Extracorporeal Life Support Organization
ECLS Guidelines

2018

Guidelines for Pediatric Cardiac Failure

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Applies To

This guideline is a supplement to "General Guidelines for Extracorporeal Life Support", and applies to the use of ECLS to neonates, infants and children with cardiac failure.

Disclaimer

This guideline describes useful and safe practice but these are not necessarily consensus recommendations for extracorporeal life support (ECLS). These guidelines are not intended as a standard of care, and are revised at regular intervals as new information, devices, medications, and techniques become available. These guidelines are intended for educational use to build the knowledge of physicians and other health professionals in assessing the conditions and managing the treatment of patients undergoing ECLS. These guidelines are not a substitute for a health care provider's professional judgment and must be interpreted with regard to specific information about the patient and in consultation with other medical authorities as appropriate. In no event will ELSO be liable for any decision made or action taken in reliance upon the information provided through these guidelines.

Reference as

Pediatric Cardiac Failure, Extracorporeal Life Support Organization, Ann Arbor, MI. [cited 2017 Feb 15]. Available from http://www.elso.org/resources/guidelines.aspx,

Further Reading

Brogan TV, Lequier, L, Lorusso R, MacLaren G, Peek G: Extracorporeal Life Support (Eds): The ELSO Red Book, Ed. 5, University of Michigan Press, Ann Arbor, MI, 2017

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I. Indications and Contraindications in Children with Cardiovascular Disease (Chapter 26, 29)

A. Use and Strategy

Cardiopulmonary Extracorporeal Life Support (ECLS) is indicated in severe, refractory circulatory failure with reversibility and/or timely, reasonable therapeutic options.

1. There are four primary strategies for ECLS use, depending on the therapeutic objective for the patient.

a) Bridge to recovery (reversible disease),

b) Bridge to bridge (goal to transition to VAD or oxygenator),

c) Bridge to organ transplantation

d) Bridge to decision (providing time for recovery, diagnosis, or determination of candidacy for alternative support /transplantation).

2. Use of extracorporeal life support for cardiac failure should be considered for patients with evidence of inadequate end organ perfusion and oxygen delivery resulting from inadequate systemic cardiac output.

a) Hypotension despite maximum doses of two inotropic or vasopressor medications.

b) Low cardiac output with evidence of end organ malperfusion despite medical support as described above: persistent oliguria, diminished peripheral pulses.

c) Low cardiac output with mixed venous, or superior caval central venous (for single ventricle patients) oxygen saturation <50% despite maximal medical support.

d) Low cardiac output with persistent lactate >4.0 and persistent upward trend despite optimization of volume status and maximal medical management.

B. Indications

Indications for pediatric cardiac ECLS generally fall into two broad categories, those related and those unrelated to cardiac surgery and catheterisation.

1. Cardiac Surgery and Catheterization

a) Pre-operative stabilization – in cases where physiological stability is likely to be achieved over time or early operative repair is likely to have a successful outcome.

b) Failure to wean from cardiopulmonary bypass.

c) Elective support during high-risk catheter procedures.

d) Low cardiac output in the post-operative period.

2. Cardio-circulatory failure due to various etiologies

a) Cardiogenic: Myocardial failure due to myocarditis and cardiomyopathy, intractable arrhythmia.

b) Distributive: Sepsis, Anaphylaxis.

c) Obstructive: Pulmonary hypertension, pulmonary embolus.

3. In-hospital cardiac arrest not responsive to conventional CPR, with rapid availability of specialist ECMO team (1).

C. Contraindications

The list of contraindications to ECLS has shrunk over the last two decades, as a number of conditions previously regarded as unsuitable for ECLS support have been shown to be compatible with satisfactory long-term survival. Use of ECLS is not recommended under certain circumstances, particularly if there is strong evidence for lack of capacity to recover or be treated.

1. Cardiopulmonary Extracorporeal Life Support is inappropriate if;

a) The condition is irreversible and/or,

b) There is no timely, reasonable therapeutic option and/or,

c) High likelihood of poor neurological outcome.

2. **Absolute** contraindications: Extracorporeal life support is not recommended in the following circumstances;

a) Extremes of prematurity or low birth weight (<30 week gestational age or <1 kg)

b) Lethal chromosomal abnormalities (e.g., Trisomy 13 or 18)

c) Uncontrollable hemorrhage

d) Irreversible brain damage

3. **Relative** contraindications:

a) Intracranial hemorrhage

b) Less extreme prematurity or low birth weight in neonates (<34wk. gestational age or <2.0 kg)

c) Irreversible organ failure in a patient ineligible for transplantation

d) Prolonged intubation and mechanical ventilation (>2 wk.) prior to ECLS

D. Special patient populations

Special consideration must be given to patients with the lowest rates of survival, highest rates of long-term morbidity, and greater degree of physiological complexity on ECLS support.

1. Unrepaired Congenital Diaphragmatic Hernia

2. Allogenic bone marrow transplant

3. Bordetella Pertussis infection

4. Single ventricle physiology

a) Stage 1 palliative surgery (S1P): ECMO support after neonatal S1P for hypoplastic left heart syndrome is now the most frequent post-operative indication for ECLS (2). In S1P patients with an arterial shunt, effective use of ECMO necessitates management of the shunt to restrict pulmonary blood flow during ECMO(3). Higher ECMO flows in the range of 150-200ml/kg/min may improve outcomes, however, if cardiac output remains insufficient on higher ECMO flows, then constriction of the shunt to limit pulmonary blood flow and promote systemic blood flow and tissue oxygen delivery may be necessary.

b) Stage 2 and 3 palliative surgery: Infants and children after surgical palliation with cavopulmonary anastomoses (Glenn or Hemi-Fontan and Fontan circulations) represent a complex physiological group, in whom stable support with ECMO can be difficult to establish. Establishing adequate flow in a patient with a Bidirectional Glenn or HemiFontan may be challenging given the separation of systemic venous return. Nevertheless, ECMO can provide stable support if a reversible process is present.

II. Extracorporeal Circuit Characteristics (Chapter 4, 5)

A. Vascular access and blood flow for cardiac support.

1. The circuit is planned to be capable of total support for the patient involved. Access is always venoarterial. The circuit components are selected to support blood flow 3 L/m2/min.

a) Neonates 100 cc/kg/min

b) Infants and children 80 cc/kg/min

c) Adults 60 cc/kg/min

2. The best measure of adequate systemic perfusion is a circuit mixed venous saturation greater than 70%. In patients without a single mixed venous oxygen saturation, such as single ventricle and shunt-dependent patients, a superior caval central venous oxygen saturation may be substituted. Achieving a desired flow is determined by vascular access, drainage tubing resistance, and pump properties.

B. Circuit components

The basic circuit includes a blood pump, a membrane lung, and conduit tubing. Depending on the application, additional components may include a heat exchanger, monitors, and alarms.

1. Pump

The pump should be able to provide full blood flow for the patient, as defined above. Any pump which meets the specifications can be used (modified roller with inlet pressure control; centrifugal or axial rotary pump with inlet pressure control; peristaltic pump).

a) **Inlet (suction) pressure.** With the inlet line occluded, the suction pressure should not exceed -300 mmHg. The inlet pressure can be very low (-300 mmHg) when the venous drainage is occluded (chattering) which causes hemolysis. Inlet pressure in excess of -300 mmHg can be avoided by inherent pump design or through a servocontrolled pressure sensor on the pump inlet side.

b) **Outlet pressure.** With the outlet line occluded, the outlet pressure should not exceed 400 mm/Hg (inherent in the pump design or by a servocontrolled system).

c) **Power failure.** The pump should have a battery capable of at least one-hour operation, and a system to hand crank the pump in the event of power failure. The pump and circuit should have a mechanism to alarm for or prevent reverse flow (arterial to venous in the VA mode) if the power fails.

d) **Hemolysis.** The plasma hemoglobin should be less than 10 mg/dl under most conditions. If the plasma hemoglobin exceeds 50 mg /dl, the cause should be investigated.

2. Membrane lung (Oxygenator)

a) The gas exchange material in membrane lungs may be solid silicone rubber, a microporous hollow-fibre (e.g. polypropylene), or a solid hollow-fibre membrane (e.g. polymethylpentene). When used for total support, the membrane lung should provide full O2 and CO2 exchange for the patient as defined in II.A.

b) Membrane surface area and mixing in the blood path determine the maximum oxygenation, described as “rated flow” or “maximal oxygen delivery”.

c) Rated flow is the blood flow rate at which venous blood (saturation 75%, Hb 12 g/dl) will be fully saturated (95%) at the outlet of the membrane lung. Maximal O2 delivery is the amount of oxygen delivered per minute when running at rated flow.

d) This is calculated as outlet minus inlet O2 content (typically 4-5 cc/dL, same as the normal lung) times blood flow. For example, a specific device has a rated flow of 2 L/min, (max O2 100 ccO2/min). If the blood flow required for total support of a patient is 1 L/min (O2 about 50 cc/min) this membrane lung will be adequate. If the blood flow required for total support is 4 L/min, this membrane lung is not adequate and the circuit will need two of these membrane lungs in parallel, or a larger membrane lung rated at 4 L/min.

3. Sweep gas

a) The sweep gas can be 100% oxygen, carbogen (5% CO2, 95% O2) or a mixture of oxygen and compressed room delivered via an oxygen-air blender.

b) The initial sweep gas flow rate is usually equal to the blood flow rate (1:1).

c) Increasing the sweep flow will increase CO2 clearance but will not affect oxygenation.

d) Water vapor can condense in the membrane lung resulting in poor CO2 clearance, and may be cleared by intermittently increasing sweep gas flow to a higher flow.

