

## Supplemental Document 1: Adult ECMO Guidelines

### Patient Selection:

Respiratory Failure with worsening gas exchange despite conventional interventions that include lung protective ventilation with use of PEEP scale as per ARDSnet protocol, prone positioning, neuromuscular blockade, and if available, inhaled nitric oxide (INO). In select cases, a trial of APRV may be appropriate.

Despite these measures, if gas exchange continues to worsen as defined by:

- PF ratio < 80 for 6 hours or PF ratio < 50 for 3 hours
- Alternatively pH < 7.25 with PCO<sub>2</sub> > 60 with plateau pressure > 30 for 6 hours

### Exclusions:

- Age > 60, this may be lower during times of critical shortages (Age > 55)
- BMI > 45 (for patients aged < 45, will extend BMI cutoff to 50)
- Poor neurologic function or unknown mental status prior to presentation
- Mechanical vent ≥ 7 days (can consider up to 10 days for pts aged < 45)
- Bleeding diathesis (inability to anticoagulate), or low platelets < 80
- Immunocompromised state:
  - Active chemotherapy or BMT within the last year
  - Auto-immune disease requiring high-intensity immunosuppression
  - Low intensity maintenance immunosuppression can be evaluated on a case by case basis (auto-immune dz or s/p liver or kidney transplant)
  - HIV: non-adherent patient or treatment refractory disease
- Malignancy with expected survival < 5 years
- Multi-system organ failure (MOF) or pending MOF with high pressor requirement and evidence of poor perfusion (i.e. high lactate)
- Unwitnessed cardiac arrest
- Chronic end organ disease:
  - Chronic renal disease stage III or worse
  - Moderate to severe COPD
  - Ischemic or non-ischemic cardiomyopathy with history of CHF
  - Severe peripheral vascular disease
  - Cirrhosis

Exclusion Extensions for patients ≤ 45 years of age

- BMI > 50 if patient has RIJ access
- Mechanical vent ≥ 10 days

### Cannulation:

ECMO consult via HAL leading to ECMO Team Activation:

- Perfusionist will be called into the hospital or notified if already in house.
- CT surgery fellow will contact family for consent.
- CVSICU team will be notified for management.
- Anesthesia team will be activated for TEE as needed.
- ICU bed will be made available
  - CCU for COVID positive patients & CVSICU for non-COVID patients

The cannulation configuration will be determined by the surgeon. Brief cannulation protocol attached as Appendix A at the end of this document.

- Bi-Caval Dual Lumen Cannula (Avalon or Crescent) to be placed with TEE guidance
- Femoral vein and RIJ configuration can be placed without echo.
- Fem/Fem VV access is the least desirable configuration

We will order a standard CXR after cannulation to get a baseline view of placement and rule out pneumothorax. If there is a PTX and chest tube is placed, the cannula will need to be repositioned for proper placement.

### **Initial VV ECMO Settings**

Adjustments will be made according to patient needs by our perfusionists

These are ideal settings but many patients with high BMIs may require higher flows

Initial Pump Speed:	3000 – 4000 RPM
Flows (determined by pump speed):	4 – 6 LPM
Blender oxygen (FdO <sub>2</sub> ):	100% O <sub>2</sub>
Sweep Gas (controls CO <sub>2</sub> elimination):	5 – 10 LPM (Max 20)
Temperature:	37 degrees Celsius
Initial PaO <sub>2</sub> goals:	60 – 90 mm Hg
pH goals:	7.30 – 7.40
No specific PaCO <sub>2</sub> goals	

## ECMO MANAGEMENT BY SYSTEMS

### NEURO:

For VV ECMO, we will keep the patients deeply sedated for the first 24 to 48 hours with a RASS goal of negative 4. If the patient is on neuromuscular blockade, this can be continued in the same time frame.

Pre-cannulation, patients will usually be on a combination of the sedatives: fentanyl, midazolam (Versed), and/or propofol. Due to sequestration of these medications in the ECMO circuit, we will immediately transition off these medications and start our ECMO sedation protocol.

