- Electronic copy is controlled under document control procedure. Hard copy is uncontrolled & under responsibility of beholder.
- It is allowed ONLY to access and keep this document with who issued, who is responsible and to whom it is applicable.
- Information security code: ☑ Open ☐ Shared - Confidential
☐ Shared-Sensitive ☐ Shared-Secret

- النسخة الإلكترونية هي النسخة المضبوطة وفق إجراء ضبط الوثائق. النسخ الورقية غير مضبوطة وتقع على مسؤولية حاملها.
- يسمح بالوصول وبالاحتفاظ بهذه الوثيقة مع مصدرها أو مع المسؤول عن تطبيقها أو مع المطبق عليهم.
- تصنيف امن المعلومات: ☑ بيانات مفتوحة ☐ شارك – سري
☐ مشارك –حساس ☐مشارك –سري

Guidelines for Extracorporeal Membrane Oxygenation (ECMO) during COVID-19

Version 1

Issue Date	18/08/2021
Effective Date	18/08/2021

Health Policies and Standards Department

Health Regulation Sector (2021)

INTRODUCTION

Health Regulation Sector (HRS) forms an integral part of Dubai Health Authority (DHA) and is mandated by DHA Law No. (6) of 2018, to undertake several functions including, but not limited to:

- Develop regulations, policies, standards and guidelines to improve quality and patient safety and promote the growth and development of the health sector in the Emirate of Dubai.
- License and inspect health facilities as well as healthcare professionals and ensure compliance to current international best practice.
- Manage patient complaints and assure patient's and physician's rights are upheld.
- Manage health advertisement and marketing of healthcare products.
- Govern the use of narcotics, controlled and semi-controlled medications.
- Strengthen health tourism and assure ongoing growth.
- Assure management of health informatics, e-health and promote innovation.

The Guidelines for ECMO in COVID-19 Patients, aims to fulfil the following overarching DHA Strategic Objectives and Program within the Dubai Health Strategy (2016–2021):

- Objective 1: Position Dubai as a global medical destination by introducing a value-based, comprehensive, integrated and high-quality service delivery system
- Objective 2: Direct resources to ensure happy, healthy and safe environment for Dubai population

- Strategic Program 10: Excellence & Quality, which promotes excellence in healthcare service delivery in Dubai while enhancing patient happiness, experience, satisfaction and trust.

ACKNOWLEDGMENT

The Health Policy and Standards Department (HPSD) developed this document in collaboration with Subject Matter Experts. HPSD would like to acknowledge and thank these health professionals for their dedication toward improving quality and safety of healthcare services in the Emirate of Dubai.

Health Regulation Sector

Dubai Health Authority

TABLE OF CONTENTS

EXECUTIVE SUMMARY

With a vision to provide excellent health care services, DHA in collaboration with its partners has implemented advanced cardiorespiratory support in the form of ECMO for patients with cardiorespiratory failure to align with international standards. A taskforce comprising of experts from public and private hospital has been formed to ensure the program is been implemented successfully.

Establishment of the "Dubai-ECMO Program" is a long-term value based, comprehensive, integrated, specialized high quality service following one of the Objectives of the Dubai Health Strategy- Direct resources to ensure happy, healthy and safe environment for Dubai population.

The main aim of the program is to extend the service in DHA and private sector, and to create an internationally recognized regional ECMO referral centre.

This program requires a dedicated retrieval team consisting of an Intensivist, Cardiothoracic Surgeon, Vascular Surgeon, Registered Nurse (RN) and a Perfusionist to transfer eligible patients from referral Hospital to ECMO Centers. This will require cross licensing of Healthcare Professionals involved and Malpractice Insurance cover. Therefore, HRS support is required in considering the aspect of case retrievals within the document.

All requests for ECMO should go through DHA Command Center and would require an ECMO referral form to be completed.

ECMO centers must nominate a point of contact for administrative purposes.

Assigning a dedicated coordinator, who will liaise with the point of contacts, referring hospitals and the clinical core team on ECMO cases.

DEFINITIONS

Acute Respiratory Distress Syndrome (ARDS): is a condition in which the lungs are damaged and do not appropriately allow oxygen into the blood.

Cannulas: are plastic tubes that are placed in the blood vessels by the surgeons to drain blood from the body to the ECMO circuit, and back again.

Cannulation: is a process of placing the cannulas into the blood vessels. This process may be performed surgically (incision made) or percutaneously (through the skin much like an IV).

Decannulation: is the process of removing the cannulas from the blood vessels. This process may be performed at the bedside in the intensive care unit.

Extracorporeal Life Support (ECLS): ECMO is an ECLS modality. .

Extracorporeal Membrane Oxygenation (ECMO): is the process by which blood is removed from the body, enters a circuit of tubing where carbon dioxide is removed and oxygen is added, is re-warmed and then pumped back into the body. This supports the body with oxygenated blood in place of the patient's own heart and lungs.

ECMO team: is the team consists of Specialized Surgeons, Perfusionist, Physicians, Nurses, and Respiratory Therapists.

Endotracheal tube: is a tube that is placed directly in the mouth leading into the lungs to help breathe and protect the patient's airway.

Pulmonary hypertension: is a condition characterized by higher than normal blood pressure in the arteries of the lungs. The high pressure is caused by the lumen (central hollow port) of the arteries narrowing. As a result, the heart works harder to pump blood through the lungs because the blood vessels will not "open up" and let the blood pass through. This may cause the heart to fail or the blood to take another route around the lungs. If blood cannot flow normally through the lungs, it is difficult for it to pick up needed oxygen. When blood does not contain sufficient oxygen, other body organs will start to fail. This condition can be fatal. Sometimes, pulmonary hypertension can be cured. ECMO is sometimes used to provide oxygen to the organs while taking the strain off the lungs and/or heart. This may allow the arteries in the lung to relax and open up.

Respiratory Distress: is trouble breathing.

Sepsis: is an infection in the blood.

Tracheostomy: is a tube that is placed directly into the neck that leads to the lungs. This tube takes the place of the endotracheal tube that is placed in the mouth. The tracheostomy tube helps to protect the larynx. It also decreases the risk of infecting the lungs with germs from the mouth.

Urgent ECLS/E-CPR: is an emergency ECMO system. It is generally used for patients who are extremely unstable and may be close to a cardiac arrest.

V-A ECMO: (veno-arterial ECMO) is a type of ECMO that drains blood from a vein, oxygenates the blood in the circuit, and returns the blood to the body through an artery. This type of ECMO can be used to support both the heart and lungs.

V-V ECMO: (veno-venous ECMO) is a type of ECMO that drains blood from a vein, oxygenates the blood in the circuit, and returns the blood through a vein. This type of ECMO is used when only the lungs need support.

Ventilator: is a breathing machine that delivers oxygen, pressure and a rate of breathing to the patient through a breathing (endotracheal) tube. Also known as a respirator or vent.

Ventricular Assist Device (VAD): is a device that will assist the left side of the heart while a patient is waiting for a heart transplant. More information will be given to you if your family member is waiting for this device.

Weaning: is the process by which the amount of support is slowly decreased, as the patient gets better. The term may be used to refer to the blood flow rate of the ECMO machine or the settings of the ventilator.

