

# EMERGING TECHNOLOGY REVIEW

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## Extracorporeal Membrane Oxygenation for Treating Severe Cardiac and Respiratory Failure in Adults: Part 2—Technical Considerations

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**I**N THIS SECOND OF 2 articles on the use of extracorporeal membrane oxygenation (ECMO) for treating severe cardiac and respiratory failure in adults, the physiology, technical considerations, and complications of this technique are reviewed. Although ECMO remains a technically and logistically demanding undertaking, recent advances in the design of circuit components, particularly the oxygenator, have improved the ease of use and durability of the technique, such that extracorporeal support can be maintained relatively safely for several weeks.

### PHYSIOLOGY OF ECMO

There are 2 basic types of ECMO: venoarterial (VA), which provides support for the heart and the lungs, and venovenous (VV), which provides support for the lungs only.

#### VA ECMO

With VA ECMO, systemic venous blood drains into the circuit via a cannula placed in the vena cava. This blood passes through the pump and the oxygenator/heat exchanger before returning to the patient via a cannula placed in a large artery (Fig 1). This mode of support is similar to standard cardiopulmonary bypass (CPB) in that both the heart and the lungs are bypassed. Systemic arterial blood flow is the sum of the ECMO circuit flow and any ejection from the left ventricle (LV). Systemic blood pressure is determined by total blood flow and arteriolar tone. Adjusting the flow and  $F_{I}O_2$  of the sweep gas controls gas exchange by the oxygen-

ator;  $F_{I}O_2$  determines oxygen tension and gas flow determines carbon dioxide tension.

In the absence of any LV ejection, the patient's systemic arterial oxygen saturation ( $SaO_2$ ) is determined entirely by the oxygen saturation of blood in the ECMO return cannula, which is normally 100%. However, if there is LV ejection,  $SaO_2$  depends on the relative flow and oxygen saturation of blood from both the ECMO circuit and blood ejected by the LV. This is important in the specific circumstance of severely impaired lung function in conjunction with femoral placement of the ECMO return cannula. In this situation, there is the potential for upper body (coronary arteries, cerebral blood vessels, and upper limbs) hypoxemia because proximal branches of the aorta receive predominantly deoxygenated blood ejected from the left heart. Even in the presence of significant LV ejection, this situation does not arise if pulmonary function is good or the return cannula is placed centrally (either directly into the proximal aorta or into the axillary artery).

Arterial carbon dioxide tension ( $PaCO_2$ ) is determined by the balance between carbon dioxide production and carbon dioxide elimination (by the oxygenator and lungs). In practice,  $PaCO_2$  is easily controlled by adjusting the oxygenator sweep gas flow, even in the absence of any alveolar ventilation.

#### VV ECMO

With VV ECMO, both drainage and return cannulae are placed in systemic veins (Fig 2). Gas exchange can be supported, even in the absence of any pulmonary function, but there is no direct support of cardiac function. (However, cardiac function is often improved with VV ECMO because mechanical ventilation is concurrently reduced and oxygen delivery to the heart is improved.) Fully oxygenated blood from the ECMO return cannula mixes with systemic venous blood, which then passes to the pulmonary artery and through the lungs. Ideally, only deoxygenated systemic venous blood enters the ECMO drainage cannula. However, depending on the positions of the cannulae, a variable proportion of oxygenated blood from the return cannula enters the drainage cannula. This is known as recirculation.

$SaO_2$  is determined by the oxygen saturation of blood entering the lungs (ie, the mixed venous oxygen saturation [ $SvO_2$ ]) and by any additional oxygenation of blood that occurs within the lungs.  $SvO_2$  is determined by the relative contributions to

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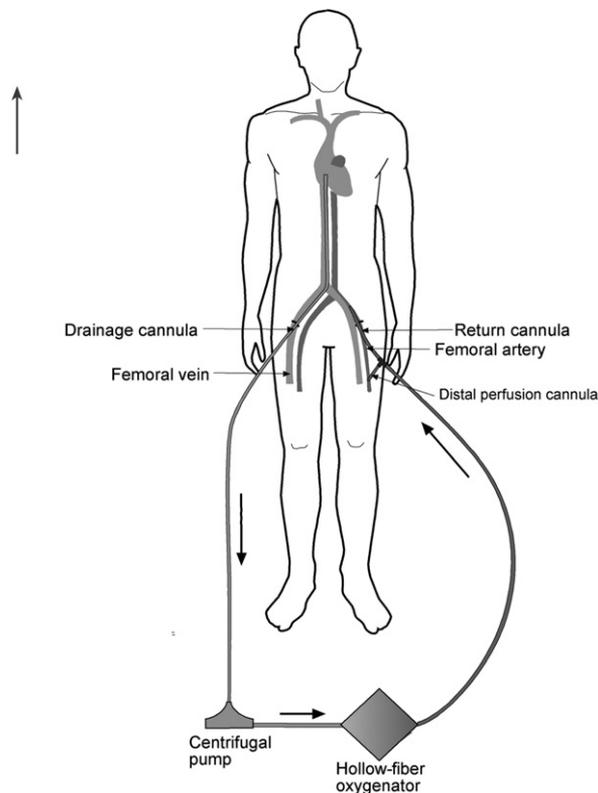
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**Fig 1. Venoarterial ECMO:** the drainage cannula is seen exiting the right femoral vein. The tip of the drainage cannula is in the right atrium. The return cannula is in the femoral artery. A distal perfusion cannula, attached to the return line via a T-connector, is shown. In this particular example, the circuit is comprised of a centrifugal pump and a hollow-fiber polymethylpentene oxygenator with integrated heat exchanger. The direction of blood flow is shown with arrows.