4. Avoiding air embolism via the membrane lung

a) Air or oxygen bubbles can pass through the membrane into the blood if the sweep gas pressure exceeds the blood pressure, or if the blood pressure is sub-atmospheric (this occurs when there is no blood flow or blood pressure, and blood drains from the membrane lung into the tubing by gravity, entraining air through the membrane lung). This is a specific problem with microporous hollow fiber devices but can also occur with silicone or polymethylpentene lungs due to very small holes in the membrane which can allow air entrainment.

b) Air embolism can be prevented by maintaining the blood side pressure higher than the sweep gas pressure. This is accomplished by including a pressure pop-off valve or pressure servo regulation control in the sweep gas supply, and by keeping the membrane lung below the level of the patient, so that if the pump stops the risk of entraining air from the room will be minimized. Even with silicone and PMP lungs, it is safest to maintain the membrane lung below the level of the patient.

5. Priming the circuit

a) The assembled circuit is primed under sterile conditions with an isotonic electrolyte solution resembling normal extracellular fluid including 4-5 mEq/L potassium. The prime is circulated through a reservoir bag until all bubbles are removed. This can be expedited by filling the circuit with 100% CO2 before adding the prime. Microporous membrane lungs are quick to prime because gas in the circuit can be purged through the micropores. The circuit can be primed at the time of use, or days before. It is not recommended to use a primed circuit after 30 days.

b) Before attaching the circuit to the patient, the water bath is turned on to warm the fluid. For patients of adequate size and

hematocrit to avoid profound anemia, ECLS is usually instituted with crystalloid prime. Many centers add human albumin (12.5 gm) to "coat" the surfaces before blood exposure.

c) For smaller children, infants and patients who are anemic prior to initiating ECLS, or for whom the volume of a crystalloid prime will precipitate anemia, packed RBCs are added to bring the hematocrit to 30-40.

(1) When blood is added to the prime, heparin is added to maintain anticoagulation (1 unit per cc prime) then calcium is added to replace the calcium bound by the citrate in the bank blood. If time allows, it is helpful to verify the electrolyte composition and ionized calcium before starting flow.

(2) For emergency cannulation, the prime can be crystalloid with hemodilution treated after initiating flow.

6. Heat exchanger

A heat exchanger is necessary to control the blood and the patient temperature at a specific level. Heat exchangers require an external water bath, which circulates heated (or cooled) water through the heat exchange device.

a) In general, the temperature of the water bath is maintained <40º Celsius, and usually at 37º.

b) Contact between the circulating water and the circulating blood is very rare, but should be considered if small amounts of blood or protein are present in the circulating water, or if unexplained hemolysis occurs.

c) The water in the water bath is not sterile and may become contaminated. The water bath should be cleaned and treated with a liquid antiseptic from time to time.

7. Monitors

Monitors are designed to measure circuit function and to alarm the operator of abnormal conditions. Most circuits will include:

a) Monitoring of blood flow is by direct measurement using an ultrasonic detector, or calculated based on pump capacity and revolutions per minute for a roller pump using standardized tubing.

b) Pre- and post- membrane lung blood pressure measurements can include maximum pressure servo regulation control to avoid over pressuring.

c) Pre- pump venous drainage line pressure (to avoid excessive negative suction pressure by the pump) can be used as a servo regulation system to prevent excessive suction.

d) Pre- and post- membrane lung oxyhemoglobin saturation measurements: The venous oxyhemoglobin saturation is a valuable

parameter for managing and monitoring both circuit and patient factors related to oxygen delivery and consumption. The post membrane lung saturation monitor will determine if the membrane lung is working at rated flow, and if function is deteriorating. Blood gases are measured from pre-oxygenator and post-oxygenator sites either by continuous on line monitoring or batch sampling. The primary purpose of measuring blood gases (as opposed to online saturation) is to determine the inlet and outlet PCO2 to evaluate membrane lung function, and blood pH to determine metabolic status.

e) Circuit access for monitors, blood sampling, and infusions. Luer connectors and stopcocks provide access to the blood in the circuit. The number of access sites should be minimized, but at least two are necessary (pre and post membrane lung). Blood access sites should be avoided between the patient and the inlet of the pump because of the risk of entraining air. It is acceptable to use the circuit for all blood sampling and infusions, although some centers prefer to give infusions directly to IV lines in the patient.

8. Alarms

a) Pre- and post- membrane lung pressure alarms. These measurements will determine the transmembrane lung pressure gradient. Clotting in the oxygenator is represented by increasing membrane lung pressure gradient.

b) Many centers use a bubble detector on the blood return line. Pressure and bubble detector alarms can be used to clamp lines and turn the pump on or off to automate these safety factors.

9. Blood tubing

a) Tubing length and diameter will determine the resistance to blood flow. Tubing is chosen to allow free venous drainage, and avoid high resistance pressure drop on the blood return side.

b) The blood flow through 1 meter of tubing at 100 mmHg pressure gradient for common internal diameter in inches is:

(1) 3/16: 1.2 L/min;

(2) ¼: 2.5 L/min;

(3) 3/8: 5 L/min;

(4) ½: 10 L/min

c) A “bridge” between the arterial and venous lines close to the patient is a useful circuit component, particularly for periods off bypass during VA access, during weaning, or during an emergency. However, when clamped the bridge is a stagnant area that can contribute to thrombosis and possibly infection. In general, if a bridge is used, it should

be maintained closed during most of the ECLS run, with a system for purging the bridge of stagnant blood when it is not in use.

10. Elective vs. emergency circuits

The characteristics of individual components are listed above.

a) Emergency circuits should be available within minutes of the call to a patient, and should be fully primed with crystalloid and ready to attach as soon as the patient is cannulated.

b) They should also include safety factors to prevent high negative pressure on the inlet side and high positive pressure on the outlet side to avoid errors during emergent cannulation and attachment.

c) The emergency circuit may include a microporous membrane lung (easy to prime), and a centrifugal pump (high-pressure limited, does not require monitors or alarms during initial set up).

d) A heat exchanger will be required for management of these patients.

III. Vascular Access (Chapter 30)

A. Modes of access.

Cardiac support requires venoarterial access. The modes of access for pediatric cardiac ECLS are:

1. Central cannulation (transthoracic via median sternotomy)

a) Can be utilized in the following scenarios;

(1) Unable to wean a patient from cardiopulmonary bypass in the operating room,

(2) Rapid initiation of ECMO

(3) To insert larger cannula to facilitate higher blood flow rates (e.g. sepsis)

b) Cannulation is via the right atrium and aorta.

c) The aortic cannula used during CPB may be too small for ECMO arterial access under prolonged conditions of normothermia, higher flows and hematocrit. This may result in high pressures in the blood return line and hemolysis. However, patients requiring post-cardiotomy ECLS may not require full flow support as during the operation, for the heart and lungs should be contributing some cardiac output and gas exchange, depending on the level of impairment.

2. Cervical (neck) cannulation

a) VA access through the jugular and carotid is used for children < 15 kg because of the small size of the femoral vessels.

3. Femoral cannulation

a) The femoral or iliac vessels may be large enough to permit appropriate vascular access in children over 15 kg of weight. Both the artery and vein will be occluded by the catheter so provision must be made for perfusion of the distal leg. Because of the small size of the distal vessels in these patients, however, providing adequate distal perfusion is difficult and not generally recommended for patients under 30 kg. Venous collateral circulation is usually adequate to avoid excessive edema and venous congestion.

B. Cannula selection

a) The term "cannula" refers to the catheter that goes directly into the vessel for ECLS, to differentiate that device from all other catheters.

b) The resistance of vascular access cannulas is directly proportional to the length and inversely proportional to the radius to the fourth power. Therefore, the internal diameter of the catheter is the most important factor controlling blood flow resistance.

c) Other factors such as side holes and tapering sections also affect resistance, and the resistance increases at higher flows, so the characteristics of each cannula must be known before cannulation.

d) Blood flow at 100 mmHg gradient for commonly used cannulas is described in the patient -specific protocols. Cannulas are chosen to provide the desired blood flow (section II A) above.

C. Cannulation

1. Methods:

Cannulas can be placed via direct surgical exposure, such as by cannulation of the right atrium and aorta via sternotomy. Direct cardiac cannulation is usually used for patients who cannot come off CPB in the OR, using the CPB cannulas. For cervical cannulation of in neonates and small children, "cut-down" exposure of the neck vessels is usually necessary. For older children, and adults, cannulation can be accomplished via percutaneous vascular access, using the Seldinger method.

2. Cannulation technique:

A bolus of heparin (typically 50-100 units per kilogram) is given just before cannula placement. In the setting of severe coagulopathy, bolus dosing of heparin is up to the attending surgeon.

a) <u>Direct "cut-down" cannulation.</u>

Cannulation is usually done in the ICU with full sterile preparation. Deep sedation/anesthesia with muscle relaxation may be useful, but is not universally necessary, depending on the ability to achieve adequate local anesthesia, and the status of the patient. Local anesthesia is used for the

skin. Dissection exposes the vessels. Direct handling of the vessels is minimized as much as possible to avoid spasm. Topical lidocaine or papaverine is helpful to mitigate spasm. Ligatures are passed around the vessels above and below the cannulation site. Heparin is given IV (50-100 units per kilogram) and the distal vessels are ligated. The proximal vessel is occluded with a vascular clamp, the vessel opened, and the cannula placed. If the vessels are very small, if there is difficulty with cannulation, or if spasm occurs, fine stay sutures in the proximal edge of the vessel are very helpful. The vessel is ligated around the cannula, often over a plastic "boot" to facilitate later cannula removal. In the femoral artery a non-ligation technique can be used (see semi-Seldinger technique).

b) Percutaneous cannulation

The Seldinger technique is used. This is particularly suited for femoral cannulation. The bilateral groins are prepped and draped in the standard sterile fashion. The femoral artery and vein are visualized using ultrasound. If the patient is hemodynamically stable (not rapidly decompensating), it is easiest to first access the distal superficial femoral artery and place the distal perfusion catheter. The common femoral artery is then accessed, and dilated to allow passage of the appropriately selected arterial cannula. Once the arterial cannula are placed, the contralateral femoral vein is accessed under ultrasound guidance, and the venous (drainage) cannula is placed and advanced to the appropriate level (so that the tip of the cannula is approximately at the IVC / RA junction). The sterile end of the lines are connected on the field, taking care to eliminate air bubbles. In the event of the acutely decompensating patient, such as in eCPR, the arterial cannula is placed first, to stabilize the patient, and the distal perfusion catheter is placed later.