ABBREVIATIONS

ARDS	:	Acute Respiratory Distress Syndrome
CAR	:	Chimeric Antigen Receptor
COVID-19	:	Corona Virus Disease-2019
CPC	:	Clinical Privileging Committee
DHA	:	Dubai Health Authority
ECLS	:	Extra Corporeal Life Support
ECMO	:	Extra Corporeal Membrane Oxygenation
HRS	:	Health Regulation Sector
ICU	:	Intensive Care Unit
MIS-C	:	Multisystem Inflammatory Syndrome in Children
RN	:	Registered Nurse
RT	:	Respiratory Technician
SARS-CoV-2	:	Severe Acute Respiratory Syndrome Coronavirus 2
V-A ECMO	:	Venoarterial Extra Corporeal Membrane Oxygenation
V-V ECMO	:	Venovenous Extra Corporeal Membrane Oxygenation.

1. BACKGROUND

Extra Corporeal Membrane Oxygenation (ECMO) also referred to as Extra Corporeal Life Support (ECLS). ECLS is now a well-established intervention used to support systemic perfusion and oxygenation in patients with cardiorespiratory failure not responding to conventional therapy. ECLS is generally considered for patients with a high risk of death (80 percent risk of death in severe ARDS or < 50 percent chance of survival in cardiogenic shock). The successful use of ECLS has risen dramatically in the last decade following an outbreak of H1N1 influenza in 2009. 1-3 ECLS is used as a bridge to destination (recovery, transplantation or death). The number of Extracorporeal Life Support Organization (ELSO)-registered centers (ELSO is a non-profit organization) have also increased significantly since 2009 and as per ELSO registry, there are 410 centers worldwide currently.

ECLS has evolved significantly in the last decade. We have a better understanding of the pathophysiology of certain diseases, ECLS technology has gotten simpler, safer, and portable. ICU care has evolved significantly in managing complex cases. The advent of a percutaneous approach to cannula insertion has made it easier and simpler to initiate ECLS in areas such as ED, ICU or Cath lab emergently if needed or at the right time. Despite ECLS not being universally adapted, there is now enough evidence to use ECLS in specialized centers doing high volume cases in appropriate patients at the right time. ECLS should be considered in patients with reversible cardio-respiratory failure who are at high risk of death when conventional therapy is failing. These cases should be referred to specialized ECMO centers with significant expertise in this technology and treatment of these complex cases. This

should be based on a Hub-spoke model in order to ensure optimal expertise is maintained and allocation of resources, optimized.

The role of ECMO support for patients with cardiopulmonary failure due to Corona Virus Disease 2019 (COVID-19) is evolving. A prominent feature of COVID-19 in critically ill patients is Acute Respiratory Distress Syndrome (ARDS).

This document has been developed for the effective use of ECMO for patients with severe cardiopulmonary failure due to COVID-19. The great majority of COVID-19 patients (>90%) requiring ECMO have been supported using venovenous (V-V) ECMO for ARDS.

Early in the pandemic, data on ECMO use was limited; however, the role of ECMO for COVID-19 related ARDS and other indications has become more apparent as the pandemic unfolds.

DHA strongly encourage participation in data submission to investigate the optimal use of ECMO for COVID-19.

2. SCOPE

2.1. ECMO services in DHA licensed health facilities.

3. PURPOSE

3.1. To assure provision of the highest levels of safety and quality ECMO services in DHA licensed health facilities.

4. APPLICABILITY

4.1. DHA licensed healthcare professionals and health facilities providing ECMO services.

5. RECOMMENDATION ONE: REGISTRATION AND LICENSURE CRITERIA

5.1. All health facilities providing ECMO services shall:

5.1.1. Adhere to all relevant federal and local laws and regulations.

5.1.2. Provision of ECMO services are based on the clinical decision by the management of the health facility.

5.1.3. ECMO services can be provided in DHA licensed Hospitals with tertiary level ICU and cardiothoracic and vascular surgical services and support.

5.1.4. Have in place internal policies and procedures for the following, but not limited to:

a. Incident reporting.

b. Service description and scope of services.

c. Patient assessment criteria.

d. Patient education and communication.

e. Informed consent.

f. Patient health record, confidentiality and privacy.

g. Hazardous waste management.

h. Infection control measures.

i. Medication management.

j. Readiness plan/Emergency response.

k. Staffing plan, staff management and clinical privileging.

l. Clinical audit and quality performance management.

m. Patient complaint.

5.2. Ensure adequate lighting and utilities, including temperature controls, water taps, medical gases, sinks and drains, electrical outlets and communications.

6. RECOMMENDATION TWO: HEALTH FACILITY REQUIREMENTS

6.1. The health facility design shall be as per DHA Health Facility Guideline 2019.

6.2. The health facility shall always have in place appropriate equipment and trained qualified healthcare professionals to perform the ECMO services.

6.3. The health facility providing ECMO services should ensure all consumables, equipment, pharmaceutical drugs/products required for each procedure are stored in a secured area.

6.4. The health facility shall be made to accommodate people of determination.

7. RECOMMENDATION THREE: HEALTHCARE PROFESSIONALS REQUIREMENTS

7.1. All healthcare professionals in the health facility shall hold an active DHA full time professional license and work within their scope of practice and granted privileges.

7.2. All physicians must hold up to date medical malpractice insurance.

7.3. The Clinical Privileging Committee (CPC) or Medical Director of the health facility shall take responsibility to privilege staff as per the DHA Policy for Clinical Privileging Policy. To be privileged and maintain privileges, to perform ECMO procedure.

7.4. The following licensed physicians are permitted to participate in caring for an ECMO Procedure:

7.4.1. The ECMO Physician

a. Is a physician who is contacted and informed by the Intensive Care Unit (ICU) when the decision is made for a patient to be placed on ECMO.

b. This physician shall have special education and training in the management of the ECMO machine and its effects on patients.

c. This physician shall manage the patient's ECMO treatment from start to finish.

d. The ECMO physician may be one of several subspecialists as mentioned below:

I. Intensivist

II. Pulmonologist

III. Cardiologist.

7.4.2. Interventional Cardiologist

a. A physician who performs ECMO placement, either in the catheterization laboratory or at the bedside. ECMO placement in an adult patient is often a procedure rather than surgery.

7.4.3. The Cardiothoracic Surgeon

a. A physician who performs surgery on the heart and lungs. These physicians may place the cannulas needed for ECMO, especially if the patient has a problem with the heart. This may take place in the operating room or at the bedside.

7.4.4. The Vascular Surgeon

a. A physician who performs surgery on veins and arteries. This physician inserts and removes the cannulas needed for ECMO but also assures that the patient's legs and arms are receiving enough blood supply and are not damaged by the large ECMO cannulas.

7.5. Other healthcare professionals involved in the ECMO procedure are as follows:

7.5.1. Perfusionist

a. Is an individual who has specialized training and certification in running the heart-lung machine in the operating room and ECMO at the bedside.

7.5.2. ECMO Coordinator/ECMO Primer

a. A Registered Nurse (RN), Respiratory Therapist (RT), or Perfusionist who specializes in the management and operation of the ECMO machine.

b. The coordinator or primer shall prepare the machine and tubing when the patient is first placed on ECMO.

c. In the event of trouble with the ECMO circuit, the ECMO Coordinator/Primer will be available to work with the ECMO specialist to fix the problem.

7.5.3. ECMO Specialist

a. A RN, RT, or Perfusionist with training in operating the ECMO machine.

b. The ECMO specialist will be present at the bedside, in the general unit, within the hospital, or on-call 24 hours a day to help manage the ECMO

circuit and its effect on the patient. In some centers, the ECMO specialist could be a bedside nurse.

