

- We recommend that ECMO centers establish descriptions for levels of diminishing ECMO capacity,<sup>34</sup> and capacity should be tightly linked to exclusion criteria, that is, when capacity diminishes, exclusion criteria become more stringent based on characteristics associated with increased mortality (Figure 2),<sup>7,15,32,44,48,49</sup> and longer run duration.<sup>50,51</sup> Of note, there is survival and run-time variability depending on the indication for ECMO and individual patient characteristics, and thus each ECMO referral should be considered on a case-by-case basis.
- Mortality increases with prolonged exposure to mechanical ventilation before ECMO<sup>44</sup>; the additional impact of prolonged exposure to high-flow nasal cannula or non-invasive positive-pressure ventilation before mechanical ventilation is currently unknown.
- COVID-19 patients receiving ECMO may consume more resources to meet personal protective equipment (PPE) requirements, and this may be a factor in patient selection by necessity when PPE is limited.
- Risks and benefits of providing ECPR for patients who have COVID-19 or whose status is unknown, for example, out-of-hospital cardiac arrest, should be carefully considered given the increased potential for PPE breach and lower historical survival with ECPR compared with most other uses of ECMO.<sup>49</sup> However, ECPR outcomes also vary considerably according to patient population based on factors that include witnessed or unwitnessed arrest, in-hospital *versus* out-of-hospital arrest, duration, and etiology of arrest. Thus, context matters in the decision of whether or not to proceed with ECPR, and centers should a priori determine whether or not they will provide ECPR for patients with COVID-19 and patients with unknown COVID-19 status.



**Figure 1.** Algorithm for management of acute respiratory distress syndrome, including indications for ECMO. \*With respiratory rate increased to 35 breaths per minute and mechanical ventilation settings adjusted to keep a plateau airway pressure of  $<32$  cm H<sub>2</sub>O. †Consider neuromuscular blockade. ‡There are no absolute contraindications that are agreed upon except end-stage respiratory failure when lung transplantation will not be considered; exclusion used in the EOLIA trial can be taken as a conservative approach to ECMO contraindications. §For example, neuromuscular blockade, high PEEP strategy, inhaled pulmonary vasodilators, recruitment maneuvers, and high-frequency oscillatory ventilation. ¶Recommend early ECMO as per EOLIA trial criteria; salvage ECMO, which involves deferral of ECMO initiation until further decompensation (as in the crossovers to ECMO in the EOLIA control group), is not supported by the evidence but might be preferable to not initiating ECMO at all in such patients. Credit: Abrams *et al.*<sup>39</sup>. ECMO, extracorporeal membrane oxygenation; EOLIA, Extracorporeal Membrane Oxygenation to Rescue Lung Injury in Severe Acute Respiratory Distress Syndrome; PaCO<sub>2</sub>, partial pressure of carbon dioxide in arterial blood; PaO<sub>2</sub>:FiO<sub>2</sub>, ratio of partial pressure of oxygen in arterial blood to the fractional concentration of oxygen in inspired air; PEEP, positive end-expiratory pressure.

- Systems should be prepared to rapidly identify changes in capacity and communicate resultant changes in exclusion criteria to their ECMO teams and regional networks to continually optimize the benefit-to-resource utilization ratio.

### Cannulation Strategies

- Conventional two-site (V-A and V-V) and multisite, e.g., veno-arteriovenous (V-AV), cannulation strategies, as well as V-V dual-lumen cannulas, as needed to address the underlying problems, are appropriate for use in patients with COVID-19.
- There may be a role for the use of dual-lumen single cannula right ventricular assist device (right atrium to pulmonary artery) in patients with COVID-19 pneumonia; however, the evidence is limited.<sup>46,47</sup>