3. Management of the distal vessels:

a) If cervical cutdown access is used, the vein and artery are ligated distally, relying on collateral circulation to and from the head. Some centers routinely place cephalad venous cannula but this is an institutional preference and is not mandatory.

b) If the access is via the femoral vessels, the venous collateral drainage is adequate but the femoral artery is significantly occluded. Distal pulses must be ascertained and documented prior to and after cannulation. A distal reinfusion catheter is strongly recommended to avoid limb ischemia. Using the Seldinger technique, a reinforced 6F cannula may be placed in the superficial femoral artery using ultrasonography guidance. If the cannula is placed by cut down, a distal perfusion catheter may be placed at the same time. In the stable patient, this may be more easily placed prior to placement of the arterial cannula. In the setting of the extremely unstable patient, such as during ECPR, the

cannula should always be placed first. An alternative to this is the use of the posterior tibial artery for retrograde perfusion. In any circumstance, the cannulating surgeon MUST determine and document adequate distal perfusion prior to the completion of the cannulation procedure.

4. Adding or changing cannulas:

a) If venous drainage is inadequate the first step is to assess intravascular volume status (consider bleeding, or other sources of blood loss) and venous cannula position.

b) If volume is adequate and the cannula is properly positioned, drainage may be limited by the resistance of the drainage cannula. In this scenario, it is best to first add another venous drainage cannula through a different vein.

c) It may be possible to change the cannula to a larger size, but removing and replacing cannulas can be difficult, and the patient may not tolerate even the short amount of time off of support. If a vascular access cannula is punctured, kinked, damaged, or clotted, the cannula must be changed.

d) If the cannula was placed by direct cut down, the incision is opened, the vessel exposed, and the cannula replaced, usually with the aid of stay sutures on the vessel. If the cannula was placed by percutaneous access, it may be possible to exchange the catheter over a guidewire in the Seldinger method.

IV. Management during ECLS (Chapter 32, 33)

A. Circuit Related. Circuit components are selected based on patient size, and the amount of flow required for support.

1. Blood flow

After cannulation, blood flow is gradually increased to mix the circulating blood with the prime; then, blood flow is increased until maximum flow is achieved. This is done to determine the maximum flow possible based on the patient and the cannula resistance. After determining maximum possible flow, (the blood flow is decreased to the lowest level that will provide adequate support. Ideally for VA access, the pump flow is decreased until the arterial pulse pressure is at least 10 mmHg (to assure continuous flow through the heart and lungs during ECLS), but this is often not possible when the heart function is very poor. The physiologic goals (mean arterial pressure, arterial and venous saturation) are set and blood flow is regulated to meet the goals.

2. Oxygenation

a) The *rated flow* is the blood flow rate at which venous blood with a

saturation of 75% and hemoglobin of 12g/dl with exit the gas exchange device with a saturation of 95%.

b) The rated flow is a standard to compare the maximum oxygenation capacity of gas exchange devices, and is determined by surface area and blood path mixing.

c) As long as the blood flow is below recommended rated flow for that gas exchange device (and the inlet saturation is 70% or higher) the oxyhemoglobin saturation at the outlet should be greater than 95%. Usually the outlet saturation will be 100% and the PO2 will be over 300mmHg.

d) If the sweep Fi02 is 100%, at or below the device rated flow, and the outlet saturation is less than 95%, the gas exchange device is not working at full efficiency (due to irregular flow, clotting). It may be necessary to replace it.

e) Oxygen delivery from the circuit should be adequate for full support (systemic saturation greater than 95% at low ventilator settings and FiO2).

f) Venous saturation should be 20-30% saturation less than arterial saturation. This indicates that systemic oxygen delivery is 3-5 times oxygen consumption.

g) In states of high oxygen demand or poor oxygen delivery (low cardiac output, impaired lung gas exchange), maintaining the hematocrit over 40% can optimize oxygen delivery.

h) Patients with already impaired oxygen delivery, such as those with palliated single-ventricle physiology, should be maintained with a hematocrit above 40%.

3. CO2 clearance

a) CO2 transfer across the membrane lung is more efficient than that of oxygen, and CO2 removal will exceed oxygen uptake.

b) CO2 clearance is controlled by the sweep gas flow rate. Increasing sweep gas flow rate increases C02 clearance but does not affect oxygenation.

c) Generally, a gas flow rate equal to the blood flow rate (1:1) is used to begin support. The gas to blood flow ratio is then adjusted to maintain the systemic pC02 at the desired range (e.g. 36-44mmHg).

d) An alternative is to use carbogen gas (5% CO2/95% O2) as the sweep gas that will maintain outlet PCO2 around 40 mmHg without titration.

e) If CO2 clearance is decreased but oxygenation is adequate, the cause is usually water accumulation within the gas compartment of the membrane lung. This may be cleared by intermittently increasing sweep

gas flow to a higher rate.

f) If the initial PaCO2 is greater than 70, the PaCO2 should be normalized over several hours rather than immediately in order to avoid swings of cerebral perfusion related to CO2 and pH.

4. Anticoagulation (Chapters 6, 7, 8, ELSO Anticoagulation Guideline)

a) The ECLS circuit is procoagulant, requiring continuous administration of a systemic anticoagulant. Inadequate anticoagulation leads to clot formation in the circuit, which can affect circuit performance, accelerate platelet deposition, and induce systemic fibrinolysis. Currently, there is a number of whole blood and plasma based tests to assess coagulation in vitro; however each have limitations when used to monitor anticoagulation in ECLS applications. A significant limitation of all of the assays discussed below is that they are not well standardized. Thus, an anti-Xa value (or ACT or PTT) performed in one machine or one laboratory, may vary greatly from results obtained from the same sample in another laboratory. Using one method of monitoring UNFH activity only, is likely no longer acceptable ECLS practice. However, using multiple tests of UNFH therapy, multiple times per day, is probably not necessary and will be very confusing for the ECLS team members. Ultimately, every ECLS program will have to come up with an approach to monitoring the anticoagulant effect of UNFH that works best for their patients in their individual center.

b) Unfractionated heparin (UNFH) has been the anticoagulant of choice for the vast majority of ECLS. A bolus dose of UNFH ranging from 50-100units/kg is given after exposure of the vessels prior to insertion of the ECLS cannula. Subsequently, UNFH is administered as a continuous infusion.

c) Measuring heparin effect.

Activated clotting time (ACT): ACT is the time (in seconds) in which whole blood clots in response to a fibrin activating reagent. Each ACT device has a specific upper limit with normal blood (120 to 140 seconds for most systems); most centres target an ACT around 1.5 times normal. ACT is measured hourly and more frequently if the ACT is changing. ACT is measured at the bedside (not sent to the laboratory) because heparin dosing decisions are often required immediately. The ACT is a test that is influenced by factors other than heparin, such as thrombocytopenia, hypofibrinogenemia, and fibrin degradation products, so supplementation of the ACT with other tests is sometimes required.

Activated partial thromboplastin time (aPTT): The aPTT assesses

the intrinsic and final common pathway of coagulation, so it is influenced by coagulation factors, heparin, and antithrombin levels. aPTT is measured in the laboratory, and is the time (in seconds) in which calcium-free plasma clots in response to a fibrin activating reagent combined with calcium. Children have developmental differences in coagulation, and aPTT does not perform as reliably in neonatal and pediatric patients compared to adults (4, 5). For neonatal and pediatric ECLS patients, aPTT values correlate poorly to anti-factor Xa levels and UNFH levels (6-8). aPTT also becomes unreliable in critical illness, because it is affected by acute phase reactants.

Anti-factor Xa assay: The anti-factor Xa assay measures the anticoagulation activity of UNFH, and depends only on heparin and AT levels. Pediatric ECLS patients with higher anti-factor Xa assays had decreased circuit and oxygenator changes, and a laboratory protocol using anti-factor Xa assay led to significantly decreased blood product use, hemorrhagic complications and increased circuit life (9, 10). However, there are other contributors to global hemostasis than fibrin formation, and the measure of anti-Xa may at times be misleading. Despite this concern, anti-Xa assay guided anticoagulation is increasing in frequency and may provide significant advantages over other methods. The majority of ELSO centers that use the anti-Xa assay as part of their anticoagulation protocol target levels of 0.3-0.7 IU/mL. As described above anti-Xa assays also vary in their responsiveness to UNFH and are subject to significant problems regarding assay standardization. Thus, adopting one anti-Xa range for all assays could lead to discrepant management results among centers. Some ECLS centers have recommended daily establishment of ACT therapeutic goal ranges based on the anti-Xa assays and AT activity levels (11-14). Anti-Xa activity can be measured more frequently if there is clinical evidence of bleeding or thrombosis.