pulmonary blood flow of the ECMO return cannula (oxygenated blood) and the systemic venous return (deoxygenated blood). Recirculation reduces the delivery of oxygenated blood to the pulmonary artery, leading to a reduction in  $SvO_2$ . Thus,  $SaO_2$  is determined by (1) ECMO flow, (2) the patient's systemic venous return (ie, his/her cardiac output), (3) the degree of recirculation, (4) the oxygen saturation of systemic venous blood, and (5) pulmonary function. Of these parameters, and in the absence of significant recirculation, ECMO circuit flow is the most important and easily manipulated determinant of  $SaO_2$ . If there is little effective pulmonary function,  $SvO_2$  is similar to  $SaO_2$ . In the absence of an abnormally elevated cardiac output or a hypermetabolic state, an  $SaO_2$  above 85% can be achieved with VV ECMO, even with minimal or absent pulmonary function. However, unless pulmonary function is relatively good (ie,  $SaO_2$  is significantly higher than  $SvO_2$ ), an  $SaO_2$  above 95% is rarely achieved.

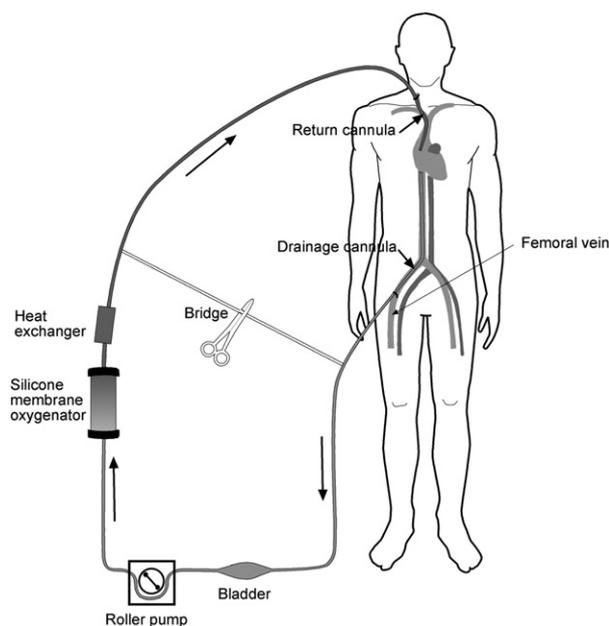
#### ECMO CIRCUITS AND EQUIPMENT

An ECMO circuit is comprised of (1) drainage and return cannulae, (2) tubing, (3) blood pump, and (4) oxygenator/heat exchanger. Apart from differences in the cannulae, identical circuits are used for both VV and VA ECMO.

#### Blood Pump

There are 2 basic types of blood pump: roller and centrifugal. They each have their advantages and disadvantages. Roller pumps have been popular in North America, whereas centrifugal pumps are widely used in Europe, Australia, and New Zealand and are gaining in popularity worldwide.

Roller pumps consist of flexible tubing inside a curved raceway. Rollers mounted on a rotating arm progressively compress a segment of tubing pushing blood ahead of the roller. A roller pump is usually used in conjunction with a blood-filled bladder sited between the drainage cannula and the pump to allow continuous pumping despite changes in the patient's intravascular volume. Blood drains passively into the bladder; if the bladder empties, the pump is shut off by a servo-controlled mechanism, thus preventing the development of high negative pressure in the drainage tubing. With hypovolemia, pump speed and therefore blood flow decrease. Roller pumps are afterload independent. Thus, with VA ECMO, a change in the patient's systemic vascular resistance (SVR) does not influence blood pumping. However, if the return tubing becomes obstructed, high pressure can develop distal to the pump, potentially causing tubing rupture. Because drainage into the bladder occurs under the influence of gravity, roller pumps must be kept below the level of the patient, which is an important consideration when transporting patients on ECMO. With roller pumps, there is a direct relationship between pump speed and blood flow; thus, a flowmeter within the circuit is not required.



**Fig 2. Veno-venous ECMO:** the drainage cannula is seen exiting the right femoral vein. The tip of the drainage cannula is at the level of the diaphragm. The return cannula is in the right internal jugular vein with the tip just inside the right atrium. In this particular example, the circuit is comprised of a roller pump with bladder, a silicone membrane oxygenator, and a separate heat exchanger. A bridge is also shown.