### Ongoing Care During ECMO

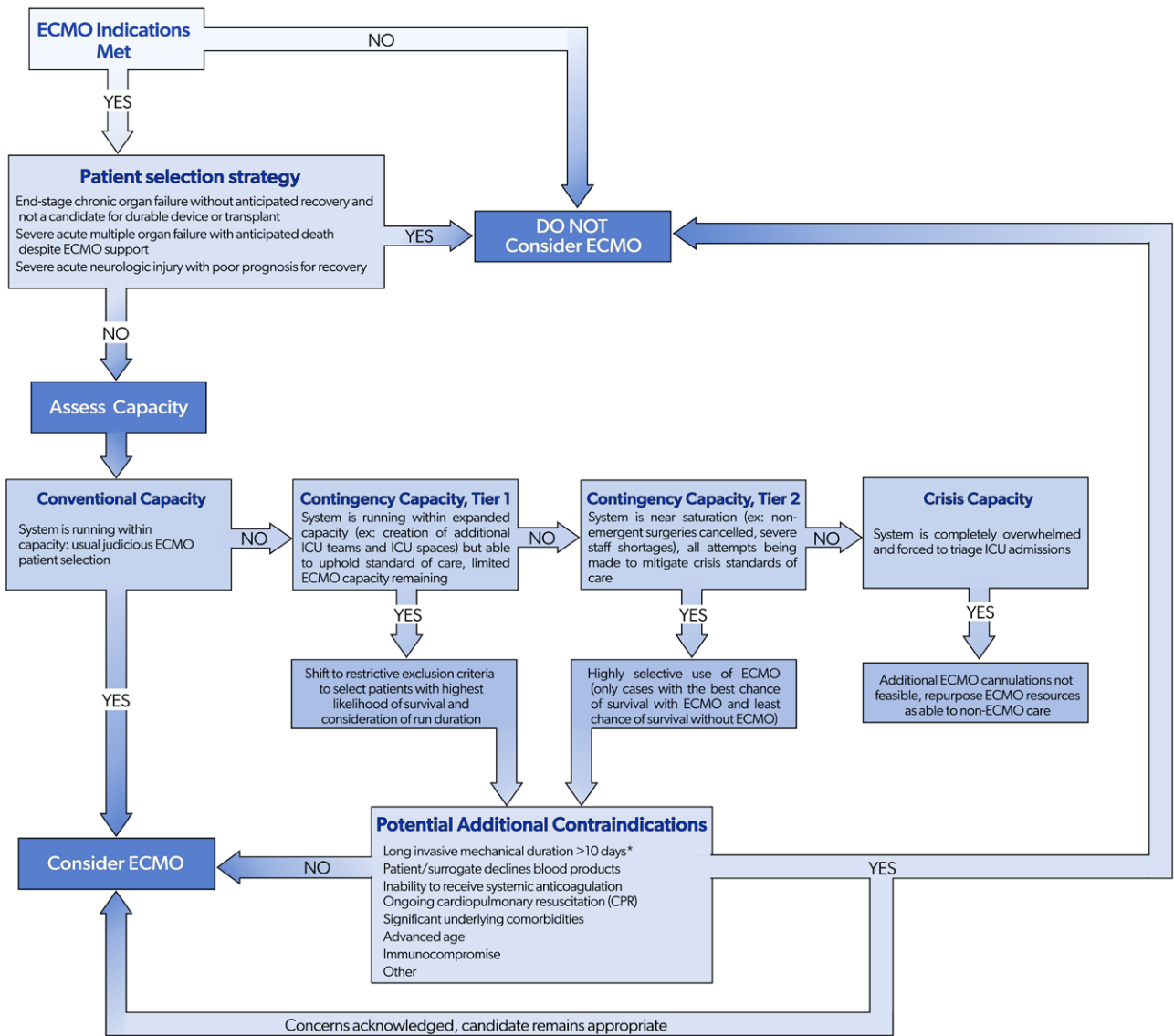
Routine management of the patient receiving ECMO is outside the scope of this guideline, and we refer to previously published guidelines<sup>2</sup> and reviews<sup>37,52,53</sup>. Recommendations on disease modifying agents are also outside of the scope of this guideline, and we refer to published national and international guidelines.<sup>54–56</sup> A concise list of COVID-19 ECMO-specific recommendations is provided in Figure 3.

### Pulmonary

- There are no data to suggest deviation from commonly performed ventilator management (very low-pressure, low-volume ventilation) for patients receiving V-V ECMO with COVID-19.<sup>2,57</sup>
- Percutaneous tracheostomy appears to be safe and feasible for patients with COVID-19.<sup>58–60</sup>
- Prone positioning during ECMO is feasible<sup>61</sup> and 81% of COVID-19 patients in one study were placed in the prone position.<sup>6</sup> Preliminary data demonstrate a potential association of prone positioning on ECMO with lower mortality.<sup>15,62,63</sup> However, a recommendation cannot be offered at this time.
- An early extubation strategy with awake ECMO may be feasible for patients with COVID-19.<sup>46,47</sup> However, there is currently no data to support this strategy over one in which the patient remains endotracheally intubated during ECMO.

