The Role of Echocardiography in the Management of Patients Supported by Extracorporeal Membrane Oxygenation

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Extracorporeal life support can be viewed as a spectrum of modalities based on modifications of a cardiopulmonary bypass circuit to provide cardiac and respiratory support, which can be used for extended periods, from hours to several weeks. Extracorporeal membrane oxygenation (ECMO) is among the most frequently used forms of extracorporeal life support. It can be configured for venovenous blood flow, to provide adequate oxygenation and carbon dioxide removal in isolated refractory respiratory failure, or in a venoarterial configuration, when support is required for cardiac and/or respiratory failure. Echocardiography plays a fundamental role throughout the entire journey of a patient supported on ECMO. It provides information that assists in patient selection, guides the insertion and placement of cannulas, monitors progress, detects complications, and helps in determining cardiac recovery and the weaning of ECMO support. Although there are extensive published data regarding ECMO, particularly in the pediatric population, there is a paucity of data outlining the role of echocardiography in guiding the management of adult patients supported by ECMO. ECMO is likely to become an increasingly used form of cardiorespiratory support within the critical care setting. Hence, clinicians and sonographers who work within echocardiography departments at institutions with ECMO programs require specific skills to image these patients. (J Am Soc Echocardiogr 2012;25:131-41.)

Keywords: Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation (ECMO) is a complex rescue therapy used to provide cardiac and/or respiratory support for critically ill patients in whom maximal conventional medical management has failed.[1,2] ECMO is based on a modified cardiopulmonary bypass circuit and can provide prolonged cardiopulmonary support for days to weeks and even months.[3,4]

Extracorporeal life support using a bubble oxygenator was first used for neonatal respiratory support by Rashkind *et al.*[5] in 1965. The first successful use of ECMO in an adult was reported in 1972.[6] In 1975, Bartlett *et al.*[7] achieved the first successful use of ECMO for neonatal respiratory failure. ECMO in neonatal respiratory failure has been supported by randomized trials.[8-10] Use in adult respiratory failure is more controversial, as early randomized trials showed poor outcomes.[10-12] Use has been limited to highly specialized centers. More recently, the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure trial[13] and selected case series have shown improved outcomes, with survival of 75% to 85% in refractory respiratory failure.[14,15] It has been used successfully in patients with chronic lung disease, as a bridge to lung transplantation.[16] Although ECMO after cardiotomy remains its most common use in adult patients,[17,18] it is also used in patients with reversible cardiac failure, as a bridge to a definitive cardiac assist device or cardiac transplantation,[19] for extracorporeal cardiopulmonary resuscitation,[3] and for periprocedural support of high-risk percutaneous coronary interventions. Case series have shown survival of 65% to 69% for patients with cardiogenic shock secondary to myocarditis.[20,21] ECMO retrieval services are also now in use.[22,23]

The Extracorporeal Life Support Organization registry through January 2011 records 44,824 ECMO cases: 29,216 in neonates, 11,212 in children, and 4,396 in adults.[21] There has been an increase in reported cardiac and respiratory cases in the past 2 years, and improvements in equipment design (particularly oxygenators) and improved medical management have allowed extended duration of ECMO support.[2,4,24] ECMO may be instituted in critical care units, cardiac catheterization suites, or emergency departments as well as operating rooms.

Despite its important role in the management of critically ill patients, there are few published data outlining the use and experience of echocardiography in critically ill adults requiring ECMO. In this review, we outline the role of transthoracic echocardiography

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Abbreviations

CXR = Chest x-ray

ECMO = Extracorporeal membrane oxygenation

LV = Left ventricular

RV = Right ventricular

TEE = Transesophageal echocardiography

TTE = Transthoracic echocardiography

VA = Venoarterial

VAD = Ventricular assist device

VV = Venovenous

(TTE) and transesophageal echocardiography (TEE) in managing patients supported by ECMO. We discuss how echocardiography provides information that assists in patient selection, guides the insertion and correct placement of cannulas, monitors progress, detects complications, and helps in determining cardiac recovery and the weaning of ECMO support. We present an overview of aspects of ECMO relevant to echocardiography. It should be noted that institutional practices will vary widely, and the reader is referred to Van Meurs *et al.*[4] for the definitive review of ECMO practice.

COMPONENTS OF AN EXTRACORPOREAL MEMBRANE OXYGENATION CIRCUIT

An ECMO circuit typically consists of large-bore tubing with

- a cannula for drainage from the venous system,
- a blood pump and control unit,
- an oxygenator for the addition of oxygen and removal of carbon dioxide,
- a heater and cooler unit, and
- a cannula to return blood to the venous or arterial system.

ECMO circuits can also be used in series with renal replacement devices, allowing fluid removal dialysis and plasmapheresis during cardiopulmonary support. In adults, the arterial cannulas used typically range in size from 17 to 23 Fr, and the venous cannulas range in size from 19 to 29 Fr if placed percutaneously and 32 to 36 Fr if placed centrally. Cannula sizes are determined by flow rate requirements, patient and vessel size, and the flow characteristics of the cannula. Roller pumps have been used extensively, but the use of centrifugal pumps is increasing, with blood flows up to 7 to 10 L/min at a maximal speed of 5,000 rpm.[2] Figure 1 depicts the components of a typical ECMO circuit.

