Extracorporeal Life Support Organization COVID-19 Interim Guidelines

A consensus document from an international group of interdisciplinary ECMO providers*

Disclaimer

The ELSO COVID-19 Guidelines have been developed to assist existing ECMO centers to prepare and plan provision of ECMO during the ongoing pandemic. The recommendations have been put together by a team of interdisciplinary ECMO providers from around the world. Recommendations are based on available evidence, existing best practice guidelines, ethical principles, and expert opinion. This is a living document and will be regularly updated when new information becomes available. ELSO is not liable for the accuracy or completeness of the information in this document. These guidelines are not meant to replace sound clinical judgment or specialist consultation but rather to strengthen provision and clinical management of ECMO specifically in the context of the COVID-19 pandemic.

Foreword

The tulip bulbs I planted last fall are now blooming red and yellow, and the cherry trees are covered with blossoms. I am elated for Mother Nature's annual gift, yet I know that this season is already unlike any others. The emergence of SARS-CoV-2 and the disruption in our routines and expectations have made it spring, interrupted. Still, as history teaches us during times of great challenge, we find our heroes.

The frontline hospital team members and hospital support staff are performing heroically as the medical community struggles to understand and manage a new illness. Despite the many variables and unknowns related to COVID-19, ECMO professionals have faced the challenge of treating the most seriously ill patients with ingenuity and dedication. This guideline exemplifies the priorities of the global ECMO community to share the knowledge gained through our experiences of success and – just as importantly – failure.

I am grateful to the ELSO COVID-19 Working Group, a collaboration of sixty interdisciplinary ECMO providers from around the world, and the ELSO staff for their hard work. I also thank the reviewers for lending their time and expertise while leading the fight in some of the most severely affected parts of the world.

Our hearts go out to the families affected by this unprecedented pandemic. The team of experts who authored the guideline is resolute in defining "best practices" to fulfil our responsibilities to our fellow clinicians, our patients, and their families. In the months and years to come, we will be proud of our response to the call to serve.

The resilience of the human spirit will prevail. Spring will continue to thrill us. Society will adapt and endure.

Mark T. Ogino, MD
President, ELSO

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1. Introduction

The World Health Organisation declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak a pandemic on March 11, 2020[1]. Patients infected with the novel virus develop coronavirus disease 2019 (COVID-19) leading to a significant increase in hospital and intensive care unit (ICU) admissions globally[2]. A vast majority of intensive care admissions are due to hypoxaemic respiratory failure with up to 88% (n=1591) of patients requiring invasive mechanical ventilation in the Italian cohort[3]. Invasive ventilation rates of 30-71% have been reported in other settings[4-8]. A small proportion of these patients fail maximal conventional therapies and may require extracorporeal membrane oxygenation (ECMO) support. As the pandemic has evolved, there has been a steady increase in ECMO use[9,10]. At the time of writing this guideline, there were 858 COVID-19 patients supported with ECMO [9,10]. (Mean age 52 years, 95% V-V ECMO, 5% V-A ECMO and other configurations).

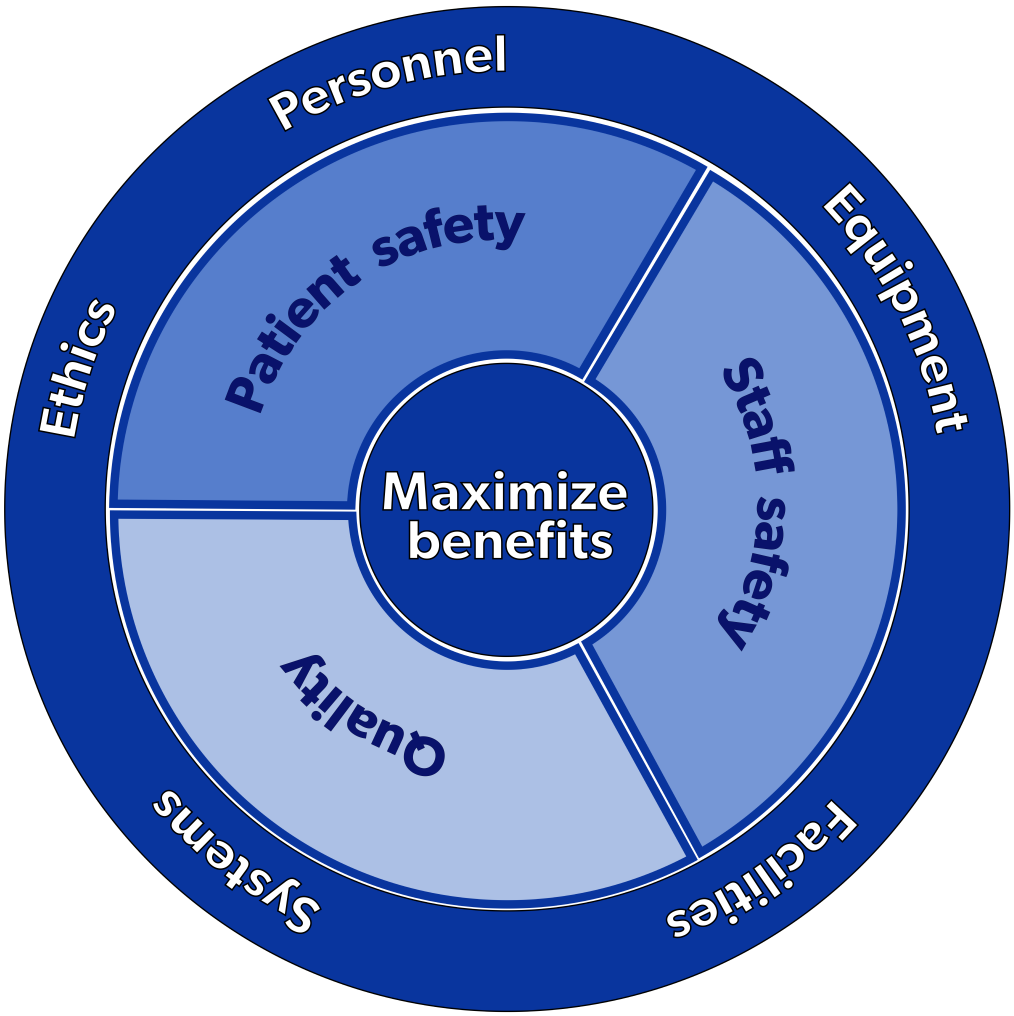

Figure 1. *Key considerations on which these guidelines are based.*

The pandemic of a novel and highly transmissible respiratory virus is placing significant stress on health care systems around the world. Intensive care units are forced to rapidly increase capacity in order to accommodate a large number of critically ill patients requiring organ support, most notably mechanical ventilation. In this setting, provision of ECMO may be challenging from both resource and ethical points of view[11]. The interim recommendations presented here balance the need to provide high quality ECMO care to those who may benefit most while being cognizant of available resources and maintaining an environment of patient and staff safety (Figure 1). While there is paucity of high-quality evidence to guide ECMO practice in many areas, these recommendations are based on available evidence[12-14], existing best practice guidelines[15-24], experience from previous infectious disease outbreaks [25-29], ethical principles[30-35], and consensus opinion from experts. In addition, the ELSO COVID-19 Working Group Members completed a survey on patient selection criteria for ECMO to build consensus. The guidelines fall into these three categories:

Recommended: the technique/intervention is beneficial (strong recommendation) OR the intervention is a best practice statement.