### Hematologic and Hemodynamic Monitoring

- COVID-19-induced coagulopathy appears to include both thrombotic and bleeding events.<sup>64–66</sup> Specific ramifications for ECMO include circuit clotting,<sup>67,68</sup> higher than previously reported rates of pulmonary embolism,<sup>6</sup> and intracranial hemorrhage.<sup>69–72</sup> However, when normalized

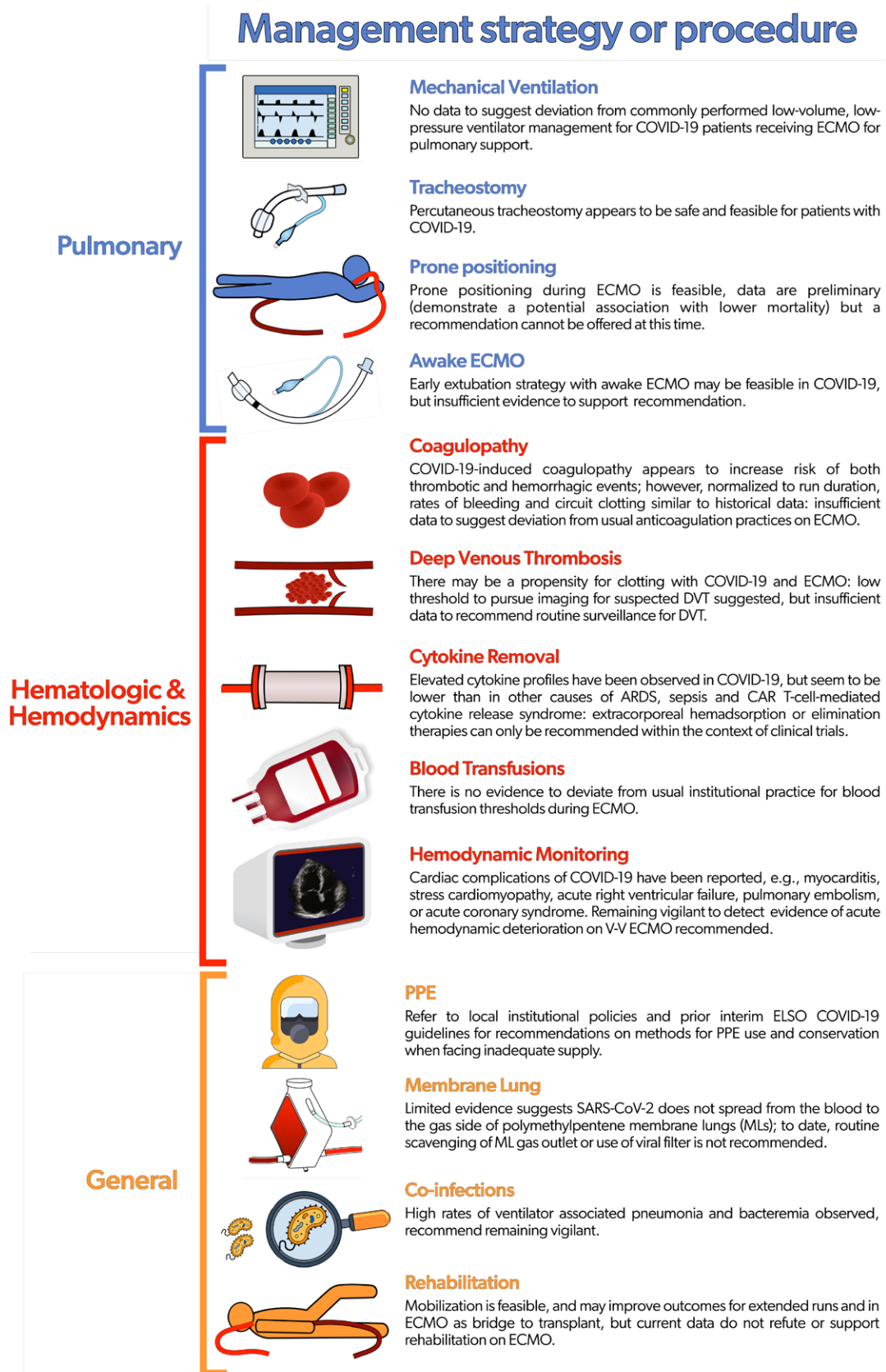


**Figure 2.** Contraindications algorithm for V-A and V-V ECMO use (COVID-19 and non-COVID-19) during a pandemic based on system capacity. \*The impact of duration on high-flow nasal cannula and/or noninvasive mechanical ventilation in addition to invasive mechanical ventilation is unknown. COVID-19, coronavirus disease 2019; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; PaCO<sub>2</sub>, partial pressure of carbon dioxide in arterial blood; PaO<sub>2</sub>:FiO<sub>2</sub>, ratio of partial pressure of oxygen in arterial blood to the fractional concentration of oxygen in inspired air; PEEP, positive end-expiratory pressure; V-A, venoarterial; V-V, venovenous.