Thromboelastography (TEG®) and Thromboelastometry (ROTEM): The thromboelastogram is a whole blood POCT of the viscoelastic properties of clot formation that measures the integrity of the coagulation cascade from the time of fibrin formation to fibrinolysis and importantly includes the contribution of platelets. TEG®/ROTEM provides information relating to multiple phases of coagulation in whole blood, which is extremely relevant to ECLS patients since there may be more than one reason for coagulation abnormalities(15). TEG® can be done with and without an agent

that inactivates heparin, so the anticoagulant effect of heparin can be separated from other factors. TEG can be done at the bedside on fresh blood or in the laboratory in calcium-free blood (adding calcium to the activator)

Antithrombin III assay: Heparin acts by "activating" a plasma molecule called antithrombin III (usually called AT3). Infants have developmentally low AT3 activity and antigen levels as compared to older children and adults. The optimal AT3 activity for any patient receiving UNFH anticoagulation for ECLS is unknown. However, in infants and children with escalating UNFH requirements, UNFH doses >35-40 units/kg/hour, and/or clinically sub therapeutic anticoagulation, acquired AT deficiency may be a contributing factor to the patient's heparin resistance. Low AT3 can be treated by giving fresh frozen plasma, cryoprecipitate, or recombinant AT3. AT3 concentrates (plasma derived or recombinant) are now available and some centers routinely administer AT replacement for AT activities < 30 to 80%, while others will treat low AT activity only if there is evidence of reduced UNFH effect clinically or based on low ACT, low anti-Xa levels or minimal UNFH effect on kaolin and heparinase TEG samples. Of the ECLS programs that routinely replace AT as part of their anticoagulation protocol, without consideration of other tests of UNFH effect, most target levels ranging from >50% to >100%. Some programs recommend >50% for all patients, while others prefer >80% for neonates and >100% for infants and children. The UNFH infusion can be decreased prior to administration of AT concentrates because of the potential for augmentation of UNFH's anticoagulant effect.

d) Heparin induced thrombotic thrombocytopenia (HIT)

Heparin-induced thrombocytopenia (HIT) is a rare condition due to heparin associated antibodies, and is characterized by thrombocytopenia and an increased risk of thrombus formation. It is frequently suspected due to the ubiquitous use of heparin and the high incidence of thrombocytopenia in critically-ill patients but the true incidence of HIT in ICU patients is estimated to be only 0.3-0.6% (16). Laboratory testing for HIT is insensitive and/or technically difficult so pretest probability should be high before ordering any blood test. Several scoring systems have been proposed to determine pretest probability but the "4Ts" is the most studied(17). A persistent, precipitous fall in platelet count 5 days or more after initiation of heparin in the presence of thrombotic complications should prompt assessment and discontinuation of heparin and

substitution of an alternative anticoagulant. Direct thrombin inhibitors are gaining acceptance as the first alternative to heparin in cases of HIT (see below).

e) Reversing heparin:

Heparin effect can be reversed by protamine. During ECLS, protamine reversal is almost never indicated because precise protamine dosing is difficult and circuit clotting can occur if heparin is reversed to normal coagulation status.

f) The Potential Role of Novel Anticoagulants

Direct thrombin inhibitors (DTIs): Direct thrombin inhibitors (DTIs) are a relatively new class of short-acting anticoagulants used in HITT patients, and many centers are using DTIs as the primary anticoagulant. DTIs bind to active sites on thrombin directly, and demonstrate more predictable pharmacokinetics and greater reduction of thrombin generation, as compared to UNFH. These novel anticoagulants have several theoretical advantages over UNFH, especially in children(18). First, DTIs bind thrombin directly, independent of AT, making them more reliable in patients with low or fluctuating AT activity. Second, DTIs do not bind to other plasma proteins or cells and as a result are not prone to day-to-day changes in serum chemistry or cell counts. Therefore, DTIs may provide a more predictable dosing regimen that allows for consistent anticoagulant effect with less bleeding compared to UNFH making them useful in ECLS. Third, DTIs inhibit both clot–bound and circulating thrombin that can lead to improved efficacy. One potential problem, which potentially limits the use of DTIs, more so in CPB than ECLS, is the lack of a pharmacologic antidote or reversal agent such as protamine in the case of UNFH. However, unlike in CPB, the need to reverse anticoagulation during ECLS would rarely occur. If needed, in cases of severe bleeding, given their relatively short half-lives, DTIs can be decreased or discontinued. Three synthetic DTIs, argatroban, bivalirudin and lepirudin, have been used in CPB, ECLS and VAD supports; however, the availability of lepirudin is currently limited. Published doses of Bivalirudin used in pediatric ECLS include an initial bolus dose of 0.05-0.5 mg/kg followed by an infusion rate of 0.03-0.1 mg/kg/hr, which was subsequently adjusted to maintain APTT 1.5-2.5 times values, or within the physician-defined range (19, 20).

New oral anticoagulants: Direct factor-Xa inhibitors ('xabans') are

a new class of anticoagulant drugs which directly inhibit factor X without using AT as a mediator. Preclinical data showed that rivaroxaban affects thrombin generation in umbilical cord blood at similar doses as those used in adults suggesting that dosing may be both feasible and simpler in neonates than dosing of UNFH(21). A number of oral factor-IIa inhibitors including dabigatran and apixaban are also in preclinical stages. However, their enteral administration and the paucity of pediatric studies will likely limit their use in pediatric ECLS for the near future.

g) Nitric Oxide (NO) and Other Circuit Releasing Compounds:

An ideal anticoagulation strategy for ECLS would be to modify the extracorporeal circuit to make it as non-thrombogenic as vascular endothelium. Among other things, endothelial cells produce prostacyclin and nitric oxide (NO) which, inhibit thrombin induced platelet adhesion and activation as a way to maintain the fluidity of blood. Both prostacyclin and NO, exogenously added to extracorporeal circuits along with UNFH in an effort to inhibit the interaction between platelets and extracorporeal surfaces, have been shown to reduce platelet activation and consumption (22). MAHAMA/NO was the first compound to be incorporated into a polymer matrix applied to an extracorporeal circuit that upon exposure to blood locally released NO at its surface and without systemic heparinization. The MAHAMA/NO-doped circuits showed significantly decreased platelet consumption when compared to both the heparinized and non-heparinized control groups Additionally, delivery of nitric oxide to the cardiopulmonary bypass circuit has been demonstrated to reduce the incidence of post-operative low cardiac output, could potentially mitigate ischemia reperfusion injury and end-organ dysfunction when added to the ECMO circuit(23, 24).

h) Platelets:

Thrombocytopenia (platelet count < 150,000) is common in ECLS patients. It may be a consequence of the primary disease, drugs, and other treatment, or caused by blood surface exposure. Circulating platelets adhere to the plastic surfaces, and undergo a “release reaction” which attracts other platelets. These aggregates of “effete” platelets circulate in the blood and are removed by the liver and spleen. If the platelet count is less than 20,000 spontaneous bleeding can occur. The usual practice is to transfuse platelets to keep the count greater than 80,000. Even though the platelet count is over 80,000, platelet function may be impaired. A kallikrein inhibitor (aprotinin or tranexamic acid) may improve platelet function if bleeding is a problem (see Bleeding, Section B7).

i) Fibrinogen:

Fibrinogen can become depleted during ECLS. Fibrinogen levels are measured daily and maintained within the normal range (250 to 300 mg/dl) by infusion of fresh frozen plasma or fibrinogen. The primary disease, or clots in the circuit, may cause fibrinolysis resulting in circulating fibrin split products. These molecules act as anticoagulants and can add to the risk of bleeding. If fibrin split products are detected and/or if bleeding is excessive, fibrinolysis can be inhibited with anti-fibrinolytics (see Bleeding, Section B7).

j) Surface coatings:

Extracorporeal circuits and devices are available with surface heparin coating or coating with other polymers intended to minimize blood surface interaction. These modified surfaces may decrease blood surface interaction somewhat, but systemic anticoagulation is still required when using the surface coatings currently on the market. It is possible to manage ECMO without systemic anticoagulation if bleeding cannot be controlled by other measures. During ECLS with no systemic anticoagulation blood flow should be maintained high, and a primed replacement circuit should be available if the circuit clots.

5. Circuit monitors, alarms, and safety (Chapters 4 and 5)

(1) **High outlet pressure.** The higher the perfusion pressure, the higher the risk of leak or blowout. 400 mmHg is typically the highest safe level. If the post pump pressure is greater than 300 mmHg at the desired flow rate, the cause might be high systemic blood pressure in the patient (in VA mode), high resistance in the blood return access cannula, high resistance in the conduit tubing from the membrane lung to the cannula, or high resistance in the membrane lung. If the outlet pressure suddenly increases setting off the high- pressure alarm, the cause is usually temporary occlusion of the infusion tubing or cannula. If this occurs stop the pump, then gradually return flow while determining the cause of the sudden increase in resistance.

(2) **Air in the circuit** might be seen directly or detected by a bubble detector. If air is detected in the circuit, stop the pump, clamp the lines near the patient, and put the patient on support settings. Because the patient is often totally dependent on ECLS, it is necessary to find and repair the cause of air in the circuit very quickly. The most common cause is aspiration of air into the venous drainage line at the site of cannulation or through a connector or open stopcock. Another common cause is air

bubbles in the intravenous infusion lines going into the patient. When air is entrained on the drainage side it is usually as small bubbles, and usually is caught in the membrane lung or bubble trap before getting into the patient. Air on the infusion side is a much more serious problem. The most common cause is air entrainment in the membrane lung. This can occur if the membrane lung is higher than the patient and if the blood side pressure drops below the gas side pressure.

(3) **Clotting.** Clots appear as dark immobile areas and can be detected by careful examination of the extracorporeal circuit with a flashlight. Clot formation occurs at sites of turbulence or low flow; connectors, infusion lines, bridges. The significance of clots will depend on the location (pre or post membrane lung) and size. Clots larger than 5 mm or enlarging clots on the infusion side of the circuit (post membrane lung) should be removed by replacing that section of the circuit or by changing the entire circuit if there are multiple clots. Platelet/fibrin thrombi appear as white areas on the circuit at connectors and stagnant sections. These are clots that have not accumulated red cells, usually because they are in areas of very high flow.