7.5.4. The ICU Nurse

a. A RN who is available at the bedside watching the patient, administering medications and giving the patient any other care he/she may need. In some centers, the ICU nurse will also be the patient's ECMO specialist.

7.5.5. The Respiratory Therapist

a. A RN who shall be present to provide breathing treatments and help manage the breathing machine for the patient.

NOTE: The ECMO process flowchart is elaborated in **Appendix 1**.

8. RECOMMENDATION FOUR: TYPES OF ECMO

8.1. There are two (2) types of ECMO. Venoarterial (V-A) ECMO can be used for heart and lung support, while venovenous (V-V) ECMO is used for lung support only. The ECMO team will decide which type will help the patient, based on the specific illness.

8.1.1. Venoarterial (V-A) ECMO provides support for the patient's heart and lungs by allowing most of a patient's blood to move through the circuit without going through the patient's heart. This type of ECMO takes blood out of a large vein and returns it into a large artery, allowing oxygen-rich blood to circulate through the body even if the heart is too weak to pump it. Therefore, two cannulas must be placed in either the neck or the groin(s).

8.1.2. Venovenous (V-V) ECMO provides lung support only, so the patient's heart must still function well enough to meet the body's needs. Two cannulas are placed into veins in spots close to or inside the heart. With V-V ECMO, the surgeon-cannulating physician has an option of using a special type of cannula with two lumens (pathways inside the tubing). This allows blood to leave and return to the body in one place, creating the need for only one entry site instead of two. Blood from the ECMO system returns to the body before the heart, and the patient's own heart pumps the blood throughout the body.

9. **RECOMMENDATION FIVE:** PATIENT SELECTION CRITERIA

9.1. **Veno-venous ECMO (V-V-ECMO)**

9.1.1. It is primarily used in patients with isolated pulmonary disease as a bridge to recovery or transplant. Acute respiratory failure known as Adult Respiratory Distress Syndrome (ARDS) is the severest presentation in adults. The mortality from severe ARDS remains high at 40% despite advances in ICU care. Interventions in ARDS management that are shown to improve survival, include low tidal volume, high PEEP, prone positioning and the use of neuromuscular blockers. The aim of these interventions is to avoid Ventilator Induced Lung Injury (VILI) usually by maintaining safe plateau pressures. Despite these conventional measures, some patients fail to respond/improve leading to increasing hypoxemia (resistant hypoxemia) and/or hypercarbia. In order to maintain acceptable oxygenation and blood gas parameters,

physicians are often forced to increase settings on the ventilator, but these changes often result in detrimental effects to the lungs, leading to delayed or no lung recovery. Hence, ECLS is used to minimize the usual complications of VILI, as well as improving oxygenation and blood gas parameters. Driving pressure and mechanical power can be maintained in acceptable ranges while on ECMO, thereby avoiding VILI and therefore resulting in a higher survival rate. From the above, one can see that the use of ECLS provides an added safety factor in ventilated patients. This may result in faster lung recovery. As well as decreasing VILI, the aim is also to lessen other complications of ventilation such as muscle weakness and delirium caused by paralysis and sedation. On ECMO, the patient may be awake, communicating, feeding and possibly be extubated early, where appropriate. Therefore ECLS has given physicians the option of supporting a patient in acute respiratory failure with both modalities, ventilation and ECMO, or leaving the patient only on ECMO without a ventilator, which was not possible in the past. With this approach, complications from prolonged immobilization can be avoided, by having patients mobilized. In patients where extubation is not feasible, tracheostomy can be performed while they are on ECMO. Early physiotherapy and active mobilization is safe and feasible on ECLS and improves outcomes.

9.1.2. As per 2019 ESLO registry data (multicenter from various countries across the world), the overall survival of patients treated with VV-ECMO is 59% (expected mortality = 80%). In 2009, the CESAR trial reported a significant improvement in 6-month disability-free survival with referral to an ECMO center, compared with conventional ventilation treated in the best available care centers in the country. 3 In a more recent study, the 2018 EOLIA trial, mortality (primary end point) in the early ECMO group was 35%, compared to 46% in the conventional group which was not statistically significant (p-0.09). However, when considering secondary endpoint (treatment failure) this was statically significant (Relative risk, 0.62; 95% CI, 0.47-0.82; P<0.001). The reason for the difference was that 35 patients in the conventional group were crossed over to ECMO due to treatment failure with conventional care. Forty-three percent of these patients actually survived, which means 57% died due to late transfer to the ECMO group. This resulted in a lower mortality in the conventional group, due to crossover. This study therefore inadvertently became a study on early versus late ECMO, rather than ECMO versus conventional therapy. Thus, from this study we can see that the initiation of ECMO early in patients with severe ARDS has shown to result in improved outcomes. 17 The EOLIA trail indicates that ECMO should be used promptly when high-risk criteria are met, rather than as late rescue therapy when death from ARDS and multi-organ failure is imminent. Hence,

these studies have provided the "evidence" that ECMO is safe and feasible in ARDS, and should now be included in the standard algorithm for the management of ARDS.

Note: Algorithm for Management of ARDS is elaborated in **Appendix 2.**

9.2. Indications for V-V ECMO:

9.2.1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is 50% or greater, and is indicated when the risk of mortality is 80% or greater (50% mortality risk is associated with a PaO2/FiO2 < 150 on FiO2 > 90% and/or Murray score >3; 80% mortality risk is associated with a PaO2/FiO2 < 100 on FiO2> 90% and/or Murray score 3-4 (1), AOI >80 (2), APSS 8 (3) despite optimal care for 6 hours or less The best outcome in ECMO for adult respiratory failure occurs when ECMO is instituted early after onset).

9.2.2. Uncompensated respiratory acidosis with PH <7.2 on maximum conventional ventilation settings

9.2.3. Persistently elevated end inspiratory plateau pressures (>30cm H2O) despite optimal medical management or worsening trend.

9.2.4. Severe air leak syndromes.

9.2.5. Need for intubation in a patient on lung transplant list.

9.2.6. Primary causes of respiratory failure: Infection: Viral, bacterial, fungus, PJP

9.3. Contraindications:

9.3.1. Absolute:

a. CNS haemorrhage that is recent or expanding

b. Non-recoverable comorbidity such as major CNS damage or terminal malignancy

c. Age: no specific age contraindication but consider increasing risk with increasing age

d. Disseminated malignancy

e. Known severe brain injury

f. Severe chronic organ dysfunction, Emphysema, cirrhosis and renal failure

g. Cardiogenic shock and severe chronic pulmonary hypertension (mean pulmonary artery pressure >50mm Hg)

h. V-V ECMO is contraindicated in cardiogenic failure and in Severe Chronic Pulmonary Hypertension (mean pulmonary artery pressure >50 mmHg)

9.3.2. Relative Contra indications:

a. Mechanical ventilation at high settings (FiO2 >90%, P-plat >30cm H2O) for seven (7) days or more. Many centers do not consider time on ventilation a contraindication.

b. Major pharmacologic immunosuppression (absolute neutrophil count <400/mm3).