### FIRST LINE:

- Hydromorphone infusion: Start at 1 mg/hr dose, prescriber managed
- Ketamine infusion: Start at 0.5 mg/kg/hr dose, prescriber managed
- Clonazepam: Start at 3mg per tube BID
- Vecuronium (if needed): 0.1 mg/kg bolus followed by 1 mcg/kg/min dose  
Titrate dose to 1 out of 4 twitches on train-of-four
- PRN doses: Hydromorphone, lorazepam (Ativan) doses

### SECOND LINE:

- Propofol: Start at 10 mcg/kg/min, prescriber managed
- Dexmedetomidine Start at 0.2 mcg/kg/hr, prescriber managed
- Oxycodone: If there is IV shortage, start at 40mg per tube Q4H

Once the patient is stabilized and well supported on ECMO, can wean off NMB and wean sedation with a goal of daily waking trials. We have encountered agitation frequently and weaning sedation has often caused interruptions in ECMO flows. We will add quetiapine (Seroquel) as needed for agitation. In select patients, the second line agents, low dose infusions of propofol or dexmedetomidine (Precedex) have been helpful. If there is delirium detected, can attempt to transition off the oral benzodiazepine and add quetiapine (Seroquel) with dose escalation as needed.

**Physical Therapy:** Early mobilization is very important to improve the chances of patient recovery but in the early stages of ECMO support, passive range of motion is all that we can accomplish. The ultimate goal will be to have patients awake and calm, on very light sedation, and able to participate in physical therapy. Achievement of this goal will require active titration of meds on a daily basis.

**Neurocritical Care Consult:** All ECMO patients will receive a neurocritical care evaluation. Please notify our ECMO neuro-intensivist, Dr. Sung-Min Cho, for any new cannulations. Ongoing neurologic monitoring will include routine NIRS, Transcranial Dopplers (TCDs) emboli monitoring, as well as CT scans, Somatosensory Evoked Potentials (SSEP), and continuous EEGs for patients with disorders of consciousness.

## RESPIRATORY:

Once cannulated, all patients will be placed on lung rest settings on the mechanical ventilator. There is no evidence of one vent mode being superior to another so there are three options:

PC: Rate 10, pressure difference 10, PEEP 10-14, FiO<sub>2</sub> 40%

VC: Rate 10, tidal volume 3-4cc/kg of PBW, PEEP 10-14, FiO<sub>2</sub> 40%  
Goal plateau pressure of  $\leq 24$  and driving pressure  $\leq 14$

APRV: P high 20-24, P low 10, T high 4-6 s, T low 0.5-0.8s, FiO<sub>2</sub> 40%

Recruitment maneuvers are not recommended. Inhaled nitric oxide or inhaled epoprostenol (Veletri) will be turned off. Rest settings will continue until patient's lungs show signs of recovery. If sedation can be weaned and patient is spontaneously breathing, can use PS, VS, or wall CPAP.

Oxygenation is dependent on ECMO flows matching patient's cardiac output. Flows that are 2/3 or greater of CO will maintain adequate PaO<sub>2</sub>. PaO<sub>2</sub> goals will be 60 – 90 mmHg but if unattainable and the patient does not show signs of hypoxemia, can change PaO<sub>2</sub> goals to > 50 and saturation > 85%. If oxygenation goals are lowered, can consider having higher hgb goals to improve oxygen carrying capacity of blood. Continue monitoring for signs of tissue ischemia including NIRS and lactate levels.

Hypercapnia is allowed with a specific pH goal of 7.30 – 7.40, mild acidosis preferred to facilitate oxygen offloading at the tissue level. If tachypnea persists with sedation wean, can trial a higher pH at 7.40 – 7.45. Persistent hypercapnia for prolonged duration can also promote bicarbonate retention by the kidneys. This compensatory metabolic alkalosis could impact weaning patient off ECMO when lungs start to recover. It may be necessary to add acetazolamide (Diamox) to the regimen to prevent high bicarb retention. At the time of cannulation, overly rapid correction of PCO<sub>2</sub> will be avoided with slow sweep gas titration.

**Tracheostomy:** This procedure should be considered at time of ECMO cannulation and family should be consented concurrently. If not performed at time of cannulation, can be coordinated with thoracic surgery team. The ideal timing of tracheostomy is unknown but we have favored earlier trachs given the anticipated lengthy need for ECMO and mechanical ventilatory support.

**Bronchoscopy:** Should perform this procedure as clinically indicated, for airway clearance and BAL cultures. Daily bronchoscopies are not necessary. Can reuse the disposable scopes that will be in each ECMO room but please clean with saline through the channel and alcohol swabs before and after each use to limit infections.