(4) **Electrical power failure**. If electrical supply is lost the circuit should be designed to automatically switch to battery operation. An alarm should sound when the circuit switches to battery operation. The battery will operate the circuit for 30-60 minutes while the cause of the problem is being identified. The major power requirement is the water bath for the heat exchanger. When operating on battery power, it is wise to turn off the water bath. If the electrical circuit and the battery fails, the alarm will be a low flow alarm or alarms attached to the patient (saturation or blood pressure). In that case it will be necessary to crank the pump by hand.

(5) **Unplanned decannulation** is a life-threatening emergency identified by major bleeding at the cannulation site, air in the drainage circuit (if the drainage cannula is coming out) and loss of volume and perfusion pressure if the infusion cannula is lost. Decannulation is prevented by securing the cannulas to the skin in at least two locations, and checking the position of the cannulas and cannula fixation at frequent intervals and adequately sedating the patient. If decannulation occurs, come off ECMO immediately by clamping the lines close to the patient, control bleeding by direct pressure, and reinsert the cannula as soon as possible.

(6) **Hemolysis** is suspected if the urine has a pink tinge (which could be due to bladder bleeding, not hemolysis) and verified by

plasma Hb measurement. Normally plasma hemoglobin should be less than 10 mg/dl. Higher plasma hemoglobin can be caused by a condition primary to the patient, or by circuit components. The pump itself will not cause hemolysis unless inlet (suction) pressures are greater than minus 300 mmHg, which can happen if the pump suction exceeds the blood drainage. The pump can also cause hemolysis if there are clots in the pump chamber (which can occur in centrifugal pumps). Hemolysis can occur if blood is flowing at a high rate through a very small orifice. This can occur if the blood return cannula has a very high resistance or if there is a high level of occlusion in the post pump circuit. Hemolysis can also occur if a hemofilter or plasmapheresis device is attached to the circuit and run at high flows. If hemolysis occurs, the source should be found and corrected.

(7) **Emergency drills** addressing all these problems should be conducted by the team at regular intervals

(8) **Safety.** ECMO is a technology dependent therapy utilized in critically ill patients. A successful outcome is highly dependent on repetitive safe practices by a diverse team (e.g. physicians, ECMO specialists, perfusionists, nurses). Policies that support a safe ECMO program include: regular emergency skills lab sessions, team training, using a pre-procedure "time out" to verify key elements and post-ECMO debriefings.

6. Component and circuit changes.

It may be necessary to stop ECLS to remove and replace small components such as stopcocks and connectors, large components such as the pump chamber or membrane lung, or the entire circuit. If the patient is dependent on ECLS, this can be done in less than one minute.

a) Commence conventional ventilation and vasoactive support.

b) Get at least one helper and assemble all the clamps and components.

c) Clamp the lines near the patient, and clamp the lines above and below the component to be changed.

d) With sterile technique, cut out the component and insert the new component, filling the tubing with saline and eliminating all bubbles.

e) When changing or adding a membrane lung, the lung must be primed with crystalloid solution before attaching to the circuit.

7. Patient Transport (Chapter 66)

Traveling poses risks. Do procedures in the ICU whenever possible.

a) **In hospital.** It may be necessary to travel to radiology, the

operating room, or the cath lab. Be sure that the battery is fully charged and the hand crank is available for the pump. Turn off the water bath to save electricity. Use a small full tank of oxygen for the sweep gas. Switch the circuit to battery power and portable oxygen before moving the patient from the bed. Before moving the patient, switch the patient monitors to a portable monitor for EKG, blood pressure, and Sa02. Minimize the number of intravenous infusions as much as possible. Bring a self-inflating bag, separate oxygen tank, and emergency drugs. Plan the trip before leaving the ICU. Hold elevators, clear hallways, and be sure the receiving unit is ready. When moving the patient and the ECLS cart, one person is assigned to keep one hand on the gurney and the other on the cart to reduce tension on the tubing.

b) **Hospital to hospital**. In addition to all the details listed above, the transport team must be entirely self-contained for hospital to hospital transfer. This includes spare parts for all components, a variety of cannulas and sizes, operating instruments, and medications. Arrange for hospital privileges in the referral hospital. Send instructions to the referral hospital regarding family, consent, and blood, platelets, and plasma preparation, OR team if necessary, etc.

c) Traveling to the catheterization lab or the operating room or the CT scanner is often required, so the access tubing and circuit must be planned with that in mind (elevators, battery power, monitors outside of the ICU, etc.).

B. Medical management of Neonates and Children with Cardiovascular Disease (Chapter 32, 33)

Medical management is directed at maximising myocardial perfusion to aid recovery, maintaining or improving end-organ function, and addressing important residual lesions if present.

1. Important Considerations for the Cardiac ECLS patient

a) Myocardial Stunning: Acute loss of preload and sudden increase in afterload following ECMO initiation can lead to worsened cardiac function and minimal to no pulse pressure. Expected time to recovery is 3-7 days.

b) Ventricular distension- If the left ventricular function is inadequate to open the aortic valve, left ventricular diastolic pressure and left atrial pressure will gradually increase, as the left side of the heart fills with bronchial venous flow, thebesian flow and any blood passing from the right to the left. When the left atrial pressure reaches 25-30 mmHg, pulmonary edema will ensue. This process takes 4-8 hours in most cases. Additionally, increased intracavitary pressure may decrease

myocardial perfusion pressure and cause subendocardial ischemia. Decompression should be considered, via a left ventricular vent or catheter based creation and/or dilation of an atrial communication (e.g. septostomy).

2. Cardiovascular assessment and monitoring

a) Rhythm and Heart rate

(1) MCS is usually capable of preserving cardiac output in the face of dysrhythmias.

(2) Dysrhythmia resulting in no cardiac ejection, can lead to ventricular distension and its complications.

(3) Conversion to sinus rhythm/ atrioventricular synchrony generally reduces myocardial demands and promotes ventricular recovery.

b) Blood pressure

(1) The patient's blood pressure is determined by two modifiable factors; blood flow (pump flow plus native cardiac output), and vascular resistance.

(2) Due to narrow pulse pressure, the mean systemic arterial pressure will be lower than normal mean arterial pressure.

(3) Adequacy of support is determined by assessment of standard clinical parameters of cardiac output and oxygen delivery: capillary refill, warmth and color of extremities, urine output and neurological status.

(4) Exact ideal blood pressure targets are not known, but initial targets can be based on predicted mean values for age and size, premorbid mean blood pressure (if known) and anatomical and physiological factors, which would then be titrated to surrogate markers of adequate oxygen delivery (lactate, MVS02, NIRS) (25).

(5) Blood flow is managed to maintain the venous saturation 70-80%.

(6) Pulsatile mechanical circulatory support (MCS) devices have a relatively normal arterial waveform. Continuous MCS devices or patients with poor ventricular function/ejection show a flat waveform. Nonetheless, it should reflect mean arterial pressure.

(7) Pulse pressure: In order to maintain some flow through the heart and lungs and prevent intracardiac and pulmonary thrombosis and LAH, flow is maintained around 80% of venous return, this is reflected by a pulse contour of about 10mmHg.

(8) Changes in arterial waveform can reflect myocardial

recovery, or an acute complication (circuit dysfunction, reduced preload, increased afterload).

c) Inotrope/ Vasoactive Medications: The requirement for vasoactive agents is almost universal in patients about to undergo extracorporeal support. After ECLS initiation, some patients will require ongoing vasoactive support, albeit at lower levels, to support cardiac function and end-organ perfusion.

(1) Enhancement of contractility in a patient severe cardiac dysfunction, in order to facilitate aortic valve opening and prevent stasis of blood in the systemic ventricle and aortic root (Epinephrine, Dobutamine).

(2) Peripheral vasoconstriction in a patient on VA ECLS for septic shock, on maximal circuit blood flow with inadequate systemic perfusion (Norepinephrine, vasopressin).

(3) Peripheral vasodilation to reduce afterload and improve circuit blood flow and systemic perfusion (Phentolamine, nitroprusside).

3. Central venous pressure and fluid management

All MCS devices are dependent upon adequate preload, and the CVP trend is a simple method of estimating intravascular volume status. CVP combined with circuit characteristics and function (increasingly negative venous pressure, low flow, circuit "chatter") will assist with guiding fluid management.

a) Examples:

(1) A low CVP coupled with impaired device flow is generally a signal to replace intravascular volume.

(2) A high CVP with impaired flow should prompt a search for conditions such as pericardial tamponade.

(3) A high CVP with preserved flow indicates hypervolemia and diuretics and/or hemofiltration should be considered.

b) However, these generalizations must also be qualified by recognizing the limitation of CVP- as it reflects not only volume status, but is also affected by cardiac and vascular compliance, and studies have noted poor correlation between CVP and actual cardiac filling volume. Volume repletion may improve circuit function, but the patient and circuit should be reassessed for potential causes of impaired venous flow such as tamponade or cannula obstruction.