Not Recommended: the technique/intervention is not beneficial OR harmful.

Consider: the technique/intervention may be beneficial in selected patients (conditional recommendation) OR exercise caution when considering this intervention.

The guidelines provided here pertain to 10 key areas specific to COVID-19 related cardiopulmonary failure and apply to neonatal, pediatric, and adult patient populations. We refer the readers to existing ELSO guidelines[15], the ELSO Red Book[17], published literature[36], and reliable printed or online resources for additional information regarding the provision and practice of ECMO. The current work is a 'living document' developed by the ELSO COVID-19 Working Group. The Group will remain active for the duration of the pandemic and during any future COVID-19 outbreaks to revise the guidelines as new information and evidence become available. The most up-to-date version of the guideline document and all previous iterations can be found on the ELSO website www.elso.org.

2. ECMO organization

We refer readers to published literature[36,37] including existing guidelines[38] to assist with organisation of ECMO programs outside the context of COVID-19.

Phases of Response

- During the pandemic, COVID-19 and non-COVID-19 patients should receive ECMO in established ECMO centers using available resources to maximize benefits[11,39].

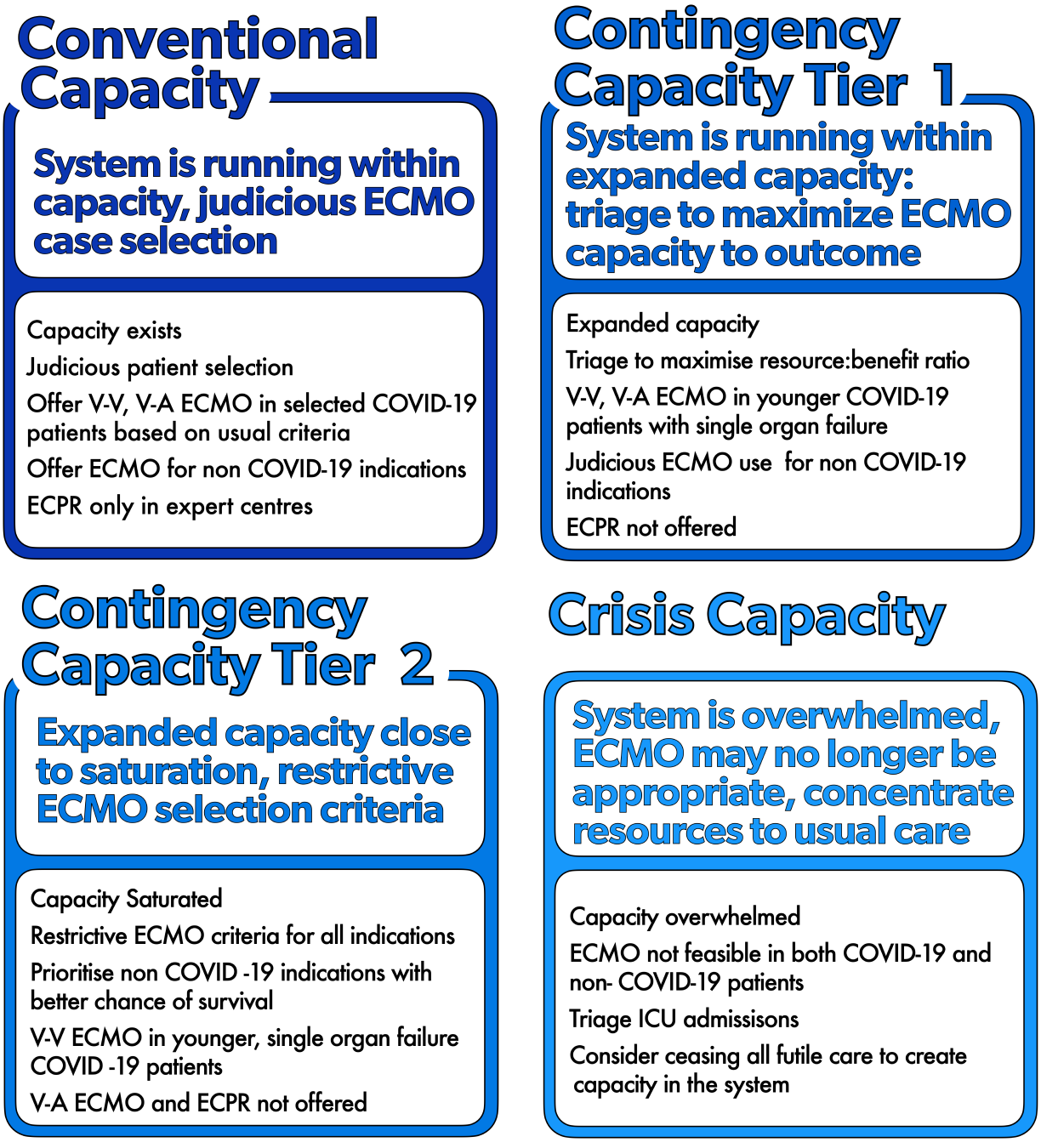

Figure 2. *ECMO provision based on system capacity*

- *We do not recommend the commissioning of new ECMO centers for the purposes of treating COVID-19 patients.*
- *We recommend responsible ECMO use based on system capacity for ECMO*.[40] When in crisis capacity (Figure 2), health care services will be overwhelmed, making resource allocation more challenging and limiting ECMO utilization. Resources are dynamic and ECMO centers may transition from conventional to crisis capacity rapidly.
- *Centers should preferentially offer ECMO to patients in whom outcomes are favourable and/or ECMO runs are relatively short* (e.g. meconium aspiration syndrome, near-fatal asthma, non-COVID-19 myocarditis, massive pulmonary embolism, cardiotoxic medication overdose, etc).

Areas of Organization

International

- The international co-operation during the COVID-19 pandemic has allowed for real-time communication of clinical experience, data, and outcomes in an unprecedented fashion. ECMO centers are encouraged to submit data to the ELSO registry to enable accurate reporting of real-time reporting of ECMO utilisation during the pandemic[9] and enroll in ongoing studies such as the ELSO endorsed ECMO for 2019 novel Coronavirus Acute Respiratory Disease (ECMOCARD) study led by the Asia-Pacific ELSO[41] and the Euro ELSO ECMO Survey[10].
- ELSO Chapters should regularly liaise with all relevant industry partners, regional distributors and local manufacturers to maximize resources and maintain supply chains.

National

- ECMO organization on a national level is encouraged to optimize resource utilization via coordination of government and private supply chains. Centralization through existing public bodies such as the United Kingdom National Health Service[42] and private entities such as Japan's ECMONet are crucial.

Regional

- *We recommend central coordination of ECMO services via regional networks whilst utilizing existing hub and spoke models of care and ECMO retrieval to service the*

ECMO needs of the region[11]*.* When individual institutions are overwhelmed or understaffed, it may be possible to enlist staff from areas with ongoing reserve.

- We recommend similar selection criteria be utilized in regional networks to provide equitable care across the programs.

Institutional

- ECMO programs should keep a manifest of all team members who are trained to care for ECMO patients.
- *Regular and frequent communication among ECMO directors and coordinators can help predict and prepare for ECMO needs with the possibility to centrally co-ordinate resources (personnel and equipment)*.
- The ECMO director(s) should lead the team to ensure consistency in ECMO patient selection and daily patient management at an institutional level.
- Capacity can be increased by adapting equipment usage and staffing ratios. This will depend on the care model already in use at local hospitals.
- Co-ordination and communication between medical, nursing and allied health staff is critical to quality ECMO outcomes.
- ECMO has been mainly used for adult patients with COVID-19 infection. In the event that adult ECMO programs exceed capacity, institutional, local and/or regional pediatric ECMO programs can be valuable resources.

Staffing

- We recommend maintaining a 1:1 patient : nurse ratio when patients are on ECMO. When capacity is at conventional or contingency Tier 1 levels, ECMO specialist ratio should follow institutional norms.
- When capacity is at contingency Tier 2 and Crisis levels, transitioning to a patient: specialist 2:1 ratio with the ECMO specialist overseeing more than one circuit whilst maintaining a 1:1 bedside nursing ratio may be considered. This may be achieved by cohorting of ECMO patients where possible.
- Redeployment of perfusionists to bedside ECMO care and re-integration of former ECMO specialists can expand the personnel pool.
- Teams are encouraged to maintain a senior ECMO specialist without a patient assignment to act as a float for emergency contingency management.

Equipment

- Simplification of the ECMO circuit may be used to increase circuit safety and reduce ECMO specialist workload in some settings. Examples include omitting negative pressure side pigtails, to reduce the risk of air entrainment, or blood monitoring devices, to reduce need for calibration samples. Any such changes to standard circuitry should be communicated widely to staff.
- Redeployment of devices previously used in the hospital and familiar to staff can increase capacity. For instance, pumps being used as a paracorporeal ventricular assist device may also be used for ECMO when coupled with a membrane lung. The US Food and Drug Administration has issued guidance to help expand the availability of devices (e.g. cardiopulmonary bypass devices, accessories, and components) used in ECMO therapy to address this public health emergency.[43]
- Fresh supplies of ECMO circuits and cannulas may be increasingly difficult to obtain. Communication through ELSO with manufacturers may help to identify options for resupply. Cardiac surgery and perfusion departments may be able to help with tubing and cannula supplies.
- The shelf-life of primed circuits may be extended to 60 days to conserve circuitry, provided:
  1) the circuit is constructed and primed using standard sterile techniques and
  2) the prime is electrolyte solution based, and no glucose containing solutions or albumin are used within the prime[44]. This may be more relevant to centers with smaller case volume.

3. Patient selection and timing of ECMO initiation

There is a clear indication of increased mortality with increasing age and comorbidities that should not be overlooked[3,8]. Specific considerations for patient selection will inherently be different during a pandemic due to a limited capacity to offer this resource-intensive mode of support, and thus the following should be taken into consideration.

- As disease burden increases and systems move to escalating levels of surge capacity (Contingency Capacity Tier 1 and beyond), we recommend that selection criteria become more stringent (Table 1) in order to utilize this resource for those most likely to benefit and return to an acceptable quality of life. (*Figure 2, Refer to "Ethics"*

section).

- When decompression of an overwhelmed hospital within a region is needed, preferentially relocate suitable ECMO candidates (young, single organ failure, previously healthy) to available ECMO centers.

Veno-venous ECMO

Indications for veno-venous (V-V) ECMO should not deviate from usual indications per ELSO[16] and other existing guidelines[36]. We recommend the following additional COVID-19 pandemic considerations for V-V ECMO:

- *We recommend against initiation of ECMO prior to maximising traditional therapies for acute respiratory distress syndrome (ARDS)[45], in particular prone positioning (Figure 3).*
- Our understanding of ARDS in COVID-19 is still evolving. There is considerable debate on the "atypical" nature of ARDS in this patient population[46,47] and on best mechanical ventilation strategy including adjuncts to be applied. Although, ventilation management prior to V-V ECMO initiation may have a significant bearing on outcomes[48], there is insufficient data to make any specific recommendations for mechanical ventilation strategies in context of COVID-19 ARDS and as such they are beyond the scope of this work.
- If mobile ECMO is unavailable, consider referring patients to ECMO centers "early," such as when PaO_2: $FiO_2 \leq 100$ mmHg. If the decision to transport is made too late, patients may be too unstable for transport.

Veno-arterial ECMO and other advanced extracorporeal support

In patients with COVID-19, the development of multiple direct and indirect cardiovascular complications including acute myocardial injury, myocarditis, arrhythmias, pericardial effusions and venous thromboembolism have been reported in up to 22% of patients requiring ICU care[49-52]. Elevation in high sensitivity troponin above the 99th percentile upper reference limit has been reported in 46% of non-survivors as opposed to 1% of survivors[53] and a continual rise in high sensitivity troponin has been associated with mortality[53]. COVID-19-may also be associated with hypercoagulability[54], increasing the risk of pulmonary thromboembolism[55-57].

- *Indications and patient selection criteria for veno-arterial (V-A) ECMO should not deviate from per existing guidelines[58].* Timely provision of V-A ECMO is recommended prior to development of multiple organ failure.

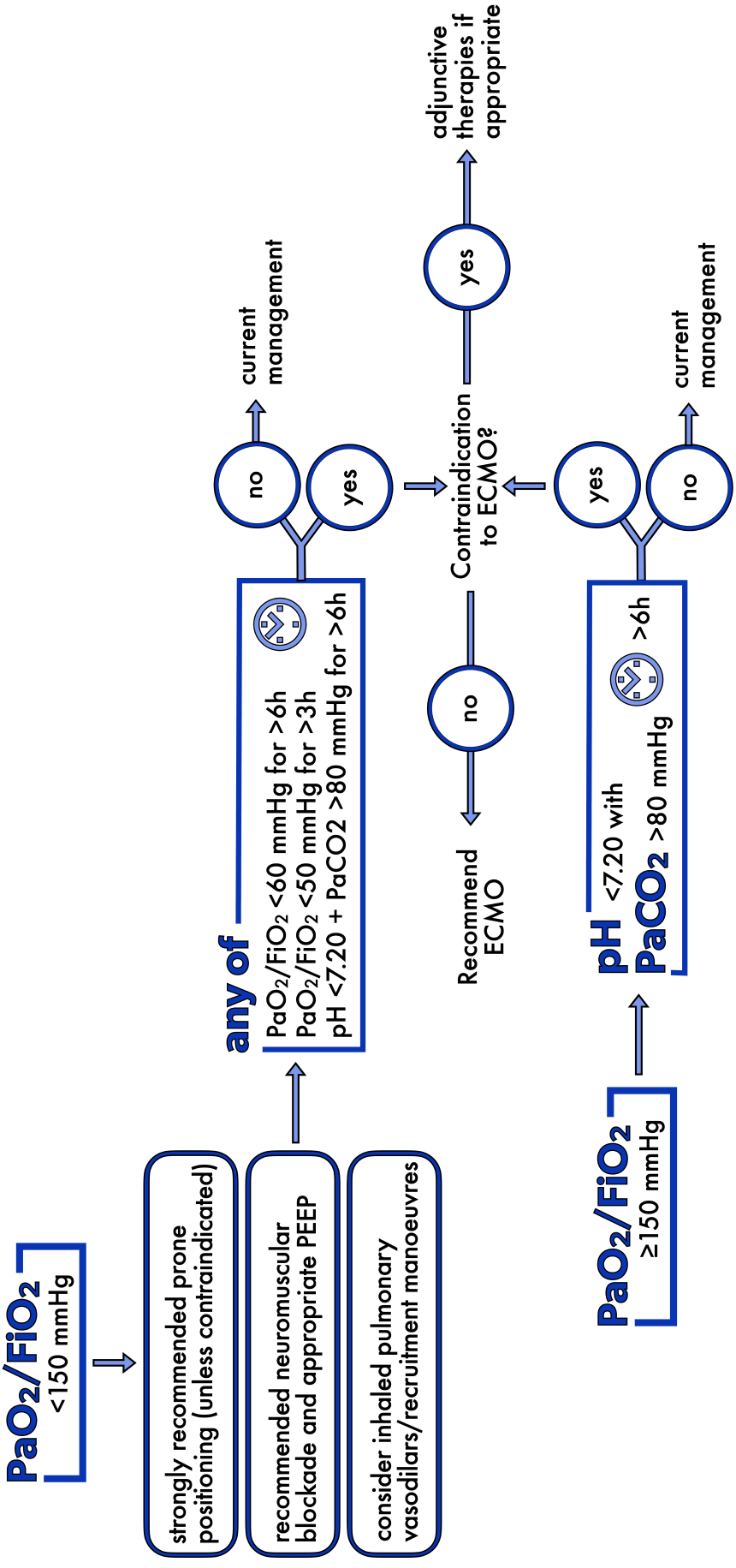

Figure 3. *Conventional VV ECMO indications for ARDS*.

- *Consider V-A ECMO in selected patients with refractory cardiogenic shock[59] (persistent tissue hypoperfusion, Systolic Blood Pressure <90 mmHg, Cardiac Index < 2.2L/min/m^2 while receiving noradrenaline >0.5mcg/Kg/min, dobutamine >20mcg/Kg/min or equivalent)*.
- The need for hybrid configuration such as V-VA ECMO[60] (venous drainage with both venous and arterial returns) is relatively infrequent. It may be considered in experienced centers for patients with ARDS in addition to suspected acute stress/septic cardiomyopathy or massive pulmonary embolism with associated cardiogenic/obstructive shock failing medical therapies.
- Patients requiring V-A ECMO support who incidentally test positive for COVID-19 but are not thought to be critically ill due to the virus should be considered for ECMO support in the usual fashion.

Extracorporeal cardiopulmonary resuscitation

- *We recommend against provision of Extracorporeal cardiopulmonary resuscitation (E-CPR) in less experienced centers or centers without an existing E-CPR program prior to the pandemic.* E-CPR in patients with out-of-hospital cardiac arrest is not recommended when systems are experiencing surge situations (Contingency Capacity > Tier 1). We recommend against the provision of pre-hospital E-CPR.
- *At experienced centers, E-CPR may be considered for highly selected non-COVID-19 patients with in-hospital cardiac arrest depending on resource availability.* However, in patients with COVID-19, the potential for cross-contamination of staff and the use of personal protective equipment (PPE) by multiple practitioners when in short supply, should be considered in the risk-to-benefit ratio of performing E-CPR. Poor outcomes with conventional CPR have been reported in COVID-19 patient population[64].
- *Emergency conversion from V-V to V-A ECMO in patients who suffer cardiac arrest during cannulation for V-V ECMO may increase risk to staff, is unlikely to result in a favourable outcome for the patient, and is thus not recommended.*

Contraindications

We recommend the following contraindications for ECMO in patients with cardiopulmonary failure due to COVID-19 (Table 1) in centers functioning under significant resource constraints. e.g. Contingency Capacity ≥ Tier 1.

Relative contraindications
• Age ≥ 65 years • Obesity BMI ≥ 40 • Immunocompromised status • No legal medical decision maker available • Advanced chronic underlying systolic heart failure • High dose vasopressor requirement (and not under consideration for V-A or V-VA ECMO)
Absolute contraindications
• Advanced age • Clinical Frailty Scale Category ≥ 3 • Mechanical ventilation > 10 days Significant underlying co-morbidities: CKD ≥ III Cirrhosis Dementia Baseline neurologic disease which would preclude rehabilitation potential Disseminated malignancy Advanced lung disease Uncontrolled diabetes with chronic end-organ dysfunction Severe deconditioning Protein-energy malnutrition Severe peripheral vascular disease Other pre-existing life-limiting medical condition Non-ambulatory or unable to perform activities • Severe multiple organ failure • Severe acute neurologic injury, e.g. anoxic, stroke • Uncontrolled bleeding • Contraindications to anticoagulation • Inability to accept blood products • Ongoing CPR

Table 1. *Indications and contraindications for ECMO in COVID-19 infected adults. BMI, body mass index; V-A, veno-arterial; V-VA, veno-venous arterial; ECMO, extracorporeal membrane oxygenation; CHD, chronic kidney disease; CPR, cardio-pulmonary resuscitation.*

These recommendations are based on data available from conventionally managed critically ill COVID-19 infected patients admitted to ICU and existing ECMO risk prediction models derived from non COVID-19 patients[3-8,61-63] . Data from COVID-19 patients supported with ECMO should soon become available to further guide patient selection.

4. Cannulation strategies and ECMO initiation

Preparation – Pre-Cannulation

- *The cannulation consent process should explicitly involve discontinuation of ECMO care in the absence of recovery of lungs, heart or both within an acceptable time frame as system capacity allows* [11,20] or if ECMO is actively harming the patient (severe bleeding or clotting for example).
- Consider performing ECMO cannulation within a designated COVID-19 environment and avoid transfers to catheterization lab or operating rooms where possible. *Cannulation should be performed by trained cannulators*.
- A dedicated person should be allocated to medically manage the patient during the cannulation process. *We recommend a maximum of 5 team members in the room/ bedspace during cannulation. Cannulation team members should wear standard, contact and airborne PPE.*
- *Awake cannulation is strongly discouraged*. We recommend that the airway be secured prior to cannulation to avoid unplanned emergent intubations during the procedure that may pose an undue risk to staff present. Appropriate use of sedation and neuromuscular blockade is recommended during cannulation.
- *Centers should develop a checklist for cannulation and cannulation team members should ensure they take all necessary supplies with them prior to entering the room. We recommend preparing a cannulation COVID-19 sprinter bag that contains all cannulae, guide wires, fluids, heparin, sterile sleeves for ultrasound probe, etc*.
- Prepare a medication bag and resuscitation trolley outside the cannulation-room. We recommend having a dedicated person in full personal protective equipment (PPE) be stationed outside the cannulation room to bring additional supplies as needed.
- Placement of a mechanical chest compression device beforehand if the patient is expected to deteriorate prior to cannulation and offering V-A/V-VA ECMO is considered appropriate in those circumstances.
- We recommend the use of plain x-ray, vascular ultrasound and echocardiography (transthoracic OR transesophageal) or fluoroscopy over a blind cannulation.[65,66]

Cannulation

V-V ECMO

- We recommend[16] that large multi-stage, drainage cannula be used (e.g. 23 Fr or

greater for adults) where possible to minimise the need for insertion of an additional drainage cannula at later stage. We suggest a single stage, return cannula (19-23 Fr for adults).

- *Dual lumen cannulae should be avoided if possible* as they take relatively longer time to insert, are associated with higher risk of thrombotic complications and malpositioning requiring repeat echocardiography with associated increased resource utilisation and personnel exposure.
- We recommend that either the femoro-femoral or femoro-internal jugular configuration be used. The femoro-femoral approach approach allows for more rapid surgical field preparation, creates efficiency of movement around the bed, and keeps the operator away from the patient's airway.

V-A and V-VA ECMO

- We recommend a femoro-femoral configuration for V-A ECMO cannulation. *A distal limb perfusion catheter is strongly recommended to reduce the risk of limb ischemia*.
- We suggest placement of three separate single lumen cannulae for the utilization of V-VA ECMO and do not recommend the use of a double lumen cannula for V-VA ECMO.
- We do not recommend the initiation of V-VA ECMO as a pre-emptive strategy. If a patient requires V-V ECMO but has no evidence of cardiac dysfunction or cardiac dysfunction is medically supportable with inotropes, placement of an arterial cannula is strongly discouraged.

5. Ongoing care on ECMO

Optimal supportive care on ECMO is critical to ensure positive outcomes. This should be guided by existing evidence and recommendations.[19,67-69]

Respiratory

Ventilator Management

- We recommend lung protective ventilation strategy targeting plateau pressure ≤ 25 cmH_20, RR 4-10 bpm, PEEP 10-15 cmH_20, driving pressure <15 cmH_20, and FiO_2 <50% to maintain saturations ≥ 85%.[12,70,71]. The ventilator management in the ECMO

arms of EOLIA trial (ECMO to Rescue Lung Injury in Severe ARDS)[12] or CESAR trial (Conventional Versus ECMO for Severe Adult Respiratory Failure)[105], offer best practice guidance. Ventilator dyssynchrony in setting of a high respiratory drive may lead to secondary lung injury and should be avoided.

Hematological

Anticoagulation

- Centers should follow existing anticoagulation guidelines[72] and institutional protocols with appropriate monitoring & dose adjustments (Figure 4).
- Since COVID-19 patients may be associated with a hypercoagulable state[57], consider targeting anticoagulation at the higher end of normal ECMO parameters.
- Caution should be exercised when using lower ECMO blood flow rates (<2L in adults) given the greater risk of circuit thrombosis in this patient population.
- Patients with a hypercoagulable status may benefit from antiplatelet agents (such as aspirin, clopidogrel, prasugrel, ticagrelor) but there is little data to recommend or refute. Both thrombocytopenia as well as prothrombotic states have been reported in patients with COVID-19[57].
- Patients with COVID-19 may have secondary hemophagocytic lymphohistiocytosis[73]. Screening should be considered for this condition, and a hematology service should be consulted for appropriate therapies.

Blood Product Transfusion

- There is no evidence to guide the transfusion thresholds in patients with COVID-19.
- We recommend judicious use of blood products, due to anticipated blood product shortages during a pandemic. *Reasonable transfusion thresholds may include: hemoglobin $\geq$ 7-8 gm/dL[74]; platelet >50000 10^9/L and fibrinogen >100mg/dl.*[72] If there is no clinically significant bleeding lower platelet counts and fibrinogen concentrations may be tolerated.
- Routine use of antifibrinolytics is not recommended due to the risk of potential thrombosis in COVID-19 patients as there have been reports of a hypercoagulable state.
- There are emerging reports of convalescent plasma transfusion[75] use in patients with COVID-19. There is no current evidence for or against such plasma transfusion therapies in patients with COVID-19 supported on ECMO.

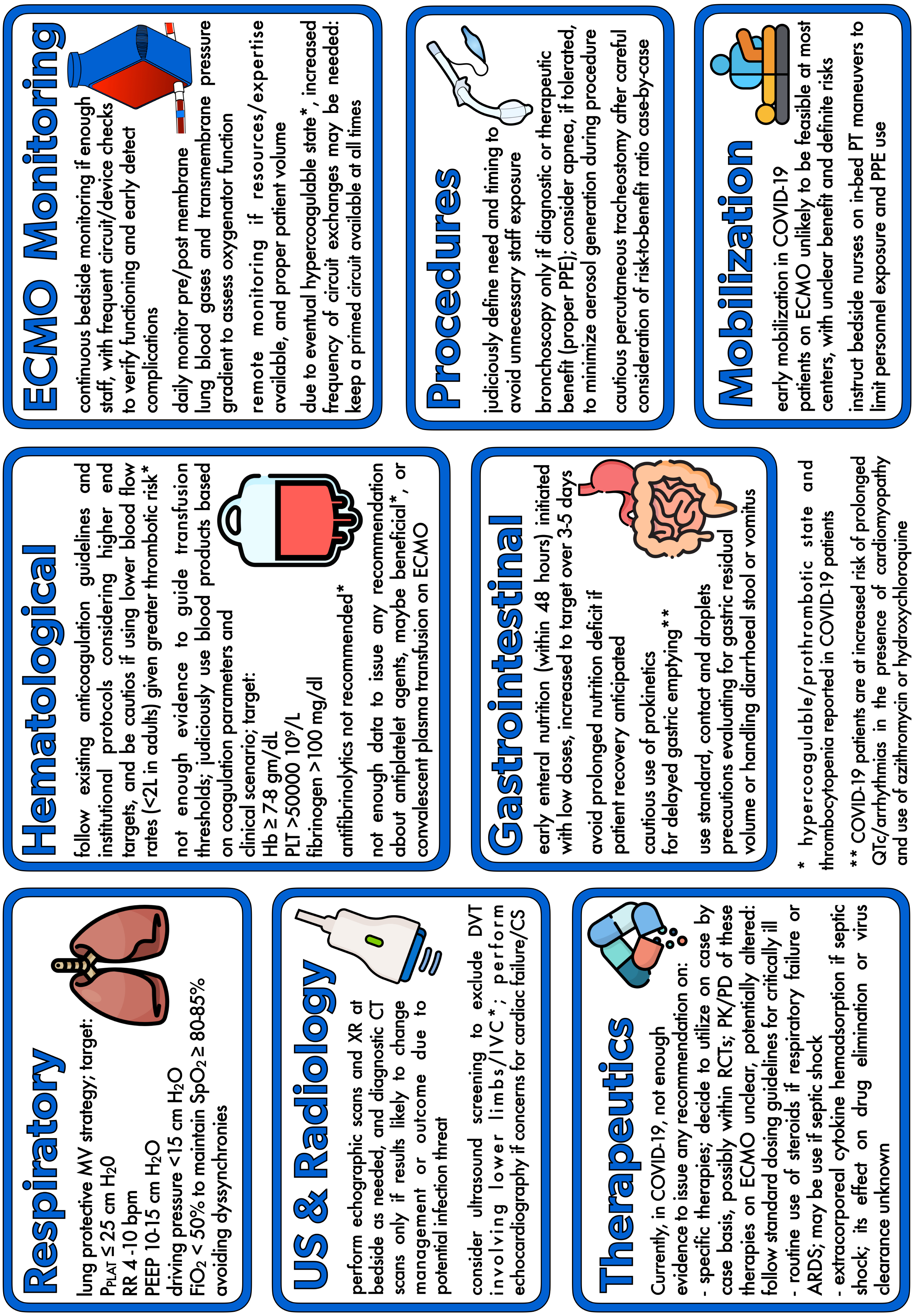

Figure 4. *Summary of patient management on ECMO.* MV, mechanical Ventilation; PPLAT, plateau pressure; RR, respiratory rate; PEEP, positive end-expiratory pressure; FiO2, inspired fraction of oxygen; SpO2, peripheral saturation of oxygen; RCTs, randomized controlled trials; PK, pharmacokinetics; PD, pharmacodynamics; ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; Hb, hemoglobin; PLT, platelets; XR, X-rays; CT, computed tomography; DVT, deep venous thrombosis; IVC, inferior vena cava; CS, cardiogenic shock; PPE, personal protective equipment; PT, physiotherapy.

Gastrointestinal

- We recommend early enteral nutrition (within 48 hours) commencing at low doses and advancing to target over 3-5 days. We recommend avoidance of prolonged nutrition deficit where it is anticipated the patient will recover[76-78].
- We recommend cautious use of prokinetics (metoclopramide) for delayed gastric emptying due to risk of prolonged QTc interval.
- We recommend standard, contact and airborne airborne precautions if evaluating gastric residual volume, due to the unknown risk of exposure to SARS-CoV-2 via gastric secretions.
- We recommend standard, contact and airborne precautions while handling diarrhoeal stool or vomitus. There is a potential, but currently unknown, risk of SARS-CoV-2 transmission from stools or vomitus. A bowel management system may be used.

Disease modifying agents

- Currently there is not enough evidence to recommend for or against the use of COVID-19 specific therapies (hydroxychloroquine, azithromycin, steroids, lopinavir / ritonavir, remdesivir or tocilizumab). Decisions to utilize such therapies should be based on a case by case basis.[79,80] *We do not recommend use of these therapies outside the clinical trial setting.* Pharmacokinetics/pharmacodynamics (PK/PD) of COVID-19 specific therapies on ECMO are unclear at this time with limited data. *Follow standard drug dosing guidelines for critically ill patients[81,82], while being cognizant of altered PK/PD on ECMO[83-85].*

Steroids

- There is not enough evidence to recommend routine steroids in COVID19-associated respiratory failure or ARDS. Steroids may be used in the context of septic shock[86,87].

Role for cytokine hemadsorption devices

- Currently, we lack definite evidence to recommend for or against the use of extracorporeal cytokine hemadsorption devices in COVID-19 patients who develop septic shock.[88] Additionally, the effect of such devices on drug elimination or virus clearance is unknown.

Mobilization

- *Early mobilization when safe and feasible may help improve recovery and maintain neuromuscular function[89].* However, in the setting of COVID-19, early mobilization of

patients during their ECMO course is unlikely to be feasible at most centers and is of unclear benefit and definite risks, which include: hemodynamic instability, dislodgement of tubes / catheters, availability of resources to facilitate mobilization, and viral transmission. Bedside nurses may be instructed on in-bed physical therapy maneuvers in an attempt to maintain standard of care while limiting personnel exposure and PPE use.

Diagnostic testing/monitoring while on ECMO

- Ultrasonography and chest or abdomen radiographs may be performed safely at the bedside as indicated. Consider screening ultrasound to exclude any deep venous thrombosis both in lower limbs and in the vena cava as COVID-19 patients may be hypercoagulable[54].
- Echocardiography should be performed as clinically indicated when there are concerns for cardiac failure or cardiogenic shock. Both left and right ventricular dysfunction have been reported in COVID-19 patients.
- Diagnostic CT-scans should be performed only if the results may change management or outcome. Transport of COVID-19 patients and cleaning of radiology rooms pose potential infection threats.

ECMO Monitoring

- Continuous bedside monitoring is optimal if staffing permits. We recommend frequent ECMO device monitoring by medical or nursing staff and ECMO specialists to verify device function and identify complications early.
- Consider daily monitoring of pre- and post- membrane lung blood gases and transmembrane pressure gradient to assess oxygenator function[90].
- Based on available resources, center expertise, and patient volume, consider remote monitoring of ECMO devices.
- The hypercoagulable state of COVID-19 patients may result in more frequent circuit exchanges. A primed circuit should be available at all times.

Procedures while on ECMO: General Principles

- *Judicious decisions regarding the need and timing of procedures is important in COVID-19 patients to avoid unnecessary staff-exposure*.
- We recommend bronchoscopy only, if it can provide diagnostic or therapeutic benefit to the patient (with appropriate PPE required). Patients can be made apneic during the procedure to minimize aerosol generation if tolerated.

- Percutaneous tracheostomy should be performed with caution after careful consideration of risk-to-benefit ratio in an individual patient.

6. Weaning from ECMO and Decannulation

Weaning from V-V ECMO

- Based on current knowledge, existing weaning guidelines[16] are suitable for weaning patients from V-V ECMO[91,92]. Given that ECMO is a finite resource, patients may have to be liberated from ECMO expeditiously where possible accepting a greater dependence on mechanical ventilation.
- During trialing off ECMO (sweep gas at 0 L/min), increase ventilator support as needed to settings that that are acceptable to facilitate coming off ECMO (V_T ≤ 6-8 mL/kg , P_{PLATI} ≤ 30 cmH_2O, PEEP ≤ 16 cmH_2O, FiO_2 ≤ 0.5, pH > 7.3, SaO_2 > 88%). If gas exchange is adequate for a 2-4 h period, the patient can be decannulated.

Weaning from V-A ECMO

- It is anticipated that most V-A ECMO runs in the context of COVID-19 will bridge to recovery. We recommend the use of existing V-A ECMO weaning protocols.[58,93]
- Bridge to durable device or to transplant can be challenging in the setting of a pandemic. As such, we recommend that multidisciplinary teams discuss exit strategies before cannulation for V-A ECMO. Family should be involved in the decision-making process along with ethics/palliative teams if possible.

Decannulation

- Full PPE precautions should be observed. Adequate care should be taken to prevent contact with bodily fluids.
- Careful assessment of bleeding and thrombotic risks is recommended prior to decannulation. Cannulas placed by cutdown should be surgically removed at the bedside, if possible. The risks of aerosol generation during electrocautery is unclear and optimal PPE should be used.
- Venous cannulae placed by percutaneous access can be removed at the bedside and bleeding controlled by topical pressure or sutures. Smaller arterial cannulas (e.g. ≤ 15

Fr) placed percutaneously may also be removed non-surgically though close coordination with relevant surgical teams is recommended.

7. Transport on ECMO

- *If adequate resources are available, centers with established mobile ECMO programs should offer ECMO transport to appropriately selected COVID-19 patients*. During the COVID-19 pandemic, critically ill patients with cardio-respiratory failure can present at non-ECMO centers and exhaust local resources. Societal recommendations include institution of ECMO or referral for ECMO in appropriately selected COVID-19 patients[11,19]. As such, programs with established mobile ECMO programs and with sufficient resources to maintain it, should continue to offer this highly specialized therapy to surrounding hospitals. Commercial support for transport between sites also exists for areas where local transport is not available.
- *COVID-19-specific criteria for ECMO cannulation should be extended for mobile ECMO candidates.* ECMO application may also be considered to facilitate transport of unstable COVID-19 patients being referred to external hospitals. Patients with COVID-19 may require transfer to other centers either for specialized procedures and consultation or due to local resource limitation and bed capacity[11].While not immediately indicated for ECMO, if such patients are not stable for transport, ECMO deployment may facilitate safe transport.
- *If performed, ECMO cannulation at remote sites should be performed with full PPE.* Cannulation of patients at external sites carries a risk of exposure to the transport team and requires strict adherence to PPE precautions[94]. Cannulation practices should follow the cannulation guidelines outlined in this document.
- *All transport team members, including EMS personnel and driver or pilot, should have PPE training and wear PPE throughout the ECMO transport.* The transport of infectious patients carries significant risk to transport personnel. Accidental exposure and contamination, with subsequent quarantine, can lead to strain on already limited personnel and resources[95]. Appropriate training has been shown to reduce self-contamination[96].
- *Minimize aerosol generating procedures during transport* and consider the use of high efficiency particulate air (HEPA) filters on the expiratory limbs of mechanical

ventilators. There is no evidence to support the routine use of a viral filter on the exhaust of the commonly used polymethylpentene based ECMO membrane lungs.

- *Develop a plan to disinfect transport vehicles* and to manage waste materials generated during transport in accordance with local regulations and in line with transport service providers.
- *Intrahospital transport of COVID-19 patients should be limited to vital diagnostic and therapeutic purposes* and appropriate planning and protective precautions should be taken to prevent exposure to staff and other patients.

8. ECMO in the neonatal and pediatric population

Patient Selection

- *COVID-19 is not a contraindication to ECMO* in this patient population.
- *We recommend using existing indications and thresholds for consideration of ECMO* as per currently published ELSO guidelines.[97-99] Some of the COVID-19 specific indications and contraindications are summarized in Table 2.
- *Candidacy for ECMO should be pre-emptively made before reaching the stage of need for ECMO.* This is based on the information that children with COVID-19 admitted to pediatric intensive care unit (PICU) are likely to have multiple co-morbidities, and this may influence consideration of ECMO support.
- *E-CPR in pediatric COVID-19 patients with severe ARDS is likely to have a poor prognosis, poses significant infection risks to staff due to aerosolization and is not recommended*. However, ECMO centres may wish to define E-CPR candidacy for in-hospital cardiac arrest upon admission of a COVID-19 positive patient to their unit.

Consent

- *The cannulation consent process should explicitly involve discontinuation of ECMO care in the absence of recovery of lungs, heart or both within an acceptable time frame*[11,20] or if ECMO is actively harming the patient (e.g. severe bleeding or clotting)
- Consent process should take into consideration the possibility that the parents/care providers may not be present for a face to face discussion.
- The ECMO consent should involve the standard components: benefits, risks and complications but should also refer to the current unavailability of published ECMO

outcomes that would guide the length of ECMO run, particularly in the event of no lung recovery and/or irreversible multiorgan failure.

Indications
• Refractory hypoxemia and worsening hypercapnia despite lung protective ventilation prone positioning high PEEP inhaled nitric oxide high frequency oscillatory ventilation • ARDS and/or ongoing requirement for vasoactive drugs (septic shock, cardiogenic shock) secondary to COVID-19 • Single organ failure with none or minor co-morbidities. AKI is not a contra-indication.
Contraindications
• Severe or multiple comorbidities • Immunocompromised status • Chronic Lung Disease • Critical congenital heart disease • Severe global developmental delay • Acute neurological complication – • intracranial hemorrhage • Irreversible severe brain damage. • Uncontrolled hemorrhage • Contraindication to anticoagulation • Severe multiple organ failure • Mechanical ventilation for > 14 days before ECMO initiation. • Lethal Chromosomal anomalies (e.g. Trisomy 13 or 18) • Extreme prematurity or low birth weight in neonates (<34wk or <2.0 kg)

Table 2. *Pediatric and Neonatal: Indications and contraindications for ECMO.*

Neonatal and pediatric cannulation

We recommend following standard cannulation techniques. Cannulation team members should wear standard, contact and airborne PPE.

- Surgery (especially sternotomy and electrocautery) is an aerosol generating procedure (AGP), and as such the use of P2/N95 respirators (without valves) along with a smoke evacuation device and eye protection is recommended. Powered Air Purifying Respirators (PAPR) are highly desirable in this setting.
- Surgical loupes are not a substitute for protective eyewear and may preclude the use of goggles or face shields. Each program will need to determine if surgical

cannulation techniques can be performed while maintaining PPE requirements. If not feasible, consideration for exclusive use of percutaneous cannulation should be discussed for patients with suspected and confirmed COVID-19 infection.

Management principles

General supportive measures

- *Management of ECMO in COVID-19 patients is similar to standard ECMO patients*.
- Anticoagulation guidelines as per institutional policy should be followed. Higher than usual intensity of anticoagulation may be indicated. A case-by-case assessment of bleeding vs. thrombotic risks is recommended pending further evidence.
- The role of chest physiotherapy and bronchoscopy during ECMO should be determined on case-by-case basis. Inline suction catheters are strongly recommended.

Implementation of blood conservation strategies

- The COVID-19 pandemic may result in a shortage of blood products. *We recommend the development of a blood conservation plan which aligns with institutional and blood supply chain emergency/disaster blood supply guidelines*. Consider the following for your local plan:
  - Restrictive transfusion thresholds, based haemoglobin (Hb) concentration and physiologic metrics and biomarkers of oxygen delivery
  - Reduced frequency of blood tests
  - A staged approach with phases for immediate introduction of blood conservation strategies and for when fresh product supplies are impacted.

Other treatments

- Therapeutic plasma exchange and IVIG are currently not recommended for COVID-19 patients unless part of a clinical trial.
- Use of medical therapies such as antivirals / hydroxychloroquine/ azithromycin/Zinc/ Vitamin C/steroids in pediatric patients should be individualized, based upon best available evidence at the time and is beyond the scope of this document.

Weaning from ECMO and decannulation

- Refer to ELSO weaning guidelines[97-99] and ECMO weaning and decannulation in adult patients for COVID-19 specific recommendations. (*refer to weaning and decannulation section*).

Family consideration and exposure

- While hospitals may be limiting or restricting visitation during the pandemic, neonatal and pediatric patients may benefit from parental presence at the bedside. We recommend one parent, with a maximum of two (depending on local institutional guidelines) be allowed to be present at the bedside. Use of videoconferencing to connect with family members or support systems (religious personnel, etc) may be beneficial.

Futility/ethical considerations

- Resource availability and lack of improvement over time may necessitate reassessment of treatment goals and redirection of care.
- Parents and family members should be made aware of this plan during the consent process.

Resource allocation considerations:

- During a pandemic, pediatric hospitals associated with adult hospitals should reserve ECMO equipment for potential non-COVID-19 neonatal and pediatric ECMO use, taking into special consideration, those diagnoses with historically excellent outcomes when supported with ECMO including but not limited to meconium aspiration syndrome and post-cardiotomy support for lesions with good outcomes. e.g. Anomalous left coronary artery from the pulmonary artery (ALCAPA).

9. Infection control and staff safety

The modes of transmission of SARS-CoV-2 are primarily through the respiratory tract and mucous membranes. There is a potential, but currently unknown, risk of SARS-CoV-2 transmission from stools or vomitus. All high-risk procedures on ECMO should be performed by experienced staff. Key infection control and staff safety measures relevant to ECMO use in COVID-19 infected patients are summarised in Table 3 and 4. Optimal PPE recommendations are subject to change as more data becomes available.

Cohort COVID-19 patients on ECMO to optimize infection control and staffing[11]
ECMO patients should be managed in negative pressure isolation rooms, when available
Neutral pressure rooms or cohorted open areas dedicated to COVID-19 patients may be used, if negative pressure isolation rooms are unavailable[100]
All laboratory samples of body fluids taken from patients on ECMO for laboratory testing, should be handled carefully. Centers should develop polices for handling of the diseased patients. Adhere to local policies on lab transfer of infectious materials.
ECMO centers should have protocols and guidelines for handling of medical wastes from a COVID-19 patient on ECMO.
Steps should be taken to enable effective two-way communication (e.g. walkie-talkies or dedicated phones) with personnel outside the isolation room for assistance or equipment[101]
All non-disposable components of the ECMO circuit must be properly disinfected after use for COVID-19 patients, as per local guidelines for surface disinfection of medical equipment.
Routine exhaust gas scavenging is not recommended. If plasma leak or other damage to oxygenator fibers is suspected, oxygenator or circuit change is recommended while donning optimal PPE. Institutional policies on environmental disinfection should be followed in such instances.
Position the ECMO circuit so that it can be monitored by the specialist though the cubicle door without opening it.
Consider performing ECMO cannulation within a designated COVID-19 environment and avoid transfers to catheterization lab or operating rooms where possible.
Dedicated ultrasound machines and echocardiography probes are highly desirable. Appropriate disinfection measures should be followed as per hospital guidelines after use.

Table 3. *Infection control measures while caring for COVID-19 infected patients on ECMO.* AAMI, Association for the Advancement of Medical Instrumentation; PAPR, powered air purifying respirators; PMP, polymethylpentene.

ECMO team members should receive adequate training in donning and doffing of PPE. [101]
Adhere to local or institutional policies on PPE use for COVID-19 patients.
ECMO initiation, and decannulation and bedside care should be performed with appropriate airborne plus contact precaution PPE including: N95/ filtering face piece 2 (FFP2) mask, gown, cap, eye protection (e.g., goggles or visor).
ECMO initiation, decannulation and all AGPs be performed with PPE and N95 masks or PAPR with full contact precautions.
While caring for COVID-19 ECMO patients wear appropriate PPE including N95/FFP2 masks, gowns, cap, eye protectors (e.g. goggles, visor) and follow contact precautions.
For procedures in which splashing or aerosol generation is anticipated, a higher level of protection (e.g. gown at AAMI level 3 or equivalent) should be considered.[18]
Labor-intensive procedures (e.g. mobilization, prone positioning, transport) carry significant risk of infection control breach to staff. We recommend that careful planning and team briefing be conducted beforehand, while keeping the number of staff performing the procedure to the minimum.
Simulation training on management of ECMO emergencies (e.g. cardiac arrest, pump failure) while wearing PPE or PAPR, since infection control breaches are more likely to occur in a stressful environment, should be scheduled. Additionally, performing procedures in full PPE should also be considered.
In the event of PPE shortage,[102] • adhere to the local hospital policies • use PAPR after appropriate training • extending the use of N95/ FFP2 masks could also be considered

Table 4. *PPE recommendations for staff caring for suspected or confirmed COVID-19 infected patients on ECMO. PPE, personal protective equipment; AGP, aerosol generating procedure; PAPR, powered air purifying respirators; ECMO, extracorporeal membrane oxygenation.*

10. Ethical dilemmas

Patient selection and timing of discontinuation of ECMO support pose significant ethical and moral challenges in regular ECMO care, but especially so during a pandemic[30,31,103]. ECMO centers should develop predetermined *consensus criteria* encompassing all aspects of ECMO care in COVID-19 patients. In addition, communication with local and regional ECMO and non-ECMO programs would be advantageous in caring for potential COVID-19 patients that would benefit from ECMO support. Reassessment of patient

selection criteria and care should be continually assessed through the pandemic and may change as capacity status changes and more is learned about the disease[35].

Ethical issues with patient selection

- ECMO should only be considered in carefully selected COVID-19 patients. (refer to patient selection section). *ECMO should not be considered in patients who are unlikely to benefit and in those with significantly reduced life expectancy from pre-existing disease[32,33].*
- ECMO is a highly technical therapy and is resource intensive. While the distribution of this therapy should be as equitable as possible, during a pandemic such as COVID-19, distribution should focus on optimal candidates for recovery.
- *We recommend involvement of supportive and palliative care teams[34], prior to cannulation and throughout the ECMO course, in situations where centers are running at contingency or crisis capacity*. Virtual meetings with use of videoconferencing tools to limit need for exposure to COVID-19 may be beneficial.

Ethical issues arising from discontinuation of ECMO for futility

- Futility is a decision made at the bedside by the treatment team on a case-by-case basis. Definitions of futility may change as we learn more about the trajectory of disease and recovery profiles in patients supported with ECMO.
- *ECMO should be discontinued if poor quality of survival is highly likely* (severe neurological insult, no heart or lung recovery with no possibility of a durable device implantation or transplant).
- Progressive multiple organ failure despite timely and optimal cardiopulmonary support indicates a poor prognosis and we recommend that goals of care be reassessed and ECMO discontinued after discussion with family.
- The definition of irreversible heart or lung failure may depend on the patient and the resources at the institution. In each case, a reasonable timeline for organ recovery or replacement should be set early in the course.
- For cardiac failure, for example, no meaningful cardiac recovery at 5-7 days in a patient who is not a candidate for durable device or transplant may be considered futile in most centers.
- For lung failure, futility of a prolonged run should be established on a case-by-case basis. Although resources may not allow prolonged ECMO runs during a pandemic, caution should be exercised when establishing futility of care in younger patients with isolated respiratory failure.

- Cessation of ECMO support can be a both morally and ethically challenging decision, and this can be heightened during pandemic-related resource constraints. Physicians should not make such decisions in isolation. We recommend early ethics team consultation, multidisciplinary team discussion with family while establishing expectations and goals of care at the time of ECMO cannulation.
- Appropriate end of life care should be provided to patients to ensure a comfortable and dignified death. Centers should develop a family visitation policy for all patients, more so during end of life care and utilize videoconferencing technology to overcome restrictions on visitations.
- *We recommend debriefing the staff in situations where there is a high risk of moral injury, acknowledging the time constraints in a pandemic. Staff should have access to psychological support as necessary*.

11. Quality assurance and ongoing research

- Quality assurance and clinical governance frameworks must be maintained with ECMO quality reviews conducted frequently to measure overall outcomes, identify problems and formulate plans for corrective actions.
- *We recommend that ELSO develop validated quality and process metrics specific to ECMO use during pandemics*.
- Collection and sharing of data is important to ensure preparedness and patient care, especially in parts of the world yet to be affected.
- The ELSO Registry should continue to serve as useful resource during a pandemic and provide valuable real-time data to track global ECMO activity and to provide preliminary guidance on patient selection and outcomes. *ELSO member centres are encouraged to enter minimum data prospectively at the initiation of the ECMO* so that valuable real-time[9] preliminary guidance may be obtained from the ELSO Registry.
- *Centers that are providing ECMO and are not ELSO members are encouraged to join ELSO and enter COVID-19 cases into the Registry. Membership fee is waived during this pandemic*.
- Understandably, ECMO centers are likely to face an increase in research participation requests during the pandemic. *We recommend that ELSO and global ECMO research networks such as the International ECMO Network[104]* develop a system of expedited

endorsement of clinical studies during the pandemic. This is important to ensure that ECMO centers prioritise participation in global data collection, clinical trials, ELSO registry based studies or other clinical studies that are most likely to yield meaningful results to guide ECMO practice.

- We recommend ECMO centers participate in the ELSO and the ECMOnet endorsed ECMOCARD (ExtraCorporeal Membrane Oxygenation for 2019 novel Coronavirus Acute. Respiratory Disease) study co-ordinated by the Asia-Pacific ELSO[41] and the EuroELSO ECMO Survey[10].
- *We recommend that ELSO develops a pandemic research plan* with ready-to-go research proposals and pre-approved ethics in place so that evidence based guidance is generated in the quickest possible time to benefit most patients.

Acknowledgements

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