Centrifugal pumps consist of a disposable pump head containing a magnetically driven impeller. The impeller spins rapidly, up to 3,000 revolutions/min, creating a pressure differential across the pump head, which causes blood to flow. A large negative pressure is generated in the drainage tubing and cannula (up to  $-100$  mmHg). Blood flow is preload and afterload dependent. Thus, there is no fixed relationship between pump speed and blood flow, necessitating the presence of a flowmeter within the circuit. With hypovolemia, the inlet pressure becomes more negative and pump speed remains static, but blood flow is reduced. During VA ECMO, a significant change in SVR alters the relationship between circuit flow and pump speed. For example, a large rise in mean arterial pressure may reduce pump flow. Similarly, pump failure during VA ECMO can lead to reverse flow within the circuit, displacing arterial blood to the venous system. For this reason, if the pump is temporarily stopped the circuit must be clamped.

Hemolysis occurs with both roller and centrifugal pumps. This is usually associated with the formation of blood clots and fibrin strands in the pump head or tubing. The plasma (free) hemoglobin and D-dimer concentrations increase, and patients may develop clinical bleeding. Hemolysis is less with centrifugal pumps than with roller pumps<sup>1,2</sup> and less with second-generation centrifugal pumps, such as the Rotaflow (Marquet Cardiovascular, San Jose, CA) and the Cobe Revolution (Sorin Group, Modena, Italy), than with the older style Bio-Medicus (Medtronic Inc, Minneapolis, MN) centrifugal pump.<sup>2-4</sup>

## Oxygenator

Membrane oxygenators may be classified by their structure, as either flat sheet or hollow fiber, and by their membrane, as either microporous or nonmicroporous. With nonmicroporous membrane oxygenators, gas exchange takes place entirely by diffusion. Microporous membranes contain millions of tiny holes through which gas exchange takes place.

In 2002, approximately 75% of adult ECMO runs were performed by using silicone membrane oxygenators with the remainder using polypropylene hollow-fiber oxygenators.<sup>5</sup> Silicone oxygenators contain a nonmicroporous silicone membrane in a rolled flat sheet construction. Silicone oxygenators have excellent biocompatibility and are durable but, compared with hollow-fiber oxygenators, provide less efficient gas exchange, are bulky, are difficult to prime, and have high resistance to blood flow.

Polypropylene hollow-fiber oxygenators are the standard oxygenators used during CPB. They are small, easy to prime, and provide highly efficient gas exchange during short-term use. However, they are microporous (ie, not true membranes, in which the blood and gas phases are completely separated), and over time the micropores become permeable to fluid causing plasma to leak into the gas phase and out the exhalation port. Gas exchange deteriorates, and a coagulopathy may develop. Polypropylene hollow-fiber oxygenators must be replaced every 2 to 3 days,<sup>3</sup> which necessitates briefly stopping ECMO support.

Recently, a new generation of oxygenator has been introduced into clinical practice, containing nonmicroporous hollow fibers constructed of polymethylpentene (PMP). These devices

have been used in Europe, Australia, and New Zealand since the early 2000s, but have only become available in the United States within the last 2 years.

PMP oxygenators combine the durability of silicone membranes with the ease of use and efficient gas exchange of hollow-fiber construction. Examples include the Quadrox<sub>D</sub> (Marquet Cardiovascular, San Jose, CA) and the Lilliput 2 (Sorin Group, Modena, Italy).

Compared with silicone membrane oxygenators, PMP oxygenators are associated with reduced red cell and platelet transfusion and improved gas exchange.<sup>6</sup> Compared with polypropylene hollow-fiber oxygenators, PMP oxygenators have improved durability and reduced requirement for blood product transfusion. In one study, the Lilliput 2 PMP oxygenator ran for a mean duration of 140 hours compared with 60 hours for the Bio-Medicus (Medtronic Inc) polypropylene oxygenator.<sup>3</sup> In the authors' experience, changing from polypropylene hollow fiber to PMP oxygenators has led to a major increase in the lifespan on the oxygenator, from 2 to 3 days to typically more than 2 weeks, and a marked reduction in blood product use. Hollow-fiber oxygenators typically contain an integrated heat exchanger, whereas silicone oxygenators require a separate heat exchanger.

## Cannulae and Tubing

To achieve adequate circuit flow, it is essential that appropriately sized cannulae are used. This is especially so for the drainage cannula, which is the main factor limiting circuit flow. Flow varies inversely with the fourth power of the radius; thus, the larger the diameter of the cannula, the better the flow. Manufacturers provide graphs of pressure drop versus flow (Fig 3) for their cannulae. Although these curves are useful to help guide cannula choice, for most adults the drainage cannula should be 23F to 25F, and the return cannula should be 17F to 21F. In the authors' experience, a 25F Bio-Medicus Multi-Stage Femoral (Medtronic Inc) venous cannula, which has numerous side holes along its length, provides excellent drain-