MODES OF EXTRACORPOREAL MEMBRANE OXYGENATION

Two types of support are commonly used in adults: venovenous (VV) ECMO and venoarterial (VA) ECMO.[1-4] VV ECMO is used for gas exchange in patients with isolated refractory respiratory failure and requires adequate native cardiac function, as it provides no direct circulatory support. Large-bore cannulas are placed in the inferior vena cava and/or superior vena cava, via the femoral and/or the internal jugular vein, to drain blood into the ECMO circuit. Gas exchange occurs in the oxygenator, and blood is returned through a large-bore cannula placed in another large vein close to the right atrium. The oxygenated blood from the ECMO circuit mixes with any blood not passing through the circuit and is pumped by the right heart through the lungs to the left heart and systemic circulation. Thus, right-heart function, pulmonary vascular resistance, and left-heart function need to be adequate to ensure systemic oxygen delivery.

VA ECMO can provide cardiac and respiratory support. In adults with preserved cardiac function and isolated respiratory failure, VV ECMO is usually preferred to VA ECMO, because it avoids the risks associated with large-bore arterial access. In VA ECMO, blood is withdrawn from the right atrium either by direct surgical cannulation or through a cannula placed in a major vein with the tip sitting in the right atrium. Oxygenation and carbon dioxide removal proceed via the oxygenator as previously described, before being pumped back through a cannula placed centrally in the ascending aorta or peripherally in a large artery. Peripheral cannulas may be placed percutaneously or surgically, depending on patient anatomy, clinical circumstances, and operator preference. Surgical placement may be by cannulation under direct vision or by a tube graft anastomosed to the artery with the cannula placed inside the graft. Specific cannula configurations in VA ECMO have advantages and disadvantages. Central cannulation (right atrium and ascending aorta) allows the use of larger cannulas, providing higher flows and reliable coronary and cerebral perfusion at the expense of requiring a sternotomy. It is thus used after cardiac surgery for patients who are unable to separate from cardiopulmonary bypass despite high-dose inotropes with or without intra-aortic balloon pump support. Peripheral cannulation avoids a sternotomy, but the flows are lower because cannula size is usually smaller. Specific issues arise with the femoral arterial return cannula position in VA ECMO. If lung function is severely impaired and cardiac function is preserved, blood passing through the lungs may not be oxygenated, and hypoxic blood ejected from the left ventricle will preferentially flow to the coronary and cerebral circulations. Adequacy of central oxygen delivery is estimated by placement of an arterial line and pulse oximeter in the right radial artery. Because flow is dependent on cannula diameter, large cannulas are used, which may completely obstruct distal flow down the leg, and the placement of a smaller backflow cannula is necessary to provide adequate blood flow distal to the cannula insertion point.[1-4] Figure 2 shows a backflow cannula in the right common femoral artery to allow perfusion to the leg distal to the cannula.

The axillary artery can be used as the return site to improve coronary and cerebral oxygenation. However, this artery is smaller than the femoral artery, and this may adversely affect flow rates.[2,4] Multiple other circuit configurations are possible. Low-flow VA ECMO is a temporizing resuscitative mode in which smaller cannulas are placed emergently to facilitate resuscitation and/or transport, before definitive management and/or full VA ECMO. An ECMO circuit can be used as a temporary right ventricular (RV) assist device after the insertion of a left ventricular (LV) assist device when there is unexpected RV failure.[25] Blood can be withdrawn from the right atrium through a percutaneous cannula and returned to the pulmonary artery, bypassing the right heart and thus allowing right-heart recovery. An oxygenator can be added for gas exchange and temperature control depending on native lung function in the perioperative period. Figure 3 demonstrates the use of ECMO as a temporary right VAD to treat right heart failure following insertion of a left VAD. Other possible configurations include venoarterial-venous (access from the venous circulation and return to both the arterial and venous circulation) and hybrid central peripheral combinations. New systems are also being developed, including specific transport systems and pumpless AV ECMO systems in which the arterial pressure drives blood across the oxygenator with blood return to a large peripheral vein.[4]

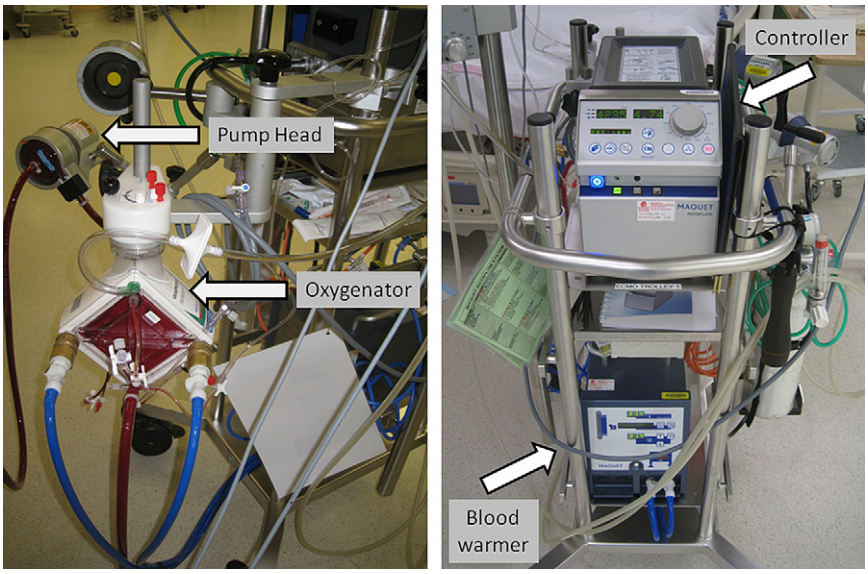

Figure 1 The components of a typical ECMO circuit.