4. Ventilation management

The primary objective is to minimize lung injury and optimize lung function in order to allow separation from ECLS once cardiac recovery has occurred.

a) Suggested protective lung strategy**:** Pressure limited ventilation, elevated levels of positive end expiratory pressure (PEEP 10cm02), maximum tidal volume 6-8mls/kg, peak inspiratory pressures 18-20cm H20, with low rate (generally 10bpm). Meticulous pulmonary hygiene is essential.

b) No single ventilation strategy is universally practiced, and the suggested target may be inappropriate in patients with an open sternum, poor lung compliance, pulmonary hemorrhage or intrathoracic hematoma.

c) It may be appropriate to allow spontaneous breathing or extubate in the absence of lung pathology if a patient is cannulated peripherally (particularly for an adult size patient with femoral cannulation).

d) Adjuncts to mechanical ventilation include bronchoscopy and prone positioning.

e) If there is a major pulmonary air leak or interstitial emphysema, the ventilator pressure can be reduced or turned off altogether for hours or days until the leak seals. This will lead to significant atelectasis in addition to the primary lung disease. If the patient develops a pneumothorax, placement of a chest tube is not an automatic response. Even placing a small tube may result in significant bleeding ultimately requiring thoracotomy. A small pneumothorax (less than 20%) with no hemodynamic compromise is best treated by waiting for absorption. An enlarging pneumothorax or a pneumothorax causing hemodynamic compromise requires external drainage. This is best done using the technique most familiar to the operator. This could be a small catheter placed by Seldinger technique, or a surgical thoracotomy with placement of a chest tube.

5. Managing gas exchange with the ECLS circuit

a) On VA ECLS, arterial blood gases reflect mixing of returning circuit blood flow with the native cardiac ejection in the aorta.

b) The returning circuit blood is typically PCO2 40 mmHg, PO2 500mmHg, saturation 100%, oxygen content 22 ccO2/dL.

c) The ratio of returning circuit blood flow to native cardiac blood flow is typically 8:1 (near total bypass).

d) Common Scenarios

(1) If native lung function is normal and the FiO2 is 0.21, this results in PCO2 40, PO2 200, sat 100%, content 21 ccO2/dL.

(2) If there is no native lung function this mixing results in PCO2 40.5, PO2 100, sat 98%, content 20 ccO2/dL.

(3) NOTE: The forgoing is true if returning circuit blood goes to the aortic root (as in subclavian, carotid, or direct arch perfusion).

If the returning circuit blood is going into the femoral artery and flow is retrograde, the mixing will occur somewhere in the mid aorta, the higher the flow rate, the higher the level of mixing.

(4) During severe respiratory failure, at typical VA flow rate (80% of full cardiac output) this can result in desaturated blood from the left ventricle perfusing the aortic arch and coronaries and fully saturated infusion blood perfusing the lower 2/3 of the body. This can occur in large children and adults. This can be managed by including SVC blood in the venous drainage, or by infusing some infusion blood into the right atrium (VVA). See patient specific protocols for further discussion.

6. Airway management

a) Upon initiating ECLS, patients are usually intubated with an endotracheal tube.

b) Tracheostomy avoids the discomfort of intubation and decreases the risk of nosocomial pneumonia. However, tracheostomy has the risk of bleeding in anticoagulated patients, so the technique is important (see B10). Further, consideration to infection of a recent or planned sternotomy wound, resulting in mediastinitis, should be given prior to moving ahead with tracheostomy.

c) Since the gas exchange is totally supported with ECLS, patients can be extubated and managed without mechanical ventilation. This facilitates activity and ambulation and is often used for patients bridging to lung transplantation.

7. Anticoagulation and bleeding

a) Bleeding is a common problem and associated with increased mortality risk (26).

b) Bleeding can impair circuit function due to inadequate preload due to hypovolaemia or tamponade physiology.

c) Risk factors include mediastinal exploration prior to ECLS, greater surgical complexity, early post-operative cannulation and longer bypass time (26, 27). If intrathoracic bleeding occurs in a patient cannulated through the neck with a closed sternum, there should be a low threshold for opening the chest in the ICU, re-exploring the operative sites, evacuating clot, and controlling bleeding as much as possible.

d) Prevention of bleeding is important throughout the ECLS course. Care providers may forget that simple venipuncture, endotracheal suctioning, passage of a catheter through the nose or urethra, can lead to uncontrollable bleeding. Because of ample blood access there is very rarely any need for needle punctures in ECLS patients. Suctioning and

passage of catheters should be done with caution, and only after assuring that the anticoagulation status is optimal (low ACT, adequate platelet counts). If invasive procedures are necessary, appropriate preparation is essential. Management of anticoagulation is discussed in section IV.A.4 above.

e) Management of bleeding

(1) Identify causes that are surgically correctable (e.g. a bleeding vessel at a cannulation site).

(2) Transfuse platelets to greater than 100,000

(3) Decrease level of anticoagulation; ACT target reduced to 160-180 seconds, or as low as 140-160 seconds.

(4) Antifibrinolytic therapy: reduces bleeding associated with activation and dysregulation of fibrinolysis in major surgery and trauma. At present, data to support routine use of antifibrinolytic therapy during ECLS is lacking, however as an adjunct to blood product and coagulation factor therapy may help reduce bleeding, particularly after surgery (28-30).

(a) ε-aminocaproic acid 100mg/kg bolus followed by a continuous infusion of 30mg/kg/hr.

(b) Tranexamic acid 100mg/kg bolus then 10mg/kg/hr.

(c) Fresh frozen plasma or specific clotting factors may be indicated if deficiencies are demonstrated.

(d) Recombinant factor VIIa (rFVIIa) has been used for torrential bleeding. Careful consideration must be given prior to rFVIIa administration, as the thromboembolic risk has not been established in the setting of ECLS and may be associated with acute circuit thrombosis.

(e) If bleeding remains uncontrolled it is reasonable to stop anticoagulation altogether. This may stop the bleeding but may also result in clotting in the circuit, so whenever anticoagulation is turned off a primed circuit should be available.

(f) Life threatening or uncontrollable bleeding may require the discontinuation of ECLS.

f) Specific sites of bleeding

(1) **Cannulation site**: This is the most common site of bleeding, particularly if access has been gained by direct cutdown. Bleeding can be minimized by doing the dissection without systemic heparin, then waiting a few minutes before cannulation if patient condition permits. Bleeding at the cannulation site may be an indication that the cannula is loose or pulling out. The possibility of decannulation should always be considered. Usually

cannula site bleeding is slow oozing related to disruption of small vessels in the skin or subcutaneous tissue. Topical pressure will often control the bleeding, although care must be taken to avoid compressing the cannula. If bleeding persists after direct cutdown access, the wound should be re-explored.

(2) **Chest drain site**: Bleeding post chest tube placement: Bleeding is a common complication even if all appropriate steps are taken during tube placement. It may occur early or after days. Accumulated blood should be evacuated, even if this requires a lower, more posterior tube. Evacuating the blood quantifies the rate of bleeding and decreases the risk of a hemothorax and later organized clot. A CT scan is indicated to determine if the tube is in the parenchyma of the lung. If it is the tube should be removed, but thoracotomy will probably be need to control the bleeding and air leak. If not all the steps outlined above may stop the bleeding. If not thoracotomy is indicated (either via thoracoscopy or directly). Even if bleeding is controlled by operation it often recurs within days. Because of this, it is wise to pack the chest open which permits frequent bedside re-exploration until the patients is off ECMO.

(3) **Surgical site**: The second most common site of bleeding is related to recent operations, particularly thoracotomy if the patient is on ECLS for postoperative cardiac failure. In this circumstance (particularly when going directly from CPB to ECLS) the first step is to place suction catheters in the operative site, seal the site with an occlusive plastic drape, and collect the blood to quantitate the rate of bleeding. Drainage blood can be collected with a “cell saver” for reinfusion. When going directly from CPB to ECLS in the OR, it is reasonable to wait until the ACT is normal or bleeding stops before starting anticoagulation. When the platelet count, ACT, and other medications are optimal, the operative site should be re-explored for active bleeding. When an operative site is explored for bleeding it is best to leave the site open with active drainage and a plastic seal closure, rather than surgical closure of the skin. (Cutdown cannulation site is an exception.) Re-exploration may be necessary many times before bleeding is controlled. There is a moderate risk of wound infection, but that risk is much lower than the risk of ongoing bleeding. See patient specific guidelines for post cardiotomy and other conditions.

(4) **Mucous membranes**: Bleeding from the nasopharynx, mouth, trachea, rectum, or bladder commonly occurs with minor trauma associated with patient care. It is difficult to control

bleeding in these areas by direct pressure but full nasal packing or traction on a Foley catheter with a large balloon in the bladder may stop major bleeding.

(5) **Gastrointestinal**: Bleeding can occur from esophagitis, gastritis, duodenal ulcer, or other sources. It is important to determine the site of bleeding by endoscopy or angiography. If the site of bleeding can be reached by an endoscope or arterial catheter, local measures should be attempted. The decision to operate to control bleeding or excise the bleeding organ is the same as in any patient with GI bleeding and a systemic coagulopathy. The coagulopathy is corrected as much as possible, and then operation is indicated if uncontrolled bleeding persists. The same is true for spontaneous bleeding into other solid organs (liver, kidney, retroperitoneal tissue) or bleeding into the thorax or peritoneal space.

(6) N**eurological**: Bleeding into the head or brain parenchyma is the most serious ECLS complication. It is usually extensive and fatal. If it is possible to take the patient off ECLS on high ventilator and drug settings, it is reasonable to operate on the skull to drain the blood, if such a procedure is indicated.

8. Other organ-specific considerations

a) **Infection**

(1) The most important risk factors for infection is the duration of support (31).

(2) Lymphopenia can occur after transfusion of large volumes of blood products, and may not adequately reflect the presence (and absence) of infection.

(3) Vigilant monitoring for endocarditis and endocardial infection is required, particularly in the setting of mechanical valves and synthetic grafts/stents.

(4) There is little evidence to support routine surveillance cultures (32).

b) **Temperature Management**

(1) Targeted temperature management can be achieved by the ECMO circuit via heat exchanger.

(2) Compressed gases supplying the oxygenator, come from a cold liquid oxygen source, and the evaporative vapor-losses across the membrane dissipate heat, also cooling the patient.