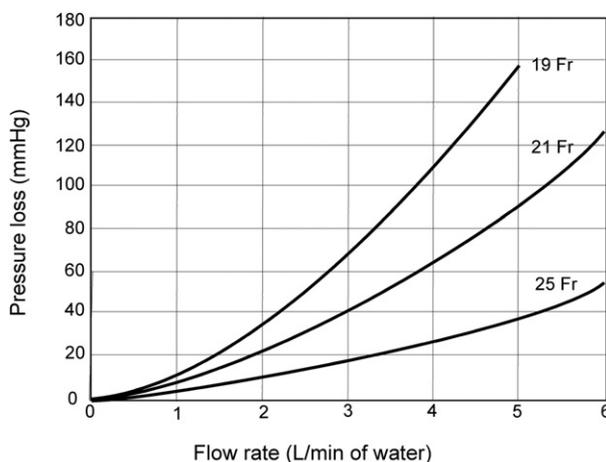


Fig 3. Pressure-flow characteristics for 19F, 21F, and 25F Bio-Medicus Multi-Stage Femoral Venous Cannulae. (Courtesy of Medtronic Inc).

age for both VV and VA ECMO, allowing circuit flows of more than 6 L/min to be achieved in most patients. Recently, double-lumen cannulae (AvalonElite Bicaval Dual Lumen Catheter; Avalon Laboratories, Grand Rapids, MI) for adult and pediatric VV ECMO have been introduced into clinical practice and are available in a range of sizes up to 31F. They are designed to be placed percutaneously using the Seldinger technique into the internal jugular vein, with the tip of the cannula situated in the inferior vena cava (IVC). Drainage holes are present in the superior vena cava and the IVC components of the cannula; the single return hole is in the right atrial component of the cannula and directed toward the tricuspid valve, with the goal of reducing recirculation.

Tubing for adult ECMO is 3/8-inch in diameter and constructed from polyvinylchloride. It is highly resistant to kinking and rupture. Direct contact between blood and the ECMO circuit leads to activation of inflammatory mediators, particularly complement.<sup>7</sup> Coating the circuit components with biocompatible substances mitigates this inflammatory response.<sup>8-10</sup> Several surface coatings are available, but the most widely used for tubing and cannulae is Carmeda BioActive Surface (Medtronic Inc) in which heparin is covalently bonded to the inner surface of the polyvinylchloride.<sup>11</sup>

Many centers also include a bridge in the circuit, which is clamped during ECMO support (Fig 2). The major advantage of the bridge is that it allows the patient to be isolated from the circuit (by clamping the drainage and return cannulae and flushing them with heparinized saline) while allowing flow in the circuit to be maintained and thereby preventing clotting of the circuit. This can be useful during weaning from VA ECMO (see later). The major disadvantage of a bridge is that it adds to circuit complexity and can be a nidus for thrombus formation.

#### TYPE OF ECMO AND CANNULATION

The choice between VA and VV ECMO is usually straightforward, VA for cardiac support and VV for respiratory failure. However, for patients with primary respiratory failure and associated severe hemodynamic instability, this decision can be difficult. As a general rule, in the absence of concomitant septic shock, hemodynamic instability associated with respiratory failure occurs as a consequence of high intrathoracic pressure and relative hypovolemia and resolves with commencement of ECMO and reduction of mechanical ventilation to rest settings.

Cannulation may be central (VA ECMO) or peripheral (VA and VV ECMO). Central cannulation for VA ECMO is usually performed in the operating room for failure to wean from CPB. In this circumstance, cannulae are usually inserted directly into the aorta and the right atrium by the surgical team. In the intensive care unit, peripheral cannulation is typically performed for both VA and VV ECMO.

#### Peripheral Cannulation in the Intensive Care Unit

Cannulation for ECMO should be performed using a strict aseptic technique, including full sterile preparation and draping and "surgical" scrub with a gown, gloves, and a mask. Ideally, 4 staff members are required for cannulation: 2 operators, 1 scrubbed assistant, and 1 nonscrubbed assistant. If cannulation

is being performed by nonsurgeons, a surgeon competent in vascular access should be available.

Percutaneous venous cannulation using the Seldinger technique is well described.<sup>12</sup> Percutaneous arterial cannulation is less well described but also has become the authors' preferred technique. The authors' practice is to perform all cannulations, including confirmation of wire placement and cannula position, under ultrasound guidance.

For VA ECMO, the return cannula is typically placed into the femoral artery and the drainage cannula in the contralateral femoral vein (Fig 1). The drainage cannula should be advanced to the right atrium to improve flow.

Leg ischemia is a risk with femoral arterial cannulation; thus, a distal perfusion cannula, which is connected to the return tubing via a T-connector (Fig 1), always should be inserted.<sup>13</sup> The authors' preferred choice is to insert a 10F to 12F cannula (eg, Bio-Medicus, One Piece, Femoral Arterial Cannula, Medtronic Inc) percutaneously under ultrasound guidance into the superficial femoral artery at the level of the mid or proximal thigh. It is much easier to place the distal perfusion cannula (or wire at least) before the return cannula is inserted because the presence of a large cannula in the femoral artery greatly reduces distal flow in that vessel and its branches. Difficulty placing the distal perfusion cannula is exacerbated further if insertion is attempted after VA ECMO has been instituted because there is reduced (or loss of) pulsatility in the distal femoral artery. This situation typically arises when VA ECMO is instituted as an emergency procedure, usually while the patient is receiving cardiac massage. Nonetheless, it is essential that a distal perfusion cannula be placed, which in this circumstance may require a formal surgical shutdown.