to ECMO run duration, rates of bleeding, and circuit clotting in patients with COVID-19 are similar to historical data, in one observational study.<sup>7</sup> Balancing hematologic derangements with ECMO anticoagulation is complex. Many centers have increased their anticoagulation targets but bleeding remains a concern, and there are insufficient data to suggest deviation from usual anticoagulation practices<sup>2</sup> for patients with COVID-19 receiving ECMO.

- There are insufficient data to recommend routine surveillance for deep venous thrombosis for patients with COVID-19<sup>73</sup>; however, we recommend a low threshold to pursue imaging for suspected deep venous thrombosis, including after decannulation, given that there may be a propensity for clotting in COVID-19 patients during ECMO.<sup>74,75</sup>

- While elevated cytokine profiles have been observed in patients with COVID-19, these seem to be lower than in non-COVID-19-related ARDS and sepsis and much lower than chimeric antigen receptor (CAR) T-cell-mediated cytokine release syndrome,<sup>76</sup> although evidence is needed to provide further insights. Therefore, extracorporeal hemadsorption or elimination therapies can only be recommended within the context of clinical trials.<sup>77</sup>
- There is no evidence to deviate from usual institutional practices for blood transfusion thresholds during ECMO.<sup>78</sup>
- We recommend remaining vigilant for acute hemodynamic deterioration during V-V ECMO. This may occur due to cardiac complications of COVID-19, for example, myocarditis, stress cardiomyopathy, acute right



**Figure 3.** Recommendations for ongoing care for patients with COVID-19 receiving ECMO. ARDS, acute respiratory distress syndrome; CAR, chimeric antigen receptor; COVID-19, coronavirus disease 2019; DVT, deep venous thrombosis; ECMO, extracorporeal membrane oxygenation; ELSO, Extracorporeal Life Support Organization; ML, membrane lung; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; V-V, venovenous.

ventricular failure,<sup>79,80</sup> pulmonary embolism, or acute coronary syndrome.

### General

- We refer the reader to local institutional policies and prior interim ELSO COVID-19 guidelines for recommendations on PPE use and conservation methods when facing inadequate supply.<sup>3,4</sup>
- There is no evidence to suggest that virions can travel out of the exhaust of a polymethylpentene membrane lung, and thus routine scavenging is not recommended, although the current evidence is limited.<sup>81</sup>
- Remain vigilant for bacterial coinfection and superinfection given high observed rates of ventilator-associated pneumonia and bacteremia in some studies.<sup>6,82–85</sup>
- Mobilization of patients is feasible while undergoing ECMO<sup>46,86–88</sup> and may be necessary to achieve favorable outcomes for patients with extended ECMO runs and those bridging to transplant. However, there are currently insufficient data to refute or support mobilization specifically for patients receiving ECMO for acute COVID-19.
- Intra-hospital transport can be safely performed, and thus traveling within the hospital should be pursued when indicated, for example, radiology, unit relocation, *etc.*<sup>89</sup>

### Weaning and Discontinuation of ECMO

- Centers should determine a priori whether they plan to offer lung or heart transplant or durable ventricular assist devices to patients with COVID-19 who are unable to wean from ECMO, as this will have implications for decision making surrounding continuation or discontinuation of ECMO in patients who are not recovering. Regional referral can be considered if transplant or durable device placement is not locally available.
- If patients are bridging to recovery, the consent process should include a discussion outlining criteria with family for when ECMO support will be stopped once it is determined to be unlikely to provide further benefit to the patient. In this case, the patient will be returned to conventional therapy or consideration given for withdrawal of life-sustaining therapies (futility and principle of proportionate therapy).<sup>35</sup>
- It is challenging to determine futility in the patient receiving V-V ECMO with single-organ failure awaiting pulmonary recovery. It is important to note that prolonged hospitalization in this cohort may not portend a higher mortality rate: patients hospitalized at 40 days had an estimated 90 day mortality of 14% in the ELSO Registry study.<sup>7</sup>
- Duration on ECMO (>90% V-V) for COVID-19 from three large observational studies was median 13.9 days (interquartile range [IQR], 7.8–23.3 days),<sup>7</sup> median 20 days (IQR, 10–40 days),<sup>6</sup> and mean 18 days.<sup>8</sup> It is important to note that successful native lung recovery has been reported after prolonged (>28 days) V-V ECMO support.<sup>90</sup>
- The role of chest imaging in determining futility while on V-V ECMO is unknown.
- Lung transplantation has been successfully pursued for some COVID-19 patients who were receiving ECMO,