**Prone positioning:** We have not routinely prone positioned patients while on ECMO but this intervention can be considered when the patient is hemodynamically stable with single organ failure and we anticipate benefit from this maneuver.

**Chronic cough:** Frequent symptom that is difficult to manage in our patient population. Guaifenesin thins secretions but this agent is not an anti-tussive. Can add inhaled lidocaine three times daily, alert respiratory therapy. Can try dextromethorphan but only if patient is COVID negative or resolved. On rare occasions, changing tracheostomy to the longer XLT model is helpful.

## **CARDIOVASCULAR:**

Hemodynamic goals with MAPs > 60-65. SBP 90-150. Pressors as needed, norepinephrine gtt first line. Can use vasopressin gtt as second line.

If hypertensive, can use hydralazine PRN but if persistent, can add labetalol. Nicardipine can also be used as needed.

Echocardiogram (POCUS) indicated with any hemodynamic instability. RV dysfunction has been relatively common, can add inotropic agent to improve pump function. Dobutamine gtt if normotensive, epinephrine gtt if hypotensive for RV support. Sildenafil can be tried to decrease RV afterload but there is no evidence for use of this drug in this setting. Unclear benefit. The placement of a PA catheter would be helpful but very challenging to float in a VV ECMO patient.

No routine afib prophylaxis but treatment with amiodarone as needed.

To improve oxygenation, heartrate control is often necessary, especially when HR > 100. **Metoprolol** 12.5mg Q6H first line with the addition of **Ivabradine** 5mg BID (max 10mg BID) as needed. Esmolol can also be tried in select patients.

## **GASTROINTESTINAL:**

Enteral access with NDT preferred. Tube feeds can be started by Day 2 of ECMO cannulation. All patients will have PESS consultation (Tricia Brown).

We will collect pre- and post-oxygenator blood gases to calculate Resting Energy Expenditure (REE) for all of our patients to determine caloric needs. This will be coordinated by our perfusionists and Tricia and are checked Monday, Wednesday, and Friday of each week.

PEG placement can be considered at time of tracheostomy.

Bowel regimen is standard with FMS as needed to prevent harm from frequent turning and instability during turns. Would recommend minimizing FMS as much as possible. If persistent loose stools remain an infection and wound care risk, FMS breaks can be instituted once weekly.

## **RENAL:**

The intravascular volume of each patient is unclear at the time of cannulation. Fluid boluses are often necessary in the first 24 to 48 hours to maintain adequate ECMO flows.

AKI is common and if CVVHD is needed, can be run off the ECMO circuit. Consult nephrology.

There is evidence having a restrictive fluid goal in patients with ARDS shortens their time on the ventilator and in the ICU but no survival benefit (FACTT Trial). This is relevant at the time of lung recovery but not beneficial during full ECMO support and lung rest. During the earlier phase, optimizing ECMO flows will outweigh the need for diuresis. However, we will prevent gross volume overload as much as possible by keeping fluid goals even on most days of stability and maintenance. Can use Lasix infusions to prevent large fluid shifts and ECMO flow limitations. Metolazone can be used every 48 hours if additional diuretic is necessary.

We are aiming for permissive hypercapnia during our ECMO support but over time, the kidneys may retain serum bicarbonate to buffer the respiratory acidosis. This may impact the patient's respiratory drive and hinder their weaning off ECMO. To alleviate the bicarb retention, we can place patients on acetazolamide (Diamox), especially when there are signs of lung recovery.

## **HEMATOLOGY:**

All patients will be anticoagulated with heparin infusion at the start of their ECMO support. Dose will be titrated by PTT goals of 50-65. This can be correlated with an Anti-Xa level of 0.3 to 0.5.

We have seen frequent bleeding complications on our ECMO patients, especially from naso and oropharynx, tracheostomy site, and GI sources. Oropharynx can be packed with TXA soaked gauze and nasopharynx with Afrin soaked gauze. For surgical site bleeds (trach, PEG, other), can start with topical hemostatic agents such as Surgicel for the first 72 to 96 hours. For any persistent bleeds, we can administer DDAVP (0.3 mcg/kg IV) and hold heparin. If reintroduction of anticoagulation causes recurrence of bleeding episodes, heparin infusion can be held indefinitely. Coagulation labs should be checked and TEG ordered.

Transfusion threshold for majority of our ECMO patients will be Hgb < 8.0 and platelets < 30. If there is a > 50% decrease in platelet count, order a HIT panel (PF4 and SRA).