Because percutaneous arterial cannulation is sometimes difficult and is associated with an appreciable risk of arterial injury and leg ischemia, some centers routinely use a "semi-Seldinger" technique in which the wires for the return and distal perfusion cannulae are placed directly into the artery via a cutdown.

An alternative technique to achieve distal perfusion is to perform a cutdown on the posterior tibial artery in the foot and insert an 8F umbilical vein cannula under direct vision. This is the technique used at the University of Michigan (R.H. Bartlett, personal communication, 2009), one of the most experienced ECMO centers in the world.

Several cannulae configurations may be used for VV ECMO. The authors' preferred technique is to place the drainage cannula in the femoral vein, with the tip advanced to the level of the diaphragm, and place the return cannula in the right internal jugular vein, with the tip at the SVC–right atrium junction (Fig 2). This arrangement (termed "femoroatrial cannulation") is associated with less recirculation and improved flow compared with the reverse (atriofemoral cannulation) configuration.<sup>14</sup> Alternative strategies include (1) femorofemoral cannulation, in which the drainage cannula is placed in the femoral vein and advanced to the distal IVC, and the return cannula is placed into the contralateral femoral vein and advanced to the right atrium and (2) the use of a double-lumen drainage and return cannula, which is placed in the internal jugular vein with the tip advanced to the IVC, as described earlier.

Echocardiographic interrogation of the cannula flow patterns using color Doppler is useful if cannula obstruction<sup>15</sup> or recirculation is suspected. Echocardiography is also useful during VA ECMO to confirm decompression of the LV (see later).

### MANAGEMENT OF ECMO

Once cannulation has been performed and the patient has been heparinized (50-100 IU/kg to achieve an activated coagulation time of 1.5-2.0 times normal), ECMO is commenced by unclamping the circuit and slowly increasing flows to the target range. Circuit flow is titrated to clinical parameters, which, for VA ECMO, is the mean arterial pressure and the oxygen saturation of blood in the drainage cannula ( $S_{D}O_2$ ), and, for VV ECMO, is  $SaO_2$  and  $S_{D}O_2$ . Standard initial settings and goals for ECMO are listed in Table 1. If adequate circuit flow cannot be achieved, despite adequate preload and adjustment of the position of the drainage cannula, a second drainage cannula needs to be placed. The initial sweep gas flow should be set to the same as the blood flow and then adjusted according to the  $PaCO_2$  and the pH.

Once ECMO is established, the ventilator is set to rest settings. For VV ECMO, the goal is to promote alveolar aeration while resting the lungs and avoiding ventilator-induced lung injury. Typical rest ventilator settings are pressure-control ventilation with a peak inflation pressure of 20 to 25  $cmH_2O$ , positive end-expiratory pressure of 10 to 15  $cmH_2O$ ,  $F_{I}O_2 < 0.5$ , and a respiratory rate of 4 to 8 breaths/min. With these settings, tidal volume is often very low (<100 mL).

As part of the response to critical illness and as a consequence of blood contact with the ECMO circuit, patients typically have a systemic inflammatory response in the first few days of an ECMO run. This may be manifested as pathologic vasodilation requiring an infusion of norepinephrine, third-space fluid losses requiring significant fluid loading, and worsening of the acute lung injury pattern on chest radiography. In patients who already have severe pulmonary dysfunction, the chest radiograph may progress to a total "white out." Once this acute phase has resolved, usually after a few days, a restrictive approach to fluid management should be used to help improve

**Table 1. Initial Settings and Goals After the Institution of ECMO**

Circuit flow	50-80 mL/kg/min
Sweep gas flow	50-80 mL/kg/min
Fractional inspired oxygen (sweep gas)	100%
Inlet pressure (centrifugal pump)	> -100 mmHg
Oxygen saturation (return cannula)	100%
Oxygen saturation (drainage cannula)	>65%
Arterial oxygen saturation	VA >95% VV: 85%-92%
Mixed venous oxygen saturation	>65%
Arterial carbon dioxide tension	35-45 mmHg
pH	7.35-7.45
Mean arterial pressure	65-95 mmHg
Hematocrit	30%-40%
Activated clotting time	1.5-2.0 times normal
Activated partial thromboplastin time	1.5-2.0 times normal
Platelet count	>100,000/mm <sup>3</sup> (>150,000/mm <sup>3</sup> if bleeding)

**Table 2. Schedule of Initial Point of Care and Laboratory Testing During ECMO**

Arterial blood gases	3-4 hourly
Pre- and postoxygenerator blood gases	Daily
Activated coagulation time	1-2 hourly
Complete blood count	6 hourly
Coagulation tests	6 hourly
Thromboelastograph	12 hourly
Blood chemistry, renal function, and liver function	12 hourly
Plasma free hemoglobin	12 hourly
Blood cultures from the circuit	Daily

pulmonary function. Continuous veno-veno hemofiltration may be used to facilitate fluid removal, even in the absence of acute renal failure. A schedule of point of care and laboratory testing during ECMO is outlined in Table 2.