with single-organ failure, but without recovery of adequate lung function. The timing for when this should be considered, and for when further attempts at awaiting native pulmonary recovery should be abandoned, remain unclear.<sup>91–93</sup>

### ECMO in Children with COVID-19

Acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in children is most commonly either asymptomatic or associated with only mild respiratory disease. Occasionally, however, this can lead to life-threatening hypoxic respiratory failure with ARDS due to severe COVID-19 or, rarely, acute heart failure and cardiogenic shock secondary to myocarditis. Furthermore, a minority can develop multisystem inflammatory syndrome in children (MIS-C) within 4 weeks of exposure to the virus, presenting with clinical and laboratory evidence of systemic inflammation, which can rapidly progress to shock.<sup>94</sup> Most children who require intensive care with acute COVID-19 or MIS-C receive targeted therapy, recover and are discharged home.<sup>95,96</sup> Rarely, children with severe disease ultimately require ECMO.<sup>97–99</sup> While the basic principles of ECMO for COVID-19 in children do not significantly differ from ECMO use for other diseases, there are some special nuances that a pandemic presents that should be considered in the decision-making process.

### Candidacy

- We recommend applying similar principles currently published in ELSO guidelines<sup>2</sup> for patient selection of pediatric COVID-19-associated respiratory failure and MIS-C.

### Cannulation

- Standard cannulation strategies appropriate for any pediatric ECMO patient should be used. There is no evidence to support alteration of cannulation strategy for patients with COVID-19.
- Appropriately sized dual-lumen or two-site cannulation approach is commonly employed for V-V support of pediatric respiratory failure patients without circulatory collapse.
- V-A support is indicated for cardiac compromise associated with COVID-19-related myocarditis and MIS-C and for patients with severe respiratory disease where adequately sized V-V cannulation cannot be accomplished.

### Management Principles

- We recommend the use of standard pediatric institutional ECMO protocols for the management of pediatric patients with COVID-19. There is no evidence to recommend changes in anticoagulation, sedation, or other protocols for patients with COVID-19.
- Management of the underlying COVID-19 and MIS-C diseases should follow institutional and national guidelines.<sup>100</sup>

### Conclusions

Patients with COVID-19 initially exhibited similar mortality when supported with V-V ECMO as compared to historical data in patients with other causes of acute severe respiratory

failure. However, mortality may be increasing and is still being determined with ongoing data collection. Data are still limited regarding V-A ECMO support in COVID-19. That said, ECMO may be utilized for adult patients with COVID-19 and severe cardiopulmonary failure when resources permit. Children may require ECMO support for severe ARDS, myocarditis or MIS-C, and ECMO patient selection and management should follow conventional guidelines. ECMO centers should consider forming networks within geographic regions to pool resources and coordinate patient referrals for ECMO. Submission of patient data is essential for ongoing research to enhance the care of patients receiving ECMO for COVID-19–related cardiopulmonary failure. When conventional capacity exists, indications and contraindications for ECMO should remain unchanged; however, as hospital system capacity diminishes, contraindications for ECMO use should become more stringent based on characteristics associated with increased mortality and longer run duration. There are no data to recommend deviation from conventional ECMO management for COVID-19 patients during their ECMO run, for example, anticoagulation, blood product transfusion thresholds, tracheostomy, endotracheal extubation, mobility, cannulation configuration, or ventilator management. The criteria surrounding ECMO discontinuation for perceived futility should be clearly discussed with patients and families.

### Acknowledgment

The authors would like to recognize and thank the team of worldwide extracorporeal membrane oxygenation (ECMO) experts led by Dr. Kiran Shekar who drafted the “Interim ECMO for COVID-19 Guidelines.” Their worldwide collaboration, expertise, and guidance helped the ECMO community during the first year of the pandemic and this manuscript builds on their important work.

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