9.4. Veno-arterial ECMO (V-A ECMO)

9.4.1. Patients with hemodynamic instability progressing to shock should be considered for V-A ECMO if the pathology is deemed reversible. Cardiogenic shock is a highly morbid condition in which impaired heart function leads to inadequate end-organ perfusion, followed by multi-organ failure and death if untreated. Mortality remains close to 50% despite prompt medical therapy. High mortality has motivated the development of mechanical means to maintain perfusion. The emphasis of ECMO support in these cases is to reduce cardiac preload while maintaining end organ perfusion. ECLS should also to be considered as part of a multi-modal approach in the management of a shocked patient, unresponsive to conventional therapy as discussed above. Introduction of ECLS in the management of shock should be guided by protocols with clear clinical criteria, inotropic score, or echocardiographic data in order to initiate ECLS early, as opposed to late/salvage therapy, which continues to have a high mortality. 19-21 V-A ECMO provides cardiopulmonary support for patients in profound cardiogenic shock, as a bridge to myocardial recovery, durable mechanical circulatory support, or heart transplant.

9.4.2. As per the ELSO registry data, overall outcome for V-A ECMO-treated patients is 42%. Patients with myocarditis showed the best outcome at 62% survival, followed by patients with cardiomyopathy at 52%. Patients with

cardiogenic shock had a 44% survival and in extracorporeal cardiopulmonary resuscitation (ECPR) patients, 34% survived. However, the registry included all forms of cardiogenic shock.

9.4.3. Other indications for V-A ECMO include sepsis, pulmonary embolus and other forms of shock. Since the publication by Brechot et al. who reported a 70% survival rate in septic patients with myocardial dysfunction, the use of ECMO in sepsis is considered more often. In this study, cardiovascular function improved significantly over time with the use of ECMO and many patients' cardiac function returned to normal. This evidence was further supported by Falk et al. who demonstrated the benefit of ECMO not only in septic cardiomyopathy, but also in septic patients with distributive shock and refractory vasoplegia.

9.4.4. ECPR is another growing indication for VA-ECMO. This involves inserting ECMO emergently in hospital, in patients with in-hospital or out-of-hospital cardiac arrest. Traditionally the survival rate from out-of-hospital cardiac arrest, refractory ventricular fibrillation, in patients receiving conventional ACLS approach, is around 8% or lower. However, with the application of ECPR, the survival has improved and is currently between 34-45% in certain expert centers.

9.4.5. In addition to ECPR the concept of the "Shock Team" has recently changed the management, and significantly influenced the outcome, of both

cardiogenic shock and cardiac arrest. In 2018, a non-industry sponsored study from the US, which included a multidisciplinary shock team (interventional cardiologist, cardiothoracic surgeon, critical care physician and heart failure specialist) and an algorithm-based approach (which included rapid identification of shock, mandatory hemodynamic monitoring, minimizing vasopressor use, early mechanical circulatory support), was undertaken. This study looked specifically at patients with cardiogenic shock. Using this approach, the survival from cardiogenic shock which was traditionally <50%, improved to over 75% (p <0.01).

9.4.6. Indications

a. Refractory Cardiogenic shock (Myocardial infarction, myocarditis) with:

I. Lactate >4.0mmol/L despite adequate fluid resuscitation, Dobutamine >10mcg/kg/min +/--Norepinephrine

II. Clinical signs associated with rapid deterioration of cardiac function:

- Nausea, abdominal pain, Alteration Of consciousness, Skin mottling
- Systolic Blood pressure <90mmHg despite inotropes
- Tachycardia, rhythm disturbances
- Ionic disturbances, Acidosis
- Hepatic/Renal failure

- Increasing doses of vasopressors or inotropes with associated end organ failure including
- Renal, liver, and worsening lactate level
- Doppler-Echocardiography +++, LVEF<20%, Signs of low cardiac output (CI <2L/min/m2, Ao VTI <7---8cm.

b. Pulmonary embolism with severe hemodynamic compromise

c. Septic Shock with evidence of cardiac dysfunction by ECHO, Persistent raised lactate level >6 hrs and ScVo2 <60% despite optimization of vasopressors, inotropes and fluids 21

d. Refractory arrhythmia

e. Vasoactive inotropic score (VIS) >50 (for 1 hour), >45 >8hours or >40 in-patient with myocarditis; VIS: ([(epinephrine + norepinephrine) mcg/kg/min] X 100+ [(dobutamine + dopamine) mcg/kg/min] + [milrinone mcg/kg/min] X 15 + [vasopressin IU/kg/min X10, 000).

9.4.7. Contraindications:

a. Absolute:

I. Futile treatment without exit strategy

II. Unrecoverable heart and not a candidate for transplant or destination therapy of VAD

III. Support

IV. Disseminated malignancy

V. Known severe brain injury

VI. Unwitnessed cardiac arrest

VII. Prolonged CPR without adequate tissue perfusion

VIII. Unrepaired aortic dissection

IX. Severe aortic regurgitation

X. Severe chronic organ dysfunction (emphysema, cirrhosis, renal failure)

XI. Compliance (financial, cognitive, psychiatric, or social limitations in Patient without social support)

XII. Peripheral vascular disease is contraindicated in peripheral VA ECMO.

Note: Contraindications algorithm for V-A and V-V ECMO use are elaborated in **Appendix 3.**

9.4.8. Cost of ECMO

a. In a time where healthcare costs are rising, costs of interventions and technology should be scrutinized as was done in a study from Canada, which performed model-based cost utility analysis in VV ECMO and compared it to standard lung protective ventilation. This study evaluated outcomes using Incremental Cost Effectiveness Ratio (ICER), which is the incremental costs associated with a new therapy needed to generate one additional QALY. Many health system payers and health

technology organizations use this methodology of economic evaluation. This study showed that VV ECMO is associated with a lifetime gain of 5.2 life years and 4.04 QALYs when compared with lung protective ventilation for the treatment of severe ARDS in young adults 45 years old. It is associated with incremental increase in costs of $145,697 CD/QALY and the ICER was $36,001 CAD/QALY with the acceptable threshold being at $50,000-100,000 CAD/QALY as per Canadian health care system. This also fits in with cost effectiveness set by National Institute for Health and care Excellence (NICE) UK with an ICER between $35,696- 53,544 CAD)/QALY. Peek et al. reported an ICER of $42,356 CAD/QALY gained with the use of referral to an ECMO center compared with mechanical ventilation, using a lifetime time horizon and UK health system perspective.

b. Cost estimates of in-hospital care of ECMO patients vary significantly. Although costs in a private delivery model and a public system are challenging, costs for ECMO in the United States generally exceeds $100,000 per patient, whereas per-patient costs in one-half of international centers are less. Despite cost concerns, data suggest that percutaneous circulatory support utilization, including ECMO, results in decreased mortality and in hospital costs for patients in cardiogenic

shock, possibly due to an avoidance of end organ dysfunction leading to shorter hospital stays.

10. RECOMMENDATION SIX: CANNULATION STRATEGIES

10.1. 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.

10.2. 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.

11. RECOMMENDATION SEVEN: ONGOING CARE DURING ECMO

11.1. Routine management of the patient receiving ECMO is outside the scope of this guideline, and recommendations on disease modifying agents are also outside of the scope of this guideline.

11.2. A concise list of COVID-19 ECMO-specific recommendations is provided in **Appendix 4.**

11.3. **Pulmonary**

11.3.1. There is 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.

11.3.2. Percutaneous tracheostomy appears to be safe and feasible for patients with COVID-19.

11.3.3. Prone positioning during ECMO is feasible and 81% of COVID-19 patients in one study were placed in the prone position. Preliminary data demonstrate a potential association of prone positioning on ECMO with lower mortality. However, a recommendation cannot be offered at this time.