### COMPLICATIONS DURING ECMO

ECMO is a complex and technical procedure that is performed on critically ill patients, and as such it has a high potential for complications (Table 3).<sup>16-23</sup> Complications may arise from clinician error or inexperience, patient pathology, or technical problems related to circuit components. Common symptoms, their potential causes, and appropriate interventions are listed in Table 4.

#### Circuit Complications

Two circuit complications are acutely life threatening: massive gas embolism and catastrophic blood loss caused by tubing rupture or disconnection. Both complications require immediate clamping of the circuit, with attendant loss of ECMO support. Emergency ventilator settings should always be prescribed for this circumstance.

#### Gas Embolism

With centrifugal pumps, a large negative pressure (up to -100 mmHg) is generated between the drainage cannula and the pump head. Air entrainment in this part of the circuit can lead to massive gas embolism. A second cause of gas embolism is cavitation, whereby gas is forced out of solution because of major obstruction within the circuit.

**Table 3. The Incidence of Various Complications During ECMO in Adults<sup>16-23</sup>**

Complication	Incidence (%)
Blood clots (oxygenerator, pump, tubing, hemofilter)	3.2-22
Bleeding (surgical site, cannulation site, gastrointestinal tract, intracranial, tracheostomy)	5.3-79
Pump failure	4.7-20
Oxygenerator failure	21
Neurologic complications (intracranial bleed, stroke, seizure, encephalopathy)	13-33
Limb ischemia	13-25
Problems during cannulation	0.8-8
Nosocomial infection	17-49
Renal failure	30-58

**Table 4. Troubleshooting ECMO: Common Problems, Their Potential Causes, and Interventions**

Symptom	Possible Causes	Intervention
Low arterial saturation	Oxygenator failure	Check pre- and postoxygenerator blood gas and pressures Replace oxygenator
	Disconnected gas supply	Check connections
	↑ Oxygen consumption (VV)	↑ circuit flows Sedate and paralyze ± cool ± transfuse blood
	↓ Lung function (VV)	See below
	Inadequate circuit flow (VV) Upper body hypoxia (VA)	↑ circuit flow ↑ circuit flows Change to VAV or VV ECMO
Low oxygen saturation in drainage line (<60%)	Low circuit flows (VV)	↑ circuit flows
	↑ Oxygen consumption (VV)	Sedate and paralyze ± cool ± transfuse blood Assess and treat for sepsis
High oxygen saturation in drainage line (>80%)	Recirculation (VV)	Perform echocardiogram Reposition cannulae Change to VA ECMO
Bleeding	Coagulopathy	Check and correct coagulopathy
	Surgical and cannulation site bleeding	Transfuse blood products Lower ACT target Stop heparin Surgical exploration with cautery
	Gastrointestinal bleeding	GI endoscopy + as above
	Airway bleeding	Airway endoscopy + above
High (negative) inlet pressure (centrifugal pump only)	Hypovolemia	Assess volume status Give fluid Sedate and paralyze
	Tamponade (VV)	Perform echocardiogram
	Tension pneumothorax	Perform chest radiograph
Hypotension	Hypovolemia or blood loss	Assess volume status Give fluid Search for site of bleeding
	Excessive vasodilation	Perform echocardiogram Assess and treat for sepsis
	Tamponade	Perform echocardiogram
	Tension pneumothorax	Perform chest radiograph
	Myocardial dysfunction (VV)	Perform echocardiogram
Deteriorating chest radiograph or pulmonary function	Systemic inflammatory response to commencing ECMO or changing circuit component	Fluid restrict if possible Wait for improvement
	Sepsis	Assess and treat for sepsis
	LV distention (VA)	Perform echocardiogram Vent the LV
High plasma hemoglobin	Clots in circuit	Check circuit, change component or entire circuit
	High negative inlet pressure (centrifugal pump)	

If gas is entrained into the circuit, the circuit should be clamped immediately and flow turned off. The patient should be ventilated fully and, in the case of VA ECMO, the circulation supported. Deairing of the circuit then can be attempted by flushing crystalloid solution into the drainage tubing and drawing effluent fluid from the oxygenator or return tubing. Fortunately, major gas embolism is rare, occurring in fewer than 2% of adult ECMO runs.<sup>21</sup>

#### Blood Clots

Blood clots can occur at several points in the circuit including the pump head, oxygenator, tubing, and bridge (Table 5).