Check daily LDH levels. If continues to trend up, could be sign of worsening hemolysis that can be secondary to microthrombi formation, DIC, or sepsis.

If the patient is a bridge to transplant, will use pediatric tubes for all blood draws and hold anticoagulation indefinitely if possible.

## **INFECTIOUS DISEASE:**

Fluconazole is recommended for fungal prophylaxis in patients with groin cannulation.

Secondary infections are common, especially klebsiella pneumonia. Patients on ECMO do not typically generate a fever so need to have a low threshold for antibiotic course when there is elevations in WBC with bacteremia or worsening pressor requirement. First line empiric antibiotics are zosyn/vanco or cefepime/vanco.

COVID treatment with remdesivir and dexamethasone will be completed after cannulation.

## **SKIN:**

All ECMO cannulas will be sutured into place and the skin will be marked to monitor for cannula migration. Please do not secure ECMO cannulas onto the bed or anywhere else. Will need to ask perfusionists to help secure cannulas.

Patient turning will be scheduled once daily during daytime hours.

Eye Care: Rewetting eye drops and lacrilube application bid, eye cover at night for patients with improper eye closure.

## **TROUBLESHOOTING**

### **ECMO Flow Limitation (Chatter or Chugging)**

The term chatter is often used when ECMO flows are transiently but frequently decreased. This occurs because the ECMO cannula is a cylindrical tube and follows 'Tube Law.' As stated, when the pressure difference between the external pressure (atmospheric) and intraluminal pressure of a tube starts to increase, the intraluminal diameter does not decrease until a threshold is reached, at which time the intraluminal diameter collapses to zero. This collapse will cause intraluminal pressure to rise allowing the tube to open and flow to resume, but as flow resumes, the pressure may drop again causing the intraluminal diameter to collapse again. This process is repeated and actually moves the venous drainage line, thus creating a limit to ECMO flows.

The Differential:

- Decreased intravascular volume (over-diuresis, bleeding, insensible losses, etc)
- Vascular wall or cannula malposition/patient repositioning
- Low MAPs causing decreased venous return
- Agitation with increased intra-thoracic/abdominal pressures (coughing, tachypnea, etc.)
- Thrombus formation limiting cannula flow
- Cannula compression or kinking
- Abdominal compartment syndrome
- Pneumothorax
- Cardiac tamponade

MANAGEMENT:

- Examine the venous drainage cannula to eliminate any kinks or external compression
- Check hemodynamics, maintain adequate MAPs to optimize venous return
- If patient is agitated, can administer bolus dose of sedative; if persistent can use NMB
- Call perfusion to turn down flows momentarily, then increase slowly
- Find lower pump speed that continues to maintain good oxygenation
- Administer IV fluid boluses to expand intravascular volume
- Can check bladder pressure, CXR, or echo if indicated

### **Suckdown Event with flows dropping < 1.0 LPM (Extreme form of chatter)**

The Differential (similar to chatter):

- Cannula malposition with vessel wall causing obstruction
- Drop in intravascular volume: bleeding or dehydration
- Shock – any cause with very low venous return
- Rapid change in intrathoracic pressures – agitation, cough, vent dyssynchrony

MANAGEMENT:

- Can pinch the outflow cannula to alleviate pressure (cannula out of ECMO to patient)
- Call perfusion immediately, will turn down pump speed then rev back up slowly
- Consider fluid bolus to expand intravascular space

- Pressors to keep MAPs > 65
- For agitation, add more sedation or start NMB

### **Persistent Hypoxemia (paO<sub>2</sub> <55, SaO<sub>2</sub> <85%)**

The Differential:

- Cannula malposition – especially dual stage cannula in RIJ (Avalon or Crescent)
- ECMO flows are too low for patient's cardiac output
- Agitation increasing heart rate, CO, and oxygen demand
- Oxygenator failure
- Chatter limiting ECMO flows as above

MANAGEMENT:

- If there is persistent chatter, troubleshoot as above
- For ECMO flow and CO mismatch, increase ECMO flows if not flow limited
- Add HR controlling agents if unable to raise ECMO flows (Ivabradine or beta blocker)
- For agitation, add more sedation or start NMB
- Check pump gas, if PaO<sub>2</sub> < 200, call surgery and perfusion about oxygenator change
- For dual stage cannulas in RIJ, can check position with CXR and echo, apply traction to cannula and assess improvement in oxygenation. If needed, can contact thoracic surgery and anesthesia for repositioning of RIJ cannula.