11.3.4. An early extubation strategy with awake ECMO may be feasible for patients with COVID-19. However, there is currently no data to support this strategy over one in which the patient remains endotracheally intubated during ECMO.

11.4. **Hematologic and Hemodynamic Monitoring**

11.4.1. COVID-19–induced coagulopathy appears to include both thrombotic and bleeding events. Specific ramifications for ECMO include circuit clotting, higher than previously reported rates of pulmonary embolism, and intracranial hemorrhage. However, when normalized to ECMO run duration, rates of bleeding, and circuit clotting in patients with COVID-19 are similar to historical data, in one observational study. 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 for patients with COVID-19 receiving ECMO.

11.4.2. There are insufficient data to recommend routine surveillance for deep venous thrombosis for patients with COVID-19; 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.

11.4.3. 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, although evidence is needed to provide further insights. Therefore, extracorporeal hemadsorption or elimination therapies can only be recommended within the context of clinical trials.

11.4.4. There is no evidence to deviate from usual institutional practices for blood transfusion thresholds during ECMO.

11.4.5. 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 ventricular failure, pulmonary embolism, or acute coronary syndrome.

11.5. **General**

11.5.1. Refer to local policies and other relevant documents for recommendations on PPE use and conservation methods when facing inadequate supply.

11.5.2. 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.

11.5.3. Remain vigilant for bacterial coinfection and superinfection given high-observed rates of ventilator-associated pneumonia and bacteremia in some studies.

11.5.4. Mobilization of patients is feasible while undergoing ECMO 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.

11.5.5. Intra-hospital transport can be safely performed, and thus traveling within the hospital should be pursued when indicated, for example, radiology, unit relocation, etc.

12. RECOMMENDATION EIGHT: WEANING AND DISCONTINUATION OF ECMO

12.1. 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.

12.2. If patients are bridging to recovery, the consent process (E.g. of a Consent Form **Appendix 5)** should include a discussion outlining criteria with family for when ECMO support is to 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).

12.3. 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 forty (40) days had an estimated ninety (90) day mortality of 14% in the ELSO Registry study.

12.4. Duration on ECMO (>90% V-V) for COVID-19 from three large observational studies was median 13.9 days (interquartile range [IQR], 23.3 days), median 20 days (IQR, 10–40 days), and mean 18 days. It is important to note that successful native lung recovery has been reported after prolonged (>28 days) V-V ECMO support.

12.5. The role of chest imaging in determining futility while on V-V ECMO is unknown.

12.6. 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.

13. RECOMMENDATION NINE: KEY RECOMMENDATIONS

13.1. V-V ECMO may be utilised for patients with COVID-19 and severe respiratory failure with expected outcomes comparable to patient support with V-V ECMO prepandamic.

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

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

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

13.5. Contraindications of ECMO use should be more stringent as ECMO capacity diminishes.

13.6. Data submission is essential to facilitate data compilation to understand the optimal care for patients with COVID-19.

13.7. Bleeding remains a concern with ECMO and there is no data to recommend deviation from conventional anticoagulation goals.

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

13.9. Potential discontinuation of ECMO in case of perceived futility should be clearly discussed with the patient and their guardian or custodian.

13.10. Rarely children can require ECMO support for severe ARDS, myocarditis, or Multisystem Inflammatory Syndrome in Children (MIS-C_, in these cases selections and management should follow conventional guidelines.

REFERENCES

1. Annich GM. Extracorporeal Life Support: a precarious balance of homeostatsis. J Thromb Heamost 2015:13 Sppl 1:S336-42. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/jth.12963 Accessed on (16 May 2021).
2. Bartlett RH. Extracorporeal membrane Oxygenation for Acute Respiratory Distress Syndrome: EOLIA and beyond. Crit care Med: Jan 2019.47:114-117. Available at: https://journals.lww.com/ccmjournal/Fulltext/2019/01000/Extracorporeal_Membrane_Oxygenation_for_Acute.16.aspx Accessed on (20 May 2021).
3. Bellani G, Laffey JG, Pham T, et al. LUNG SAFE investigators; ESICM Trials Group: Epidemiology patterns of care and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JMA 2016;315:78800. Available at: https://jamanetwork.com/journals/jama/fullarticle/2492877 Accessed on (20 May 2021).
4. Biehl M, kashiouris MG, Gajic O. Ventilator-Induced-Lung Injury minimizing its impact in patients with or at risk for ARDS. Respir Care 2013.58:927-937. Available at: http://rc.rcjournal.com/content/58/6/927.short Accessed on (19 May 2021).
5. Brechot N, Luyt CE, Schmidt M, et al: Venoarterial extracorporeal membrane oxygenation support for refractory cardiovascular dysfunction during severe bacterial septic shock. Crit Care Med 2013;41:1616-1626. Available at:

https://journals.lww.com/ccmjournal/Fulltext/2013/07000/Venoarterial_Extracorporeal_Membrane_Oxygenation.4.aspx Accessed on (16 May 2021).

6. Cabinet Secretary for Health and Sport. Regulations of Non-Surgical Cosmetic Procedures: Consultation. Scottish Government. 2020. Available at: Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/192028/Review_of_the_Regulation_of_Cosmetic_Interventions.pdf Accessed on (28 May 2021).

7. Cheng R, Hachamovitch R, Kittleson M, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a metanalysis of1,866 adult patients. Ann Thorc Surg 2014;97:610-616. Available at: https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0003497513020055?returnurl=https:%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0003497513020055%3Fshowall%3Dtrue&referrer=https:%2F%2Fpubmed.ncbi.nlm.nih.gov%2F Accessed on (26 May 2021).

8. Combes A, Hajage D, Capellier G, et al. extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. NEJM 2018.378:965-1975. Available at: https://www.nejm.org/doi/10.1056/NEJMoa1800385?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0www.ncbi.nlm.nih.gov Accessed on (24 May 2021).

9. Davies A, Jones D, et al. Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators: Extracorporeal membrane

Oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome. JAMA 2009. 302:1888-1895. Available at: https://jamanetwork.com/journals/jama/fullarticle/184800 Accessed on (24 May 2021).

10. DeWitt DS, Black KJ, Thiagarajan RR, et al: Effects of commonly used inotropes on commonly used myocardial function and oxygenation consumption under constant ventricular loading conditions. J Appl phyio (1985) 2016;121:7-14. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5504386/ Accessed on (11 May 2021).
11. ELSO Adult Respiratory Failure Guidelines, 2017, version 1.4, pages1-32. Available at: https://www.elso.org/Portals/0/ELSO%20Guidelines%20For%20Adult%20Respiratory%20Failure%201_4.pdf Accessed on (6 May 2021).
12. ELSO registry 2019 Available at: https://www.elso.org/Portals/0/Files/Reports/2020_January/International%20Summary%20January%202020_page1.pdf Accessed on (24 May 2021).
13. Falk L, Hultman J, Bromn LM. Extracorporeal Membrane Oxygenation for Septic Shock. Crit Care Med 2019 47(8):1097-1105. Available at: https://journals.lww.com/ccmjournal/Fulltext/2019/08000/Extracorporeal_Membrane_Oxygenation_for_Septic.12.aspx Accessed on (28 May 2021).

14. Gattinoni L, Vasques F, Quintel M. Use of ECMO in ARDS: does the EOLIOA trial really help? Crit Care.2018. 22:171-172 Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6034241/ Accessed on (22 May 2021).