#### Loss of Circuit Flow

Loss or reduction of circuit flow is a frequent complication of ECMO and is most commonly caused by hypovolemia. Less common causes include cardiac tamponade, tension pneumothorax, and cannula malposition. With centrifugal pumps, impending loss of circuit flow is indicated by the inlet pressure becoming more negative ( $\leq 120$  mmHg) and “chatter” of the drainage tubing. This can progress to “suck down” of the vein or RA around the drainage cannula, which results in a sudden decrease in inlet pressure ( $\leq 150$  mmHg) and an abrupt loss of circuit flow. Pump flow must be transiently reduced to release the suction effect. With a roller pump, hypovolaemia leads to

**Table 5. Signs of Blood Clot Formation at Various Sites in the ECMO Circuit**

Site	Marker of Thrombosis
Pump head (centrifugal)	Rising plasma hemoglobin Change in sound of pump
Oxygenator	Increasing pressure gradient across the oxygenator Fall in postoxygenator PO <sub>2</sub> Increase in sweep gas needed to maintain PaCO <sub>2</sub>
Tubing/bridge	Visible fibrin strands or thrombus
Nonspecific markers of blood clot formation	Increasing D-dimers or fibrin degradation products Increased bleeding

slowing or stopping of the pump caused by emptying of the bladder.

### Patient Complications

#### *Hypoxemia and Venous Desaturation*

With VA ECMO, normal SaO<sub>2</sub> usually can be achieved. However, as described earlier, the presence of significant LV ejection and impaired lung function can result in upper-body hypoxemia. This situation most commonly occurs when VA ECMO is inappropriately used for treating isolated respiratory failure or when VA ECMO has been used appropriately for cardiorespiratory failure and cardiac function has recovered. Detecting a higher SaO<sub>2</sub> in the lower body than in the upper body identifies the problem. Potential solutions include (1) increasing pump flows to reduce LV ejection, (2) changing to VV ECMO, and (3) adding an additional return cannula (ie, oxygenated blood) to the internal jugular vein, so-called venoarteriovenous ECMO. Central placement of the arterial cannula, including placement in the axillary artery, avoids this problem.

The causes of hypoxemia with VV ECMO are listed in the Physiology section. Of these, inadequate circuit flow is the most important. Hypoxemia (SaO<sub>2</sub> <85%), despite adequate circuit flows, raises the possibility of either significant recirculation or pathologically increased cardiac output and/or increased oxygen consumption. Causes of the latter include inadequate sedation, sepsis, iatrogenic overheating, overfeeding, and seizures. Recirculation is identified by the combination of a low SaO<sub>2</sub> and high S<sub>D</sub>O<sub>2</sub> (typically >75%), whereas increased oxygen consumption and high cardiac output are typically associated with low S<sub>D</sub>O<sub>2</sub>. Treatment should be directed at the underlying cause but may also include sedating and paralyzing the patient, increasing circuit flows, boosting the hemoglobin concentration (eg, to 11-12 g/dL), and active cooling (eg, to 35°C).

#### *Hemodynamic Instability*

VA ECMO can totally support the circulation in the absence of native cardiac function, whereas VV ECMO does not have any direct effect on hemodynamics. Thus, assuming that circuit flows are adequate, hypotension during VA ECMO implies reduced vascular tone, whereas with VV ECMO hypotension

may be caused by reduced vascular tone, reduced preload, or cardiac dysfunction. Even with optimal cannulae size and position, circuit flows above 7 L/min are rarely possible. Thus, severe sepsis, in which native cardiac output would normally increase several fold, can lead to marked hypotension and venous desaturation, despite “full” VA ECMO support.

A particular problem that may occur with VA ECMO is that of LV distention. Patients with mitral and aortic valve regurgitation are most at risk. The problem is often first identified by the presence of alveolar edema on the chest radiograph or edema fluid frothing up the endotracheal tube shortly after the institution of ECMO. The diagnosis may be confirmed by identifying a severely dilated LV with transesophageal echocardiography (TEE). Increasing pump flows reduces pulmonary blood flow and may ameliorate the problem. Failing this, the left heart must be vented, either surgically or in the catheter laboratory by percutaneous atrial septostomy.<sup>24</sup>

#### *Hematologic Complications*

Hemorrhage, particularly from cannulation and surgical sites, is common during ECMO. In one series of more than 400 adults, cannulation site bleeding occurred in 31.4% of patients and surgical site bleeding in 26.7% of patients.<sup>17</sup> Less common, but potentially more serious, is gastrointestinal, tracheostomy, and intracranial bleeding, which in the same series occurred in 7.1%, 13.7%, and 2.7% of patients, respectively.

Causes of coagulopathy include heparin, thrombocytopenia, fibrinolysis, uremia, and hepatic dysfunction. Disseminated intravascular coagulation and heparin-induced thrombocytopenia/thrombosis also can occur. In the presence of major bleeding, the present authors' practice is to keep the platelet count >150,000/mm<sup>3</sup>, the fibrinogen >200 mg/L, and the prothrombin ratio <1.5. It may be necessary to lower the activated coagulation time goal (to 1.2-1.5 times normal) or temporarily stop the heparin infusion. If fibrinolysis is identified (by elevated D-dimer and a characteristic appearance on the thromboelastograph), an antifibrinolytic, such as tranexamic acid, should be administered. In extreme circumstances, recombinant activated factor VIIa has been used successfully to control bleeding during ECMO.<sup>25,26</sup> However, its use also has been associated with fatal thrombosis in this circumstance.<sup>27-29</sup>

The most useful mechanism of avoiding bleeding is prevention. Thus, wherever possible invasive or surgical procedures should be avoided. For this reason, the authors' practice is to delay tracheostomy until after ECMO has been discontinued. Similarly, with “rest” ventilator settings, simple pneumothoraces do not need to be drained. If a procedure is deemed necessary, it should be undertaken by an experienced practitioner with access to cautery.