(3) The heat exchanger can be used to maintain normothermia, and also to cool for neuroprotection, to decrease patient metabolic demands, or treatment of fever.

c) **Neurologic**

(1) Neurologic complications may occur more commonly in the congenital heart disease patient population, and vigilance for neurological complications is essential.

(2) Screening cranial ultrasounds and more definitive neuroimaging (CT head) can detect intracranial haemorrhage or embolic events.

(3) Continuous EEG monitoring may be considered in patients who underwent neonatal cardiopulmonary bypass (33, 34).

d) **Analgesia and sedation**

(1) During ECLS cannulation and initiation the patient is deeply sedated and often muscle relaxed. This is to avoid spontaneous breathing which might cause air embolism during cannulation, to avoid movement that might make cannulation difficult, to minimize the metabolic rate, and for patient comfort (Original guideline).

(2) Analgesia and sedation strategies for ECLS patients are similar to strategies for all critically ill children, with a major trend towards minimizing sedation, allowing spontaneous movement and ventilation, and facilitating neurological assessment (page 373).

(3) Dosing requirements may be elevated, as drugs may be adsorbed into the circuit, tolerance can develop, and hemofiltration may remove administered drugs (Rogers 595)(35).

e) **Fluids and renal replacement therapy (Chapters 4, 41, 62)**

(1) The balance between adequate intravascular volume for ECLS circuit function and the development of progressive interstitial edema is challenging.

(2) If required, volume can be replaced with crystalloid, colloid or blood products. If blood products were required for other reasons, they would be the first choice.

(3) Excess interstitial edema leads to organ dysfunction, contributing to worsening cardiac, pulmonary gastrointestinal and renal function, and prolongs time on ECLS.

(4) Spontaneous or pharmacologic diuresis should be instituted, with the goal of resolution of edema and returning patient to their dry weight.

(5) If the response is inadequate or the patient develops renal failure, hemofiltration can be incorporated into the ECLS circuit.

(6) There is evidence that patients on hemofiltration and ECLS have worse outcomes than those just receiving ECLS alone (36, 37). It is not known if this reflects something harmful about

hemofiltration in this context, or more severe underlying disease.

f) **Endocrine**

(1) There is no evidence to support tight glycemic control for pediatric cardiac patients on ECMO (38, 39).

g) **Nutrition**

(1) Adequate caloric and protein nutritional support, as with all critically ill patients, is essential.

(2) Enteral nutrition in patients receiving venoarterial ECMO is well tolerated, provides adequate nutrition, is cost effective, and has minimal risk. (40, 41).

(3) Initiation of enteral nutritional support should begin after resuscitation is complete and perfusion is restored (usually within 12-24 hours).

(4) Parenteral nutrition can be used when the enteral nutrition is contraindicated (e.g. mechanical obstruction, bowel ischemia) or to supplement when full support cannot be achieved by the enteral route alone.

h) **Psychological and Family support**

(1) The predominant emotions for families of a patient on ECLS are fear and anxiety (42).

(2) It is important to maintain multidisciplinary support and open communication to the family to identify issues of significance to them.

(3) Goals of therapy should be discussed early and reviewed regularly, and the potential that ECLS proves unsuccessful for patient recovery needs to be communicated early.

(4) The involvement of palliative care services may assist in family support and aid in the identification of important care goals.

9. Procedures (Chapter 6)

a) Procedures from venipuncture to liver transplantation can be done with success during ECLS. When an operation is necessary, coagulation should be optimized (anticoagulation minimized) as described above. Even small operations like chest tube placement are done with extensive use of electrocautery. For the surgeon, the procedure is like operating on any coagulopathic patient.

b) Tracheostomy is often done in ECLS patients but the technique is different from standard tracheostomy. The trachea is exposed through a small incision, all with extensive electrocautery. The smallest opening in the trachea is made between rings, preferably with a needle, wire, and dilation technique. Do not incise a ring or create a flap. The operative site

(and trachea) should be bloodless after operation. Subsequent bleeding (common after a few days) should be managed by complete re-exploration until bleeding stops.

V. Weaning, Trials off and Discontinuing Pediatric Cardiac ECMO (Chapter 34)

- Separating from ECMO is a complex process that is affected by multiple patient, circuit and system factors, and requires careful planning and assessment starting from the time of ECMO initiation.
- Successful ECMO weaning is generally defined as survival after discontinuation of ECMO without the need for reinitiation of mechanical support for the next 48 hours.
- In order to avoid complications, children who fail to be weaned off VA ECMO within 10 days should have consideration of alternative forms of support.(43, 44).

1. Timing of wean

1. Local factors: determined by the ability of the ECMO team to care for the patient on ECLS support without contributing to the burden of complications, and the capacity to provide intensive care support to the fragile patient weaned from ECLS support.

2. Length of support: Most myocardial recovery occurs in the first two weeks of support. Additional gains become less likely after this period and should prompt a discussion about length of support, and if transition to VAD is indicated as a bridge to recovery or cardiac transplantation.

3. Indication for support: the clinical course of myocardial dysfunction is a major determinant of the expected timing of recovery and ultimate removal of ECMO.

a) Primary myocardial dysfunction: recovery occurs over weeks to months, or not at all. ECMO may not be the best form of mechanical support beyond two weeks, if sufficient myocardial recovery has not occurred, and conversion to VAD should be considered.

b) Recovery from myocardial dysfunction after cardiac surgery: Myocardial injury after cardiac surgery and cardiopulmonary bypass consists of inflammatory, ischemia-reperfusion, and surgical insults, and is thought to peak around 24 hours. Generally, the patient is supported for at least 48 hours with adequate tissue oxygen delivery, LV decompression, hemostasis, correction of metabolic disturbances and exclusion of residual lesions. Patients with pre-existing myocardial dysfunction prior to cardiac surgery (i.e. late presentation transposition of the great arteries with deconditioned systemic ventricle) may require a longer period of support to recover adequate cardiac function.

c) Identification of the culprit lesion: ECMO support after cardiac surgery may allow a window of stability to identify and address important residual lesions. In these instances, the patient can often be immediately weaned after repair of the residual lesion.

4. Perception of prognosis: Cannulation onto ECMO often occurs rapidly without a full understanding of the cause for deterioration. It may become apparent that there is limited or no reasonable therapeutic options or likelihood of recovery. Perceptions of prognosis often differ between team members, and these decisions benefit from a team approach.

5. Capacity to go back on support: If there is technical or logistical barriers to rapid return to ECMO support (i.e. a patient with a healed sternotomy, cannulated via the neck, where cannulation of the same vessels would be very difficult or impossible), such patients may require further optimization, and a greater certainty of successful weaning prior to decannulation.

2. Predictors of successful weaning

1. There is little published evidence to support using specific parameters to predict patient readiness to be weaned from VA ECMO. A general approach is to assess for evidence of myocardial recovery and resolution of complicating factors (SIRS, pulmonary dysfunction). -Evidence of myocardial recovery – increasing pulse pressure, increasing systolic pressure, rising end-tidal C02 (in children without systemic to pulmonary shunts), and improving function on echocardiography (45-47).

2. Echocardiography: Function measured by echocardiography whilst on full flow ECMO does not predict myocardial performance when loading conditions are altered on low flow or following decannulation. Specific echocardiographic parameters (aortic velocity time integral ≥10 cm, left ventricular ejection fraction >20-25%, and lateral mitral annulus peak systolic velocity ≥6 cm/s) under low flow conditions has been shown to be predictive of successful ECMO decannulation in adult patients with cardiogenic shock (47). In pediatric patients the target is often a qualitative assessment of improvement of function to support adequate oxygen delivery, but this is ill-defined and may vary between patients.

3. In patients whose support includes a left atrial vent or atrial septostomy the following can suggest left ventricular recovery.

a) Lower left atrial vent flows,

b) Drop in circuit mixed venous oxygen saturation,

4. Increased left ventricle native ejection when the atrial vent is clamped or removed.

3. Weaning Trial Optimization

For clinical parameters and echocardiography to accurately reflect adequate cardiac function off mechanical support, myocardial loading conditions must be optimized.

Physiological conditions prior to the wean should closely approximate those after decannulation. This process will often start several hours prior to the weaning trial.

1. Low dose inotropes and vasopressors in-line with enough time to reach the patient.

2. Confirm endotracheal tube position and function, resume conventional ventilation and ensure adequate recruitment and tidal volumes, and review the chest radiograph. In patients at risk of pulmonary hypertensive crises, inhaled nitric oxide should be initiated.

3. Pacemaker wires should be tested and connected to the pacemaker box.

4. Correction of all metabolic abnormalities, in particular potassium, magnesium, phosphate, calcium and glucose.

5. Anticoagulation should be titrated to minimize the likelihood of thrombus formation at lower flows. Thrombocytopenia and hypofibrinogenemia should be corrected prior to surgical manipulation.

4. Weaning trial

There are various strategies to reduce the contribution of the ECMO circuit to assess suitability for decannulation. For either strategy, adequacy of ventricular function is assessed by echocardiography, cardiac output, oxygenation and ventilation.

a) Clamping of the cannula proximal to the patient and circulating the circuit slowly through the AV bridge. This allows complete separation from support for briefs periods, however bridges can increase the risk of circuit clots by being sites of low and turbulent flow. A variation of this can involve flushing the cannula with crystalloid, and then instilling them with heparin to prevent thrombosis, allowing longer periods of complete separation.

b) Incremental reduction of flow with administration of fluid and titration of ventilation and inotrope/vasopressor support. With this strategy, flows should not be reduced to below 200ml/min to minimize risk of clot formation.

c) For patients whose systemic to pulmonary shunts have been partially or completely occluded as part of their ECMO strategy, readiness to wean must be judged without reduction if flows, as this will lead to desaturation.

d) Pump-controlled retrograde trial. When a centrifugal pump is utilized, it is possible to reverse the flow probe, and turn the RPM setting on the pump down to allow reverse (arterio-venous) flow retrograde through the circuit, and then use the centrifugal pump as a brake to limit this to approximately 10% of the cardiac output. The effect is that of a limited A-V shunt, but this eliminates stasis in the circuit, and prevents the need for “flashing” the circuit and interrupting the weaning trial.