**Recirculation** - When blood flow coming out of the ECMO cannula gets sucked back into the circuit via the venous drainage cannula and ECMO venous saturation is > 75% or > ScVO<sub>2</sub> by 5-10% or greater without alternative explanation (severe sepsis with tissue dysoxia or hypothermia)

The Differential:

- ECMO flows are too high and there is mismatch with cardiac output
- If dual stage cannula, then there may be malposition of the cannula in RIJ
- If fem/IJ or fem/fem configuration, the outflow and inflow may be too close in proximity

MANAGEMENT:

Check positioning of cannula with CXR/echo. Turn down the flows if oxygenation is in good range. Some degree of recirculation can be tolerated if flows and saturations are maintained.



## VV ECMO Weaning Strategy

The first signs of lung recovery will be larger tidal volumes on PC or APRV modes of ventilation. If patient is on VC, then daily checks of plateau pressures will reveal improving compliance.

Gas exchange will improve and Sweep Gas flows on ECMO can be weaned down to meet pH goals. Once the sweep is down to 1 LPM, the patient should be able to use their native lungs for gas exchange.  $FiO_2$  on the ventilator can be increased to 60% maximum during the weaning phase. PC or VC can be increased slightly to maintain lung protective settings with tidal volumes  $\leq 6cc/kg$  of predicted body weight (PBW). Pressure support or volume support can be used if the patient tolerates being awake and is breathing spontaneously.

If gas exchange is adequate with the ECMO sweep gas at 1 LPM and blender  $FiO_2$  at  $\leq 40\%$ , the sweep can be turned to zero while maintaining flows  $> 3.0$  LPM. We typically continue the sweep of zero trial for 16 to 24 hours. If the  $PaO_2 > 60$  and pH is  $> 7.30$  with  $PCO_2 < 60$ , we can decannulate.

Coordinate the decannulation procedure with the thoracic surgery team, the perfusionist, and the respiratory therapist. The blood in the circuit can be collected by the perfusionist and delivered to the patient as autologous blood.

## APPENDIX A

### VV ECMO Cannulation:

Cannulation configurations:

Cannulation configuration is dependent on indication for VV ECMO and patient's anatomy/body habitus.

- 1) Right internal jugular with dual lumen cannula (Crescent or Avalon)
- 2) Right internal jugular and femoral vein cannulation
- 3) Bilateral femoral vein cannulation

Personnel needed: ICU intensivist, surgeon, perfusion, cardiac anesthesia (if TEE guidance is needed)

Equipment needed:

- Cannulas
- Connectors
- Primed circuit
- Percutaneous insertion kits with dilators
- Heparin bolus 5000 units
- Saline
- Bulb syringe with basin for wet to wet connection
- 0 silk sutures to secure the cannula
- Ultrasound for venous access
- Chloraprep
- Sterile drape, mask, gloves, gown

Dual lumen cannulation

- Avalon cannula (range of 16-31 Fr) or Crescent cannula (range of 24-32 Fr)
- Location: Percutaneously placed into right internal jugular vein. The distal portion of the cannula should be in the IVC with the return lumen directed towards the tricuspid valve
- Need TEE guidance +/- fluoroscopy

Right internal jugular and femoral vein cannulation

- Location:
  - Return flow into through the right internal jugular cannula. Distal tip of the cannula in the right atrium or SVC/right atrium junction
  - Venous drainage via the femoral vein. The distal tip of the cannula should be just distal to the right atrium/IVC junction
- Types of cannulas needed:
  - Return cannula in the right internal jugular: 16 to 21 Fr
  - Venous drainage cannula: typically 23 or 25 Fr
- Cannulas should be 8 cm apart to minimize recirculation

- CXR/AXR needed to confirm placement

#### Bilateral femoral vein cannulation

- Location:
  - Return flow into the right atrium. Distal tip of the cannula in the right atrium
  - Venous drainage cannula with tip within the infrahepatic IVC
- Types of cannulas needed:
  - Return cannula: 16 to 21 Fr
  - Venous drainage cannula: typically 23 or 25 Fr
- Cannulas should be 8 cm apart to minimize recirculation
- CXR/AXR needed to confirm placement