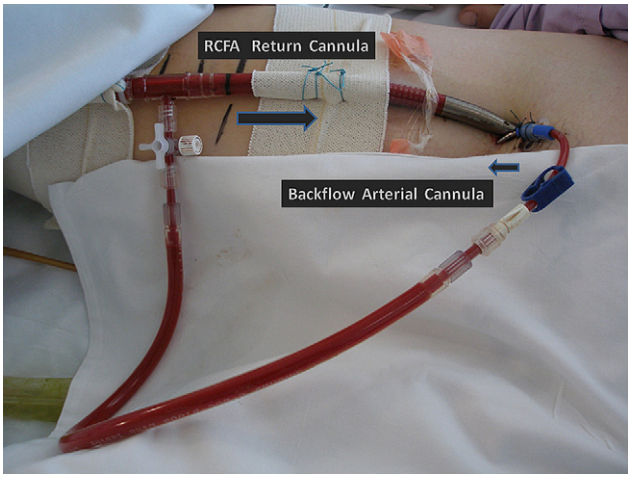

Figure 2 An arterial return cannula inserted into the right common femoral artery (RCFA) with a backflow cannula providing perfusion to the leg distal to the cannula.

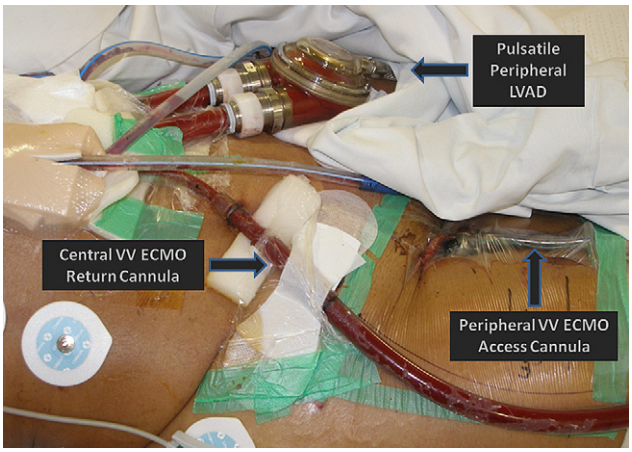

Figure 3 A patient with transient right-heart failure after LV assist device (LVAD) insertion has an ECMO circuit configured as a short-term RV assist device with the venous access cannula in the right atrium (inserted via the right common femoral vein), and the return cannula is connected to the main pulmonary artery.

INDICATIONS

Indications for ECMO can be subdivided into cardiac and respiratory indications. The role and timing of VV ECMO in adult respiratory failure secondary to acute respiratory distress syndrome are debated. Patients may be considered for VV ECMO when there is refractory hypoxemia (and/or respiratory acidosis, with pH $<$ 7.2) despite maximal conventional mechanical ventilation and treatment of reversible contributing factors. The exact values chosen in patients with acute respiratory distress syndrome will vary but would typically be partial pressure of oxygen $<$ 60 mm Hg with fraction of inspired oxygen = 1.0 despite $>$15 cm H_2O positive end-expiratory pressure, because this is associated with poor outcomes in patients with acute respiratory distress syndrome.[26] The oxygenation index ([fraction of inspired oxygen $\times$ mean airway pressure $\times$ 100]/partial pressure of oxygen [mm Hg]) is used to describe the severity of respiratory failure. An oxygenation index $>$ 35 to 40 represents failure of conventional ventilation and should trigger consideration of rescue therapies. The Conventional Ventilation or ECMO for Severe Adult Respiratory Failure trial used a lung injury (Murray) score of $>$3.0.[13,19]

Respiratory Indications

Respiratory indications are listed in Table 1.

Cardiac Indications

Typical cardiac indications (Table 2) include cardiac arrest, near cardiac arrest, cardiogenic shock and refractory low cardiac output (cardiac index $<$ 2.2 L/min/m^2), and hypotension (systolic blood pressure $<$ 90 mm Hg) despite adequate intravascular volume, high-dose inotropic agents, and an intra-aortic balloon pump.[2,3]

An advantage of VA ECMO over the insertion of a ventricular assist device (VAD) is that it can be initiated more rapidly outside

Table 1 Indications for VV ECMO

Common indications
Severe bacterial or viral pneumonia
Acute respiratory distress syndrome
Aspiration syndromes
Primary graft failure after lung transplantation
Other indications
Smoke inhalation
Status asthmaticus
Airway obstruction
Alveolar proteinosis
Pulmonary contusion
Massive hemoptysis or pulmonary hemorrhage

Table 2 Indications for VA ECMO

Common indications
Cardiogenic shock
Inability to wean from cardiopulmonary bypass after cardiac surgery
Primary graft failure after heart or heart-lung transplantation
Sepsis with profound cardiac depression
Drug overdose/toxicity with profound cardiac depression
Myocarditis
Other indications
Cardiac arrhythmic storm refractory to other measures
Chronic cardiomyopathy: as a bridge to longer term VAD support or as a bridge to decision
Pulmonary embolism
Isolated cardiac trauma
Acute anaphylaxis
Periprocedural support for high-risk percutaneous cardiac interventions

the operating room, in multiple environments. It can also be performed at peripheral centers before a patient is transported to a referral center for definitive management. Early consultation between the non-ECMO and the ECMO centers is vitally important to facilitate planning and transportation of a critically ill patient before the establishment of irreversible end-organ dysfunction. ECMO can then be used as a bridge to VAD implantation in patients who present in decompensated cardiac failure or those in acute cardiogenic shock. VA ECMO also allows support of cardiorespiratory failure, as opposed to isolated cardiac dysfunction. The Interagency Registry for Mechanically Assisted Circulatory Support data demonstrates a significant increase in mortality when VADs are inserted in patients with severe organ dysfunction.[27] In this cohort, VA ECMO improved organ perfusion, allowing time for further information to be obtained regarding patient suitability for VAD implantation or transplantation ("bridge to decision"). A VAD can be subsequently inserted when organ dysfunction has diminished through the use of VA ECMO. Similarly, if a patient recovers sufficiently and a donor heart becomes available, the patient can be transplanted off ECMO. One benefit of ECMO in the bridge-to-recovery situation is the option of peripheral cannulation as opposed to VAD cannulation, which is generally central and intracardiac and therefore associated with further muscle damage, risk for arrhythmogenic foci, and where subsequent cardiac surgery requires a repeat sternotomy. Because of the difficulties involved with inserting a VAD in the pediatric population (with size being a limiting factor) and the ability of many pediatric respiratory conditions to resolve with appropriate treatment, ECMO is a significantly more common form of support than VADs in this group of patients.[28]