5. Decannulation

Preparation prior to decannulation is vital. Personnel, equipment, medications and blood products are organized for the decannulation procedure.

1. There should be anticipation and an established plan for complications such as low cardiac output, pulmonary hypertension, bleeding, arrhythmias and the need to rapidly re-initiate ECMO.

2. All patients should have a defined plan in the event of deterioration after discontinuation of ECMO, including whether re-initiation of ECMO is indicated.

3. Patients should not be weaned off ECMO on maximal inotropic and vasopressor support (unless in the case of a "one-way" decannulation), as patients often require increased hemodynamic support in the hours following decannulation.

Figure 34-1 Sample decannulation checklist

Decannulation Checklist
Inotropes and vasopressors in line
Anesthetic and resuscitation drugs prepared
Temporary pacemaker attached to wires and checked
Euvolemic state, volume expanders drawn up
Packed red blood cells available
Platelets > 80 x 10^9/L and fibrinogen > 1.5g/L
Endotracheal tube checked
Adequate pulmonary recruitment
Normal electrolytes
Established plan if decannulation fails. Cannula of the same size in the room. Spare ECMO circuit prepared.

6. Surgical perspectives

1. When the same circuit will be used to re-cannulate for ECMO if required, the tubing beyond the connector attached to the cannula should be prepped and placed in the operative field.

2. Tissue and fluid from the cannulation site, particularly if central cannulation was utilized, can be taken for gram stain and culture.

3. Manipulation of the heart, extensive dissection and undue bleeding may destabilize the patient and should be avoided.

4. The cannulas can be removed whenever the patient is ready, but ideally after the heparin has been turned off for 30 to 60 minutes.

5. Venous and arterial cannula placed by percutaneous access can be removed directly and bleeding controlled by topical pressure. When removing a venous cannula, air can enter the venous blood through the side holes if the patient is breathing spontaneously. This is prevented by a Valsalva maneuver on

the ventilator, or by short-term pharmacological paralysis when removing the venous cannula.

6. For peripheral cannulation, vascular reconstruction may be required depending on the cannulation technique (purse string, direct closure, or oblique incision with end-to-end anastomosis).

7. For central cannulation, chest closure can be considered if ventricular function has improved significantly. Otherwise, the chest should remain open, and the purse strings for cannulation should be snared and left in the chest.

8. If a patient has been supported centrally for more than 2-3 days the edges of the wound may not be viable. Debridement should be postponed until the time of wound closure to minimize risk of bleeding.

7. Failure to wean

1. Children that do not follow an anticipated trajectory and are unable to wean from ECLS support require early and aggressive approach to investigation and management of residual lesions, inadequate hemodynamic or pulmonary support, infection and pulmonary disease.

2. Echocardiography, chest ultrasound, CT angiography, cardiac catheterization and electrophysiology studies may reveal residual lesions amenable to surgical or interventional correction (effusions, valvar regurgitation, outflow tract obstruction, coronary abnormalities, and arrhythmias).

3. Many hemodynamically significant residual lesions may only be detected by cardiac catheterization and not by echocardiography (48). Early detection of residual lesions within 3 days of ECMO support is associated with a higher rate of successful decannulation and better survival to hospital discharge.

8. Risk factors for mortality

1. Risk factors for increased mortality in ECMO patients include renal failure, lactatemia and acidosis at 24 hours of support, bleeding, and initiation of ECMO in ICU vs directly from cardiopulmonary bypass (49, 50).

2. In patients with primary myocardial dysfunction (myocarditis, cardiomyopathy) who fail to demonstrate adequate recovery, VAD support should be considered within 10 days.

3. In the setting of recovered myocardial function with persistent severe pulmonary disease, conversion to VV-ECMO should be considered.

I. Discontinuation of support

1. The possibility of stopping for futility should be explained to the family before ECLS is begun. The definition of irreversible heart or lung damage depends on the patient and the resources of the institution. In each case, a reasonable deadline for organ recovery or replacement should be set early in the course.

- For cardiac failure, three to five days of no cardiac function in a patient who is not a VAD or transplant candidate is considered futile in most centers.
- For pulmonary failure, two weeks of no lung function in a patient who is not a transplant candidate has been considered futile in many centers, although there are cases of lung recovery after prolonged (> 100 days) of ECLS.

2. Fixed pulmonary hypertension in a patient with respiratory failure after several weeks of support on VV-ECMO may also be an indication of futility, or at least an indication to convert to VA access.

VI. Special considerations

A. Myocarditis

Patients with myocarditis can be well supported, and many pediatric patients will have full cardiac recovery. Current survival to recovery is 60% in this population, and exceeds 80% in selected reports. Evidence of low cardiac output, as detailed in section I, with escalating inotropic support is an indication for ECLS. As always, careful monitoring to insure ongoing LV ejection is necessary. Left atrial and pulmonary venous hypertension can be addressed by septostomy or LV venting.

B. Single Ventricle Palliation

1. Stage 1 palliative surgery (Norwood operation): ECMO support after neonatal stage 1 palliation for hypoplastic left heart syndrome is now the most frequent post-operative indication for ECLS. In patients with an arterial shunt, effective use of ECMO necessitates management of the shunt to ensure restricted pulmonary blood flow during support. Higher ECMO flows in the range of 150-200ml/kg/min may be associated with better outcomes, however, if cardiac output remains insufficient on higher ECMO flows, then constriction of the shunt to limit pulmonary blood flow and promote systemic blood flow and tissue oxygen delivery may be necessary.

2. Stage 2 and 3 palliative surgery: Infants and children after surgical palliation with cavopulmonary anastomoses (Glenn or Hemi-Fontan and Fontan circulations) represent a complex physiological group, in whom stable support with ECMO can be difficult to establish. Establishing adequate flow in a patient with a Bidirectional Glenn or Hemi-Fontan may be challenging given the separation of systemic venous return. Nevertheless, ECMO can provide stable support if a reversible process is present. In general, cannulation of the systemic venous return in the right atrium will provide stable flow in the immediate postoperative setting.

3. Patients with Fontan physiology and new cardiac or respiratory failure can be supported with ECMO in the perioperative setting, or if they present with potentially respiratory or cardiac failure later in life.

C. Toxins

(Chapter 57)

Although many cardiotoxic poisonings can be treated with specific antidotes, some patients presenting in cardiogenic shock may still require ECLS as a bridge to recovery. Since cardiac impairment is temporary and limited in these cases, use of ECLS is recommended for those patients who remain in refractory shock despite maximal medical treatment. Patients who experience cardiac arrest following toxic overdose have better outcomes than patients presenting with cardiac arrest from other causes.

D. Drowning

(Chapter 27)

ECMO has been used to support children and adults with accidental drowning and hypothermia. Although the survival in some reported series is low, neurologically intact survival has been reported as >50% in some series, with better outcomes in those patients who did not require cannulation during cardiac arrest (ECPR).

E. Sepsis

(Chapter 9)

Sepsis in newborns can present with profound respiratory distress due to impaired ventilation and coagulopathy, complicated by PPHN. ECMO can support patient's refractory to medical therapy (iNO, HFOV, and vasopressor infusion). Survival for neonatal sepsis requiring ECMO is currently 73% in the ELSO database, and early initiation is recommended for patients with medically refractory disease. While supported, treatment of the inciting cause is critical.

F. Transplant

1. ECMO can support patients with profound cardiac failure prior to transplantation, however, studies examining bridge to transplantation with ECMO have generally shown poor survival, and bridging with left ventricular assist devices (LVAD) has been shown superior in comparison. It should be noted that the comparisons have been made based on historical controls, which may not take into account the complexity of the patients supported with ECMO, or the selection of the patients, which were bridged using LVAD. Nevertheless, careful judgement is necessary when planning bridge to device or transplant with ECMO.

2. ECMO can also support patients with post-transplant dysfunction preventing separation from bypass, particularly those with primary graft dysfunction. In these patients, ECMO is associated with an approximately 50% recovery and survival. Patients with severe acute rejection generally have poorer outcomes, but may be supported to VAD or re-transplantation.

G. Cardiac catheterization and surgical procedures (Chapter 29)

1. Diagnostic and interventional cardiac catheterization, can be performed on ECMO support. In pediatric patients, the most common indication for catheterization on ECMO is evaluation for residual lesions following corrective surgery. Early correction of residual lesions is associated with shorter duration of support and improved survival on ECLS, so interventional diagnostic procedures should be considered when noninvasive studies are non-diagnostic.

2. The use of ECMO support during cardiac catheterization procedures, when the procedure may precipitate hemodynamic instability, is an evolving, but established use of ECMO support (for example trans catheter valve replacement and endovascular stent deployment). Complex airway surgery may also be facilitated by the use of ECMO, without the need for the full anticoagulation and hemodilution of CPB. The details of cannulation and support (location, timing, duration of support following procedure) vary depending upon location.

H. ECPR

While outcomes for ECPR (ECLS initiation following initiation of CPR and PALS support) are worse than those for "elective" VA ECMO initiation, reasonable survival can be achieved. The outcomes for patients who arrest due to an underlying cardiac pathology are better than for patients who have a non-cardiac (i.e., respiratory or metabolic) etiology of arrest. Out of hospital cardiac arrest still portends a grave prognosis, and centers should consider ECPR for these patients carefully.

VII. Expected results

A. Series in the literature and ELSO registry data.

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