15. Khoshbin E, Roberts N, Harvey C, et al. poly-Methyl-Pentene oxygenators having proved gas exchange capability and reduced transfusion requirements in adult extracorporeal membrane oxygenation. ASAIO J 2005;51:281-287. Available at: https://journals.lww.com/asaiojournal/Fulltext/2005/05000/Poly_Methyl_Pentene_Oxygenators_Have_Improved_Gas.17.aspx Accessed on (16 May 2021).

16. Ko Y, Cho YH, Park YH, et al. Feasibility and safety of early physical therapy and active mobilization for patients on extracorporeal membrane oxygenation. ASAIO J 2015.61:564-568. Available at: https://journals.lww.com/asaiojournal/Fulltext/2015/09000/Feasibility_and_Safety_of_Early_Physical_Therapy.13.aspx Accessed on (19 May 2021).

17. Napp LC, Kuhn C, Bauersachs J. ECMO in Cardiac arrest and cardiogenic shock. Herz 2016.42:27-44. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5306351/ Accessed on (12 May 2021).

18. Noah MA, Peek GJ, Finney SJ, et al. Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 Influenza A (h1N1). JAMA 2011.306:1659-1668. Available at:

https://jamanetwork.com/journals/jama/fullarticle/1104507 Accessed on (11 May 2021).

19. Peek GJ, Mugford m, Tiruvoipati R, et al. efficacy and economic assessment of conventional ventilator support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicenter randomized control trail. Lancet (London, England) 2009.37:1351-1363. Available at: https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0140673609610692?returnurl=https:%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0140673609610692%3Fshowall%3Dtrue&referrer=https:%2F%2Fpubmed.ncbi.nlm.nih.gov%2F Accessed on (17 May 2021).

20. Rupprecht L, Lunz D Phillip A et al. Pitfalls in percutaneous ECMO cannulation. Heart Lung Vessel 2015;7:320-326. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4712035/ Accessed on (16 May 2021).

21. Theile H, Ohman EM, Waha-Thiele S, Zeymer U, Desch S. Management of cardiogenic shock complicating myocardial infarction: an update 2019. European Heart Journal (2019) 40, 2671–2683. Available at: https://academic.oup.com/eurheartj/article/40/32/2671/5528526?login=true Accessed on (25 May 2021).

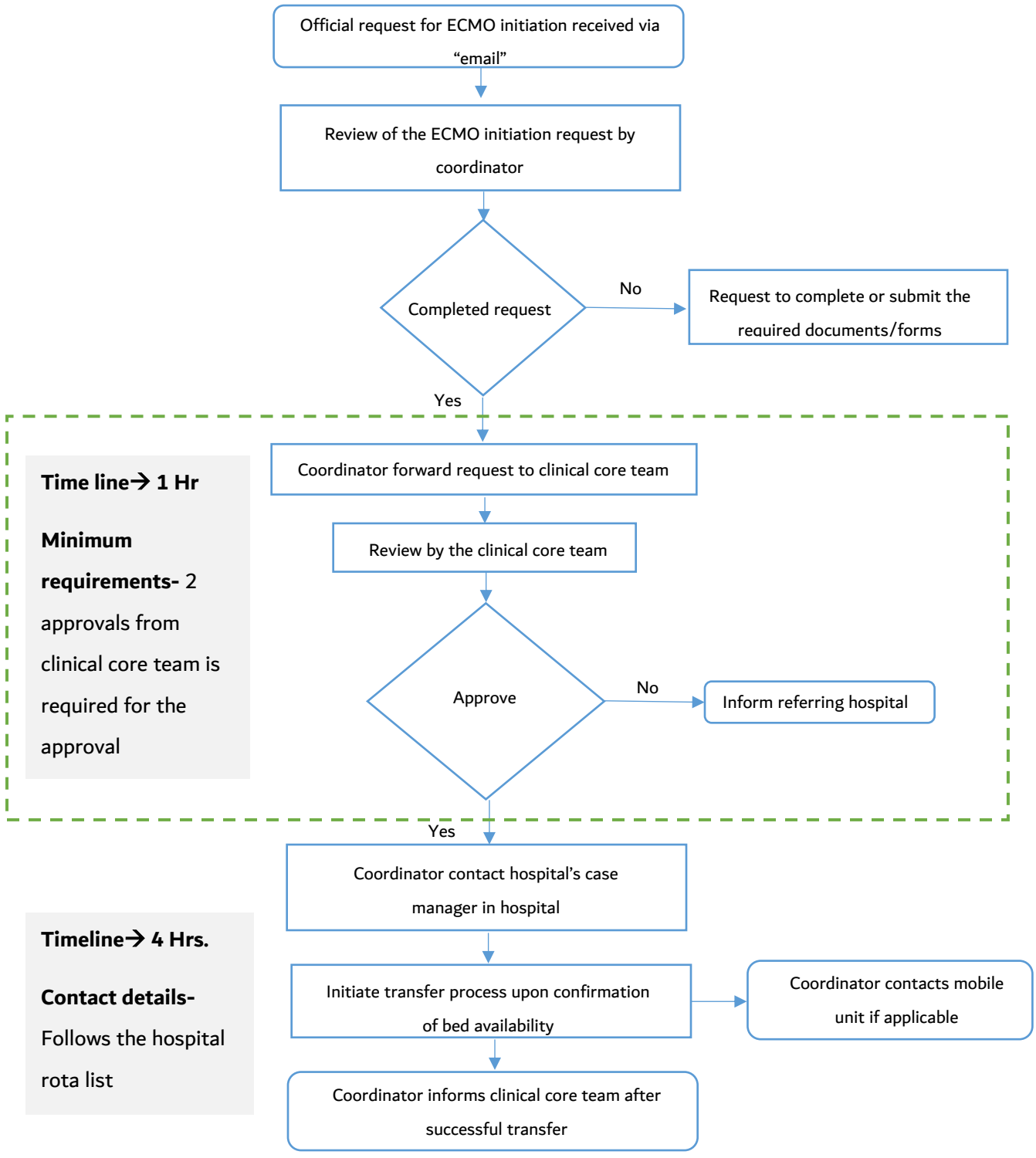
22. Turner DA, Cheifetz IM, Rehder KJ, et al. Active rehabilitation and physical therapy during extracorporeal membrane oxygenation while awaiting lung transplant: a

practical approach. Crit Care Med 201.39: 2593-2598. Available at: https://journals.lww.com/ccmjournal/Fulltext/2011/12000/Active_rehabilitation_and_physical_therapy_during.1.aspx Accessed on (22 May 2021).