Table 3 Absolute contraindications to VA and VV ECMO

Absolute contraindications to all forms of ECMO
Progressive and nonrecoverable disease and not suitable for transplantation
Severe neurologic injury or intracerebral bleeding
Absolute contraindications to VA ECMO
Unrepaired aortic dissection
Severe aortic valve regurgitation
Absolute contraindications to VV ECMO
Severe cardiac failure
Cardiac arrest
Severe pulmonary hypertension (mean pulmonary artery pressure > 50 mm Hg)

CONTRAINDICATIONS TO EXTRACORPOREAL MEMBRANE OXYGENATION

Potential contraindications to ECMO include nonrecoverable disease in patients who are not candidates for bridging or transplantation. Patients with irreversible neurologic injuries, those with advanced multiple-organ failure, and those who have contraindications to anticoagulation may not be suitable candidates for ECMO. The upper age limit is debated and will vary with the reversibility of the underlying condition. Similarly, an upper weight limit in adults (such as 125 kg) is debated, because cannulation may be difficult and flows may be inadequate.[1] Absolute (Table 3) and relative (Table 4) contraindications are also specific to each type of ECMO support.

COMPLICATIONS

ECMO is associated with significant complications related to the critically ill patient subset in which it is used and the therapy itself.[1] Common complications include bleeding, thromboembolic events, and sepsis.[2] Less common complications include limb ischemia, hemolysis, and mechanical failure (such as oxygenator or cannula or device thrombosis). Rarer but potentially catastrophic complications include intracerebral bleeding, circuit rupture, accidental decannulation, and air embolism.[4]

ECHOCARDIOGRAPHIC IMAGING OF PATIENTS ON EXTRACORPOREAL MEMBRANE OXYGENATION

Because ECMO is based on the principles of oxygenation and hemodynamic support via blood flow within large-bore cannulas placed in or near the heart in patients with cardiorespiratory failure, echocardiography would be expected to have a fundamental role throughout the care of patients supported on ECMO.

Echocardiography before ECMO Commencement

Echocardiography helps exclude new reversible pathology, which may account for a patient's hemodynamic instability (such as cardiac tamponade, undiagnosed cardiac valve pathology, and LV dysfunction), avoiding the need for ECMO support. It also provides

Table 4 Relative contraindications to ECMO

Age > 75 y
Inability to anticoagulate
High-dose immunosuppression
Cardiopulmonary resuscitation duration > 60 min
Established multiple-organ failure
Multiple trauma with multiple bleeding sites

information regarding contraindications, such as aortic dissection. The presence of significant aortic valve regurgitation may have a detrimental impact on LV unloading in VA ECMO, in which LV afterload is increased. Pathology in the aorta, such as severe aortic atherosclerotic disease, may influence VA ECMO cannulation site (central vs peripheral) or technique (surgical vs percutaneous). The positioning of a venous cannula in the right atrium for VA and VV ECMO also dictates that right-heart anatomy be evaluated for any structural abnormality that may adversely affect the function and position of the cannula. Notable findings would include a prominent patent foramen ovale, atrial septal defect, interatrial septal aneurysm, prominent Chiari network, presence of a pacemaker or implantable cardioverter-defibrillator leads, and tricuspid valve pathology (such as tricuspid stenosis or a tricuspid valve replacement). By assessing cardiac function, echocardiography can help determine whether VV ECMO is sufficient or whether VA ECMO should be considered in conditions such as pneumonia with severe septic cardiomyopathy.

Echocardiography during ECMO Initiation and Cannulation

Echocardiography also has a key role during ECMO cannulation, as it assists in the correct placement of ECMO cannulas. It provides real-time feedback as to the degree of ventricular unloading and interventricular septal motion at the commencement of ECMO support. TTE may not provide the required spatial resolution to guide ECMO initiation and TEE may be required. There are multiple possible cannula configurations, so clear communication between the operator and the echocardiologist as to the intended cannula insertion strategy is vital. In VV ECMO, when one cannula is used for access and one to return blood, the optimal position of the access cannula tip is in the proximal inferior vena cava, before entry into the right atrium. The optimal position for the return cannula is in the mid right atrium and clear from the interatrial septum and tricuspid valve. Figure 4, and Videos 1 and 2 (view video clips online) are TEE images of a VV ECMO return cannula positioned in the mid right atrium, with colour Doppler demonstrating flow out the end and side holes. If the access cannula is more proximally placed than the return cannula, or if the two cannula ends are too close together, recirculation will occur, resulting in little oxygenated blood passing into the pulmonary and systemic circulation. Figure 5 is a plain abdominal x-ray showing the appearance of the access and return cannulae in a VA ECMO circuit. Figure 6 is a plain chest demonstrating a return cannula in the right atrium in a VV ECMO circuit.

Incorrect cannula positioning may require reoperation or manipulation to achieve an appropriate location. These can result in increased risk for bleeding and infection and will also delay the delivery of ECMO support. Venous cannulas are more likely to be incorrectly positioned than arterial cannulas. Abnormal sites include against the interatrial septum, through a patent foramen ovale and into the left atrium, in the coronary sinus, and across the tricuspid valve or subvalvular apparatus. Cannula malpositioning may also result in vascular or cardiac injury and inadequate flows.