#### *Infection and Sepsis*

Infections in patients receiving ECMO are common (Table 3) and occur with an increased frequency compared with other surgical intensive care unit patients.<sup>22</sup> However, sites of infection (most commonly bloodstream, lower respiratory tract, urinary tract, and wound) and causative microorganisms (typically gram-negative bacilli and staphylococci) are similar to other intensive care unit patients.<sup>22,23</sup> Cardiac surgery patients are at

an increased risk of nosocomial infections compared with other ECMO patients.<sup>23</sup>

Signs of sepsis may not be obvious in patients on EMCO; in particular, fever may be absent because of the servo control of body temperature by the heat exchanger. Thus, even subtle signs of infection (eg, deteriorating hemodynamics or leukocytosis) warrant an aggressive search for a septic cause. Broad-spectrum empiric antimicrobial therapy (eg, a carbapenem plus vancomycin) should be instituted early until the results of microbiological cultures become known.

#### *Neurologic and Musculoskeletal Complications*

Neurologic complications associated with ECMO include intracerebral hemorrhage, ischemic stroke, and seizures.<sup>18,22</sup> Of these, intracranial hemorrhage is the most feared and is usually fatal. The reported incidence of intracranial hemorrhage varies between 1.6% and 18.9%.<sup>16-20</sup> Risk factors for intracranial hemorrhage include thrombocytopenia (platelet count <50,000 mm<sup>3</sup>) and female sex.<sup>16</sup>

### DISCONTINUING ECMO

#### VV ECMO

Recovery of pulmonary function usually takes 1 to 3 weeks but occasionally longer. Signs of recovery of pulmonary function are (1) an improvement in SaO<sub>2</sub> for a given circuit flow (or a reduced circuit flow required to achieve the target SaO<sub>2</sub>), (2) a progressive increase in SaO<sub>2</sub> above SvO<sub>2</sub>, (3) improving lung compliance, and (4) an improving chest radiograph.

Once the patient can sustain an SaO<sub>2</sub> above 90% on circuit flows of 1 to 2 L/min, a trial off ECMO is warranted. The authors' approach is to fully ventilate patients with modest ventilator settings (eg, F<sub>i</sub>O<sub>2</sub> ≤0.5, peak inflation pressure ≤25 to 30 cmH<sub>2</sub>O, respiratory rate 12-18/min, and positive end-expiratory pressure of 10 cmH<sub>2</sub>O), keep the circuit flows at 1 to 2 L/min, and then stop the sweep gas. After 2 to 3 hours, if the blood gases and lung compliance are satisfactory, the circuit flows are reduced to zero and the patient is decannulated.

Patients who are failing to improve after 1 to 2 weeks should receive aggressive diuresis. The insertion of a pulmonary artery

catheter may be useful in patients who are failing to improve. Progressive pulmonary arterial hypertension may indicate irreversibility.<sup>17</sup> The presence of right ventricular failure and a mean pulmonary arterial pressure more than two-thirds systemic is almost always indicative of irreversibility.<sup>30</sup>

#### VA ECMO

An early sign of recovery of myocardial function is the presence of pulsatility on the arterial waveform. Patients are usually weaned from ECMO onto modest inotropic support (eg, epinephrine, 0.05-0.1 μg/kg/min). The planned inotropic regimen should be started several hours before weaning. Circuit flows are slowly reduced to 1 to 2 L/min, and, with TEE imaging, cardiac function and hemodynamics are assessed. If the patient is stable after 1 to 2 hours of minimal support or no support if the cannulae are clamped and flushed and the bridge is opened, he/she may be decannulated.

The majority of patients who are able to be weaned from VA ECMO for cardiac failure do so within 2 to 5 days.<sup>18,31-33</sup> Patients with an ejection fraction <30% after 2 days of ECMO are significantly less likely to be successfully weaned than those with an ejection fraction >30% (8% v 54%, *p* < 0.001).<sup>31</sup>

### CONCLUSION

There are many similarities between VA and VV ECMO. However, there are also important differences in the physiology, potential complications, achievable clinical goals, and techniques of weaning between these 2 forms of extracorporeal support. Understanding these similarities and differences is essential to the safe conduct of ECMO. A major determinant of success with ECMO is ensuring that appropriate cannulae are placed in the appropriate vessel so that adequate circuit flow can be achieved to support the patient. Clinicians must be skilled, knowledgeable, and fastidious so that the risk of iatrogenic injury is minimized. Good teamwork is essential. However, despite the complexity and inherent risk of the technique, recent developments in circuit components have greatly improved its ease of use and durability, such that, in experienced hands, ECMO can be run for several weeks in relative safety. For selected patients, ECMO is a truly lifesaving therapy.

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