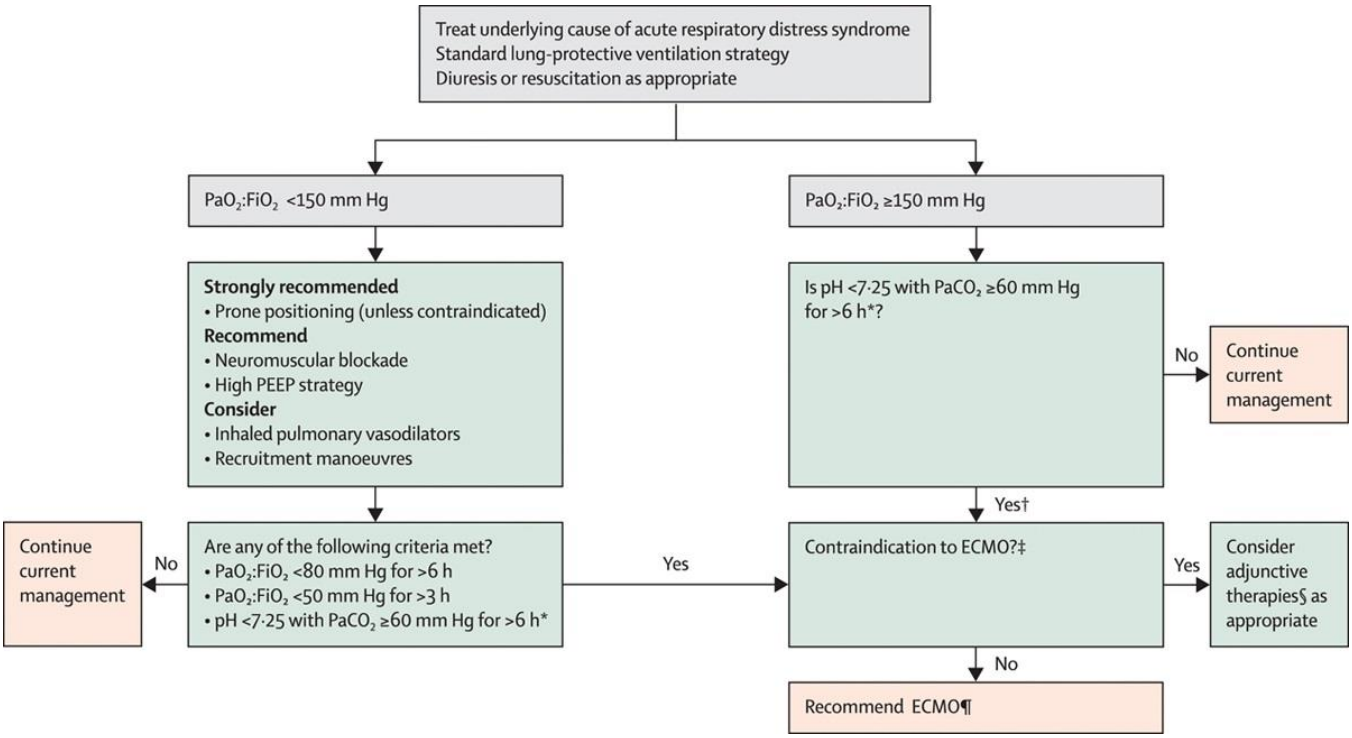
23. Yannopoulos D, Bartos JA, Raveendran G, et al. Coronary artey disease in patients with out-of-hospital refractory ventricular fibrillation cardiac arrest. J Am Coll cardiol. 2017;70(9):1109-1117. Available at: https://www.jacc.org/doi/full/10.1016/j.jacc.2017.06.059 Accessed on (18 May 2021).