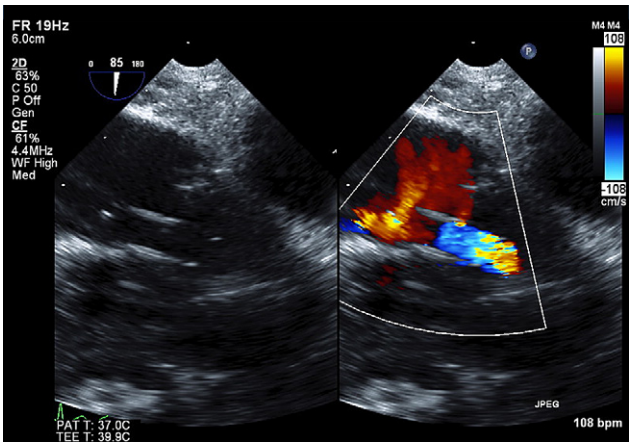

Figure 4 Two-dimensional transesophageal echocardiographic image of a VV ECMO return cannula in the right atrium. Note the additional flow out the cannula side holes.

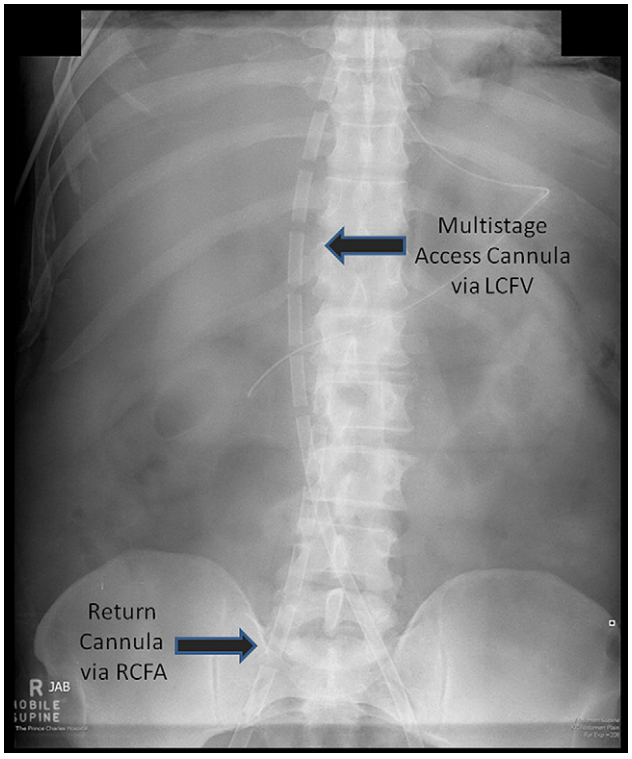

Figure 5 Plain abdominal x-ray showing a venous access cannula inserted via the left common femoral vein (LCFV) into the right heart and an arterial return cannula inserted via the right common femoral artery (RCFA) into the abdominal aorta.

Imaging is recommended for placement of the Avalon Elite cannula (Avalon Laboratories, LLC, Rancho Dominguez, CA).[29] These dual-lumen cannulas range in size from 13 to 31 Fr and are inserted via the right internal jugular vein. One lumen has specifically located holes that drain blood from the inferior vena cava and superior vena cava. The other lumen returns blood to the right atrium through a side hole that is positioned to face the tricuspid valve. Meticulous positioning is required so that the cannula tip is located in the inferior vena cava just below the cavoatrial junction and the return side hole is positioned to enable return flow across the tricuspid valve.[30]

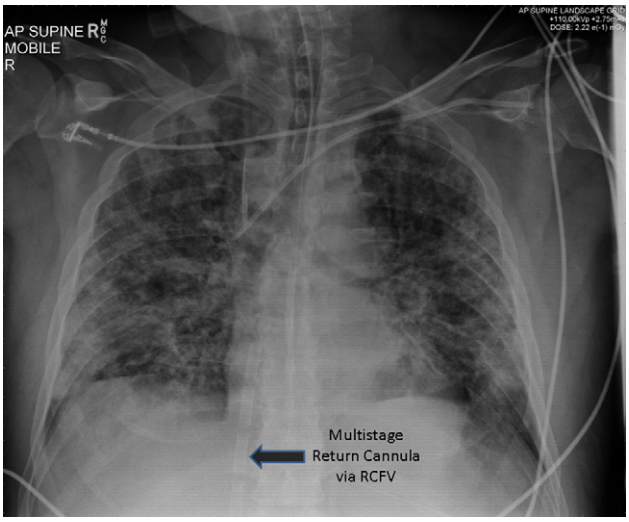

Figure 6 Plain CXR demonstrating a return cannula in the right atrium in a patient on VV ECMO. *RCFV*, Right common femoral vein.

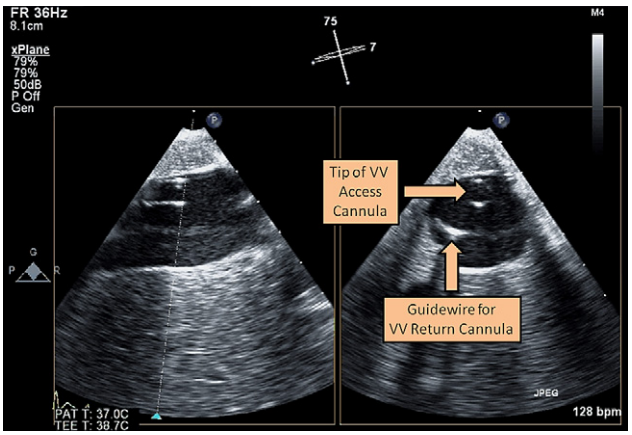

Figure 7 Simultaneous biplane imaging of the inferior vena cava during VV ECMO cannulation, demonstrating a guidewire for the return cannula and the tip of the access cannula.

When commencing a patient on ECMO, guidewires are initially inserted percutaneously and positioned within the heart or great vessels, before the passage of cannulas over these wires. Because of the strong echocardiographic artifacts that can be generated from these wires and cannulas, close attention must be paid to their placement. Figure 7 demonstrates the benefit of biplane imaging available with three-dimensional TEE in determining the spatial orientation of guidewires and cannulas within the inferior vena cava.

A delay in the delivery of the cannula over a guidewire due to difficulty passing the cannula through a peripheral vessel can result in guidewire thrombus formation. This may then be mobilized during passage of the cannula along the wire, resulting in a pulmonary embolus.

In peripheral VA ECMO, the access cannula is optimally located in the mid right atrium, to provide unobstructed flow of central venous blood into the circuit. Again, as for VV ECMO, TEE is useful to guide positioning. The return cannula is usually placed in the contralateral femoral artery and the tip located in the iliac artery or abdominal aorta. This region cannot be visualized with TEE. However, imaging for placement of this cannula is usually not required. TEE can confirm that the guidewire used in percutaneous arterial cannulation is in the lumen of the aorta before dilatation, reducing the risk for extra-arterial cannula placement. Alternatives to echocardiography and blind placement would include placement using an image intensifier in a cardiac catheter laboratory or hybrid operating room. Occasionally, the arterial return cannula may be passed through a synthetic "chimney" graft onto the femoral or axillary artery. Flow orientation and velocity can usually be readily assessed in this location using vascular ultrasound imaging.

Numerous studies assessing cannula positioning have been performed in the pediatric population. Stewart *et al.*[31] studied the use of two-dimensional TTE and agitated saline contrast TTE to determine correct cannula placement and assessment for intracardiac shunting for VV ECMO in 18 infants. At the time of insertion, agitated saline contrast TTE was performed by injecting contrast into the proximal port on the arterial aspect of the cannula. The optimal site of the cannula was found to be in the right atrium, 5 mm from the tricuspid valve, with the tip oriented toward the lateral right atrial wall. This position resulted in the best venous flow and minimized the degree of right-to-left shunting. Five infants had successful cannula repositioning using TTE, because of deviation from the optimal position that had caused a reduction in cannula flow. Thirteen infants had a degree of right-to-left shunting through the interatrial septum. These particular issues are relevant to ECMO support provided by a single cannula with a double lumen. In the majority of adults on VV ECMO, separate access and return cannulas are typically used.

An 8-year review of 193 pediatric patients supported on ECMO was performed by Kuenzler *et al.*[32] to ascertain whether intraoperative echocardiography improved ECMO cannula placement. Overall, 21 cannulas (10.9%) were not correctly positioned. One hundred one procedures were performed without echocardiographic guidance, and 18 (17.8%) of these required surgical repositioning. Only three of 92 cases (3.3%) performed with intraoperative echocardiographic guidance required surgical repositioning ($P = .003$). More recently, Thomas *et al.*[33] reviewed the use of chest x-ray (CXR) compared with echocardiography for cannula positioning in pediatric patients on ECMO. Of the 33 patients who underwent TTE for cannula-related issues, 24% required readjustment of positioning. In none of these patients did CXR reveal incorrect cannula positioning. Of the 58 patients who underwent TTE for unrelated issues, 7% were found to have abnormal cannula positions. Although CXR is a readily available and economical investigation, with less operator expertise required than for TTE, it lacks sensitivity in detecting cannula positioning. This problem is heightened by the fact that some ECMO cannulas do not have a radiopaque tips. Consequently, reliance on CXR for determining cannula location may result in underestimation of the proximity of the cannula, and echocardiography provides better spatial orientation of cannulas. Additionally, TTE provides incremental information about cardiac filling, function, and associated ECMO complications that is not possible with CXR. Echocardiography also avoids exposure to ionizing radiation. As such, echocardiography offers an alternative to plain CXR in the assessment for correct cannula positioning.[33,34]

Echocardiography and Monitoring ECMO Response

After the institution of ECMO support, there are numerous alterations in hemodynamics, dependent on the type and cannulation location in the ECMO circuit. During peripheral VA ECMO, LV

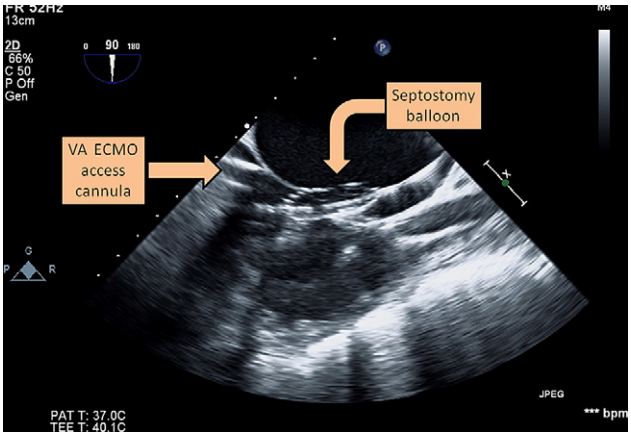

Figure 8 Septostomy balloon being inflated across the interventricular septum under transesophageal echocardiographic guidance.

preload usually decreases (because of decreased pulmonary blood flow), but LV afterload increases (because of the pressurized return of blood via the arterial return cannula). In cases of very severe LV dysfunction, especially when associated with severe mitral regurgitation, the left ventricle may become more distended, and the aortic valve may not open. This will be indicated by a loss of pulsatility on arterial pressure monitoring. This can lead to stasis and thrombosis in the ascending aorta, LV cavity, and pulmonary veins. A left-heart venting procedure or percutaneous balloon atrial septostomy has been described in this situation.[35,36] Figure 8 shows a septostomy balloon inflated across the inter-atrial septum. Video 3 (view video clip online) demonstrates an "unvented" left ventricle in a patient with severe ischemic LV failure supported on VA ECMO. Note the dilated and impaired left ventricle, minimal aortic valve opening, severe spontaneous echo contrast in the ascending aorta, and severe mitral regurgitation (both in systole and diastole). Video 4 (view video clip online) demonstrates a balloon septostomy being performed under transesophageal echocardiographic guidance in an attempt to decompress the left ventricle.

Failure of the aortic valve to open during peripheral VA ECMO support is a significant concern. In this situation, anticoagulation is increased and afterload is decreased while optimizing native LV output (by reducing ECMO flows and judicious use of inodilators), to facilitate aortic valve opening and resolution of spontaneous echo contrast in the left ventricle. Changing the ECMO circuit to a VAD should also be considered in this situation.

During VV ECMO, the pulmonary circulation receives blood with increased oxygen content. As blood is taken from and then returned to the right heart, there is no significant change to RV preload, and there is no adverse affect in hemodynamics in the normal left heart. VV ECMO increases the mixed venous oxygen saturation. This may have two beneficial effects. First, it may decrease pulmonary vascular resistance, leading to lower RV afterload. Second, it may indirectly improve LV function by increasing oxygen delivery to the left heart and hence coronary arterial circulation.

The majority of research focusing on ECMO-induced changes in hemodynamics has been carried out in the pediatric population. Martin and Short[37] studied the effect of VV ECMO on cardiac performance in 19 infants with persistent pulmonary hypertension. Clinical and echocardiographic hemodynamic parameters were obtained before and during ECMO support and <24 hours after ECMO support. LV and RV stroke volumes both decreased by 50% at ECMO initiation but had returned to their baseline levels at 72 hours. Because of the steady heart rate throughout the study, the alterations in RV and LV cardiac output paralleled the corresponding changes in stroke volumes. Pulmonary artery systolic pressure remained elevated in the first 48 hours after ECMO, decreased between 48 and 72 hours of support, and was normal after ECMO. This transient early drop in cardiac performance with VA ECMO may be due to coronary perfusion from desaturated mixed venous blood shunted through poorly functioning lungs as well as increased afterload from the return of the VA ECMO circuit.

Strieper *et al.*[38] prospectively evaluated 15 infants requiring VV ECMO to determine the impact of VV ECMO on cardiac performance. There was no deterioration in cardiac function, measured by aortic flow velocities, LV dimensions, LV fractional shortening, or the velocity of circumferential fiber shortening. All infants had pulmonary hypertension before VV ECMO. By 72 hours, there were significant improvements in pulmonary artery mean and peak velocities and time to peak pulmonary velocities in patients on ECMO. Estimating the pulmonary artery systolic pressure using tricuspid regurgitation velocity could not be reliably performed, because of the high-velocity flow within the cannula in the right atrium. The improved delivery of mixed venous oxygenated blood via VV ECMO to the left heart (and hence coronary arteries), along with the absence of increased afterload seen in VA ECMO, may account for favorable cardiac performance in the setting of VV ECMO. In a study by Balasubramanian *et al.*,[39] cardiac function in 10 adult patients requiring VV ECMO for severe acute respiratory failure was assessed using echocardiography. This was performed before ECMO and during and after the cessation of ECMO. There were no significant changes in LV fractional shortening, circumferential fiber shortening velocity, meridian wall stress, or peak aortic flow velocity.

RV function may be adversely affected by sepsis and increased pulmonary vascular resistance in response to significant hypoxemia. Echocardiography can be useful in documenting the effects of improving oxygenation and acid-base status on the adequacy of RV function when VV ECMO is used. Video 5 (view video clip online) depicts TEE demonstrating severe RV dysfunction before VV ECMO, used to treat acute respiratory failure secondary to Wegener's granulomatosis. Video 6 (view video clip online) depicts TTE demonstrating normalization of RV systolic function after 48 hours of VV ECMO.

Echocardiography and the Detection of ECMO Complications

Patients supported on ECMO are critically unwell and thus at increased risk for complications due to the underlying disease process, critical illness, anticoagulation, or the device itself, particularly after cardiac surgery. Echocardiography can assist in the detection and management of specific complications that may arise during ECMO support. It is usually the first investigation requested when there is suspicion of ECMO dysfunction, particularly for thrombosis, cannula displacement, or tamponade. A significant number of transthoracic and transesophageal echocardiographic studies are performed on patients who are on ECMO.[40] Because of the limitations of spatial resolution with TTE, TEE is usually required to detect these complications. It enables rapid assessment of cannula positioning, cardiac filling and function, chamber compression from tamponade, and cannula-associated thrombi.

The detection of cardiac tamponade and the significance of pericardial effusions or collections can be difficult in patients supported on ECMO, as the heart is in a partially bypassed state. There may

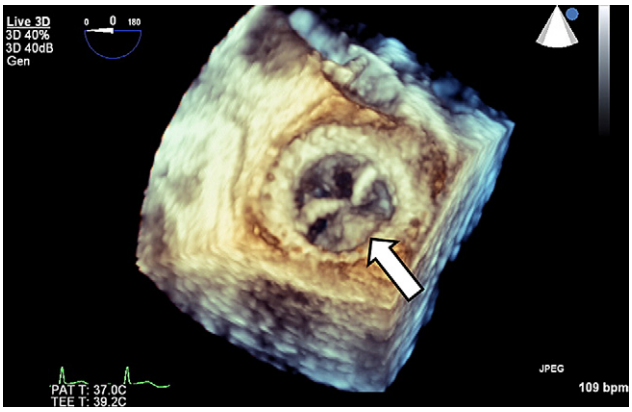

Figure 9 Three-dimensional TEE of biologic mitral valve replacement, from the left atrial aspect. Note the thickened and immobile leaflet (*arrow*) due to heparin-induced thrombocytopenic thrombotic syndrome.

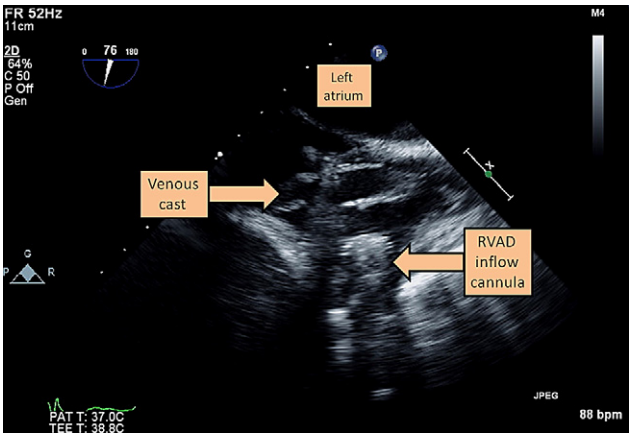

Figure 10 In situ venous cast in the right atrium after removal of a venous ECMO cannula and conversion to a definitive RV assist device (RVAD).

be significant compression of a cardiac chamber from a pericardial hematoma, but if this does not adversely affect cannula flow, it may be of no hemodynamic significance. Hulyalkar *et al.*[41] described a case in which cardiac tamponade was detected using TEE during VA ECMO support in an adult. The presence of a significant pericardial collection, which may even result in cardiac chamber compression and may not necessarily affect hemodynamics or ECMO flow while on support, may become a significant factor when contemplating weaning from ECMO.

The cannulas used in ECMO can be large, which predisposes them to being a common cause of complications, especially thrombosis or venous and arterial obstruction. The literature describing this is limited to one study and a collection of case reports. In a retrospective study by Zreik *et al.*,[42] seven of 60 pediatric patients on ECMO developed superior vena cava thrombus detected using TTE. Three patients had clinically evident superior vena cava syndrome, and the other four had thrombi detected incidentally during TTE for other indications. Comparing the two groups, there were no differences in the type of ECMO, cannulation size, anticoagulation regimen, or duration of ECMO. In light of the inability to predict which patients will develop superior vena cava thrombus, the authors recommended TTE in all pediatric patients after ECMO. Ranasinghe *et al.*[43] reported a case of a 25-year-old man with Wegener's granulomatosis vasculitis requiring VV ECMO. Low flows within the circuit and desaturation resulted in TEE being performed, revealing a mobile thrombus within a jugular venous cannula. Figure 9, and Video 7 (view video clip online) demonstrates a three-dimensional en-face TEE image of a biological mitral valve replacement with a thickened and restricted leaflet (arrow) due to HITTS induced thrombosis.

Katz *et al.*[44] reported a case in which a 51-year-old woman required VA ECMO after single lung transplantation. High negative pressures (−150 mm Hg) were required to maintain adequate flow from the venous cannula. TEE revealed that the venous cannula had passed across the interatrial septum and was draining the left atrium. It also revealed a thrombus in the distal cannula as well as at the right atrium. Echocardiography was used to reposition the venous cannula to within the inferior vena cava. An agitated saline bubble study confirmed the presence of a patent foramen ovale.

Thrombus formation associated with venous cannulas may either reduce ECMO flow or complicate the clinical course by causing a pulmonary embolism. Additionally, on removal of a venous

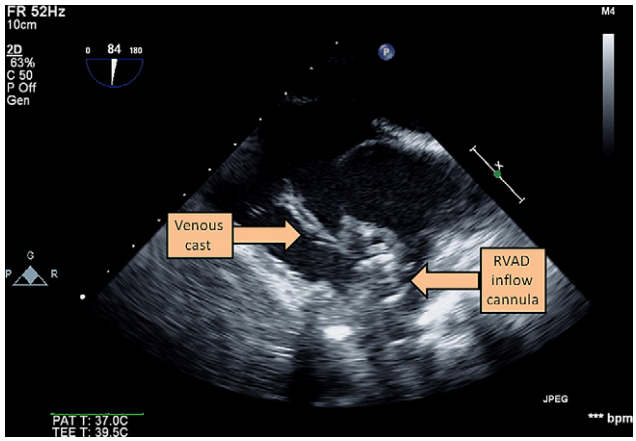

Figure 11 Embolization of the ECMO cannula venous cast into the inflow cannula of the RV assist device (RVAD).

ECMO cannula, organized thrombi that had formed around the cannula may then be left behind in the heart. Figure 10, and Video 9 (view videos clip online) demonstrate this, showing a thrombus cast that was retained in the right atrium after removal of a venous access cannula. This then embolized into the inflow cannula of a subsequently inserted RV assist device, resulting in significantly reduced RV assist device flow (see Figure 11and Video 10 [view video clip online]). Finally, if the venous cannulas are removed at the time of surgery (such as during VAD insertion or cardiac transplantation), it is recommended that intraoperative TEE of the inferior vena cava be performed to assess for the presence of a venous cannula cast. If missed, this may subsequently cause a pulmonary embolus, but if detected, it can be easily removed at the time of surgery.

Echocardiography during