APPENDICES

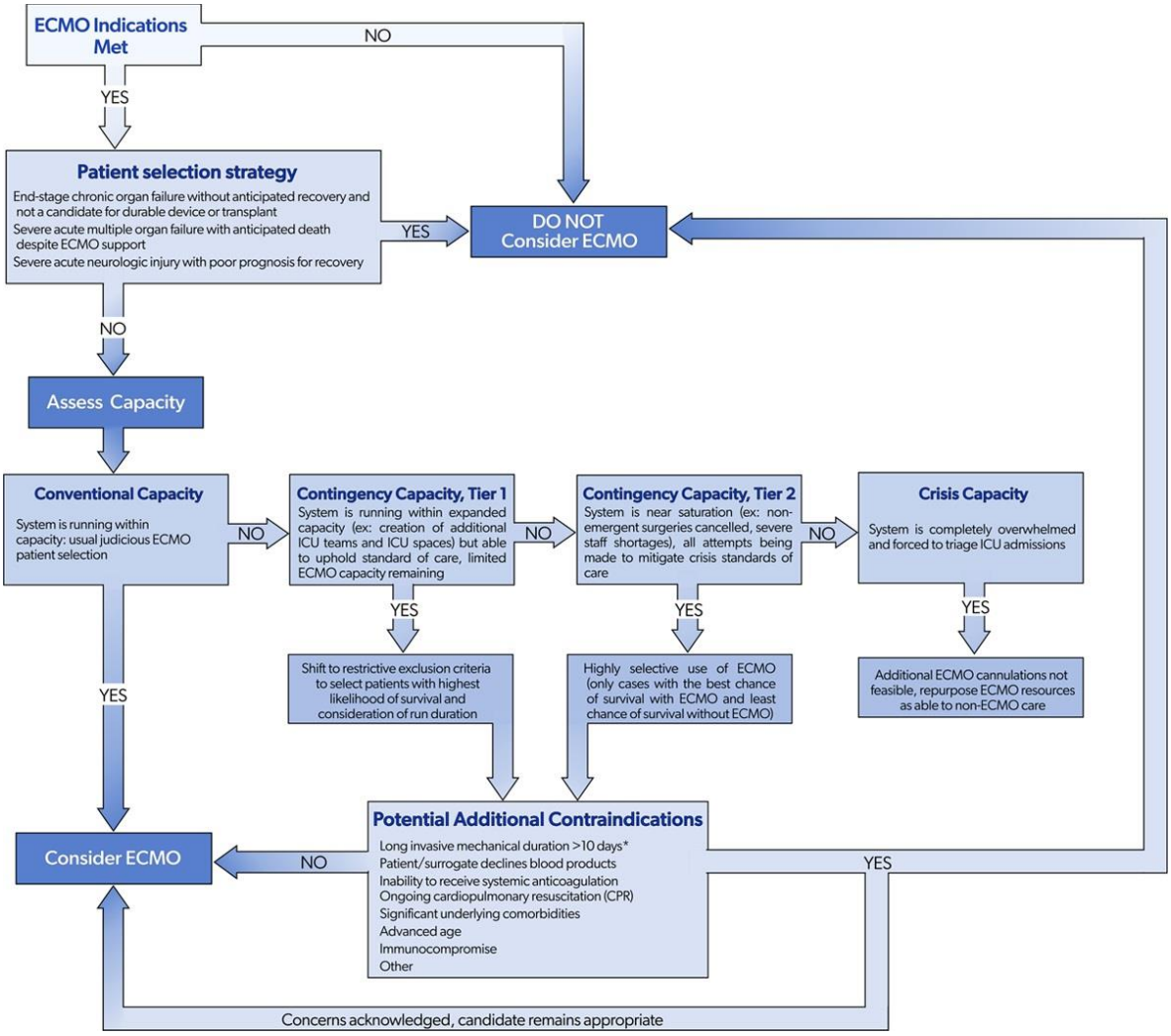
APPENDIX 1: ECMO PROCESS FLOW CHART



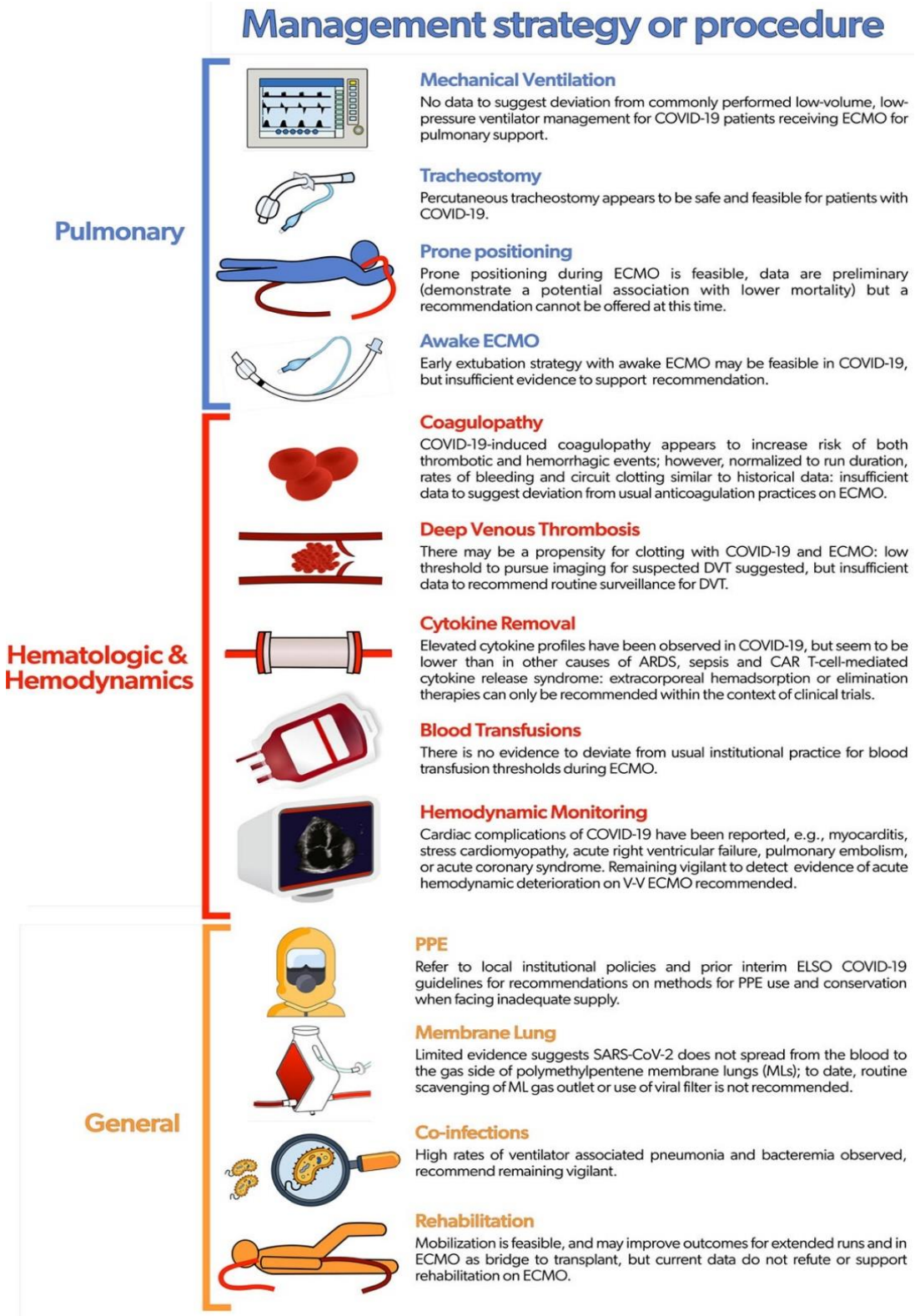
APPENDIX 2: ALGORITHM FOR MANAGEMENT OF ARDS



APPENDIX 3: CONTRAINDICATIONS ALGORITHM FOR V-A AND V-V ECMO USE



APPENDIX 4: RECOMMENDATIONS FOR ONGOING CARE FOR PATIENTS WITH COVID-19 RECEIVING ECMO



APPENDIX 5: ECMO INITIATING REQUEST FORM FOR HEALTHCARE PROFESSIONALS

Kindly fill the form below if the patient is meeting the following eligibility criteria for ECMO management

- Refractory Hypoxemia with P/F ratio <100

OR

- Uncompensated respiratory acidosis with PH <7.3 On maximum conventional ventilation settings
- >18 yrs. and <65 yrs.
- Duration of MV < 7days
- Reversible pathology?
- Neurologically intact before intubation
- No present or past medical history of
  - ✓ End stage lung disease
  - ✓ End stage liver disease
  - ✓ Terminal malignancy
  - ✓ Irreversible brain damage
  - ✓ Established multi organ failure

Name:	**Emirates ID #:**
Age:	**Weight:**
Gender:	**Date of Admission:**
Hospital Name:	**Treating Doctor:**
History of underlying irreversible lung disease (e.g. Interstitial lung fibrosis, COPD on home oxygen or BiPAP): ☐ YES ☐ NO	
History or known case of immunocompression ☐ YES ☐ NO	
Diagnosis: ☐ Bacterial Pneumonia ☐ Viral Pneumonia ☐ ARDS secondary to extra pulmonary sepsis ☐ Lung contusion due to Trauma ☐ Aspiration Pneumonia ☐ Drowning ☐ Acute Severe Asthma ☐ Pancreatitis ☐ Others (please specify) _____	
Duration of the mechanical ventilation from onset of ARDS (must be less than 7 day)	
Ventilator Settings	
<u>Supine</u> Mode _____ PEEP _____ Plateau Pressure_____ Respiratory rate _____	**<u>Prone</u>** Mode _____ PEEP _____ Plateau Pressure_____ Respiratory rate _____
Proning: Start date _____ Frequency _____	

Current Mechanical Ventilator Settings: (P/F ratio must be less than 100 mg)

☐ Supine: _____

☐ Prone: _____

ABG (Arterial Blood Gases) Results (in *supine* position)

Date: ___/ ____/_____

Results:_____

Date: ___/ ____/_____

Results:_____

Date: ___/ ____/_____

Results:_____

ABG (Arterial Blood Gases) Results (in prone position)

Date: ___/ ____/_____

Results:_____

Date: ___/ ____/_____

Results:_____

Date: ___/ ____/_____

Results:_____

Inotropes

☐ YES ☐ NO

Type of inotropes/ vasopressors (+ dosage) _____

Nitric Oxide

☐ YES ☐ NO

Neuromuscular Blocking Agent

☐ YES ☐ NO

Organ Failure:

☐ YES ☐ NO

Details:_____

_____

Echocardiogram

Date ___/ ____/_____

Findings:

_____

_____

Sofa Score: _____

CNS

Glasgow Coma Scale	SOFA Score
15	0
13-14	1
10-12	2
6-9	3
<6	4

CVS

MAP or administration of Vasopressors requires	SOFA Score
MAP >70mm Hg	0
MAP <70mm Hg	1
Dopamine >5mcg/kg/min or Dobutamine any dose	2
Dopamine <5 µg /kg/min or Epinephrine ≤ 0.1 µg/kg/min or Non epinephrine ≤ 0.1 µg/kg/min	3
Dopamine > 5 µg /kg/min or Epinephrine > 0.1 µg/kg/min or Non epinephrine > 0.1 µg/kg/min	4

Hepatic

Bilirubin (mg /dl) (micromole/L)	SOFA Score
<1.2 (<20)	0
1.2-1.9 (20-32)	1
2.0-5.9 (33-101)	2
6.0- 11.9 (102 -204)	3
>12.0 (>204)	4

Hematology

Platelets X 10^3/micro 1	SOFA Score
>150	0
<150	1
<100	2
<50	3

	<20	4	

Renal

Creatinine (mg/dl) (µmol / L)	SOFA Score
<1.2 (<110)	0
1.2-1.9 (110-170)	1
2.0-3.4 (171-299)	2
3.5-4.9 (300-440) or < 500 ml/ d> 5.0 (> 440) (or < 200 ml/d)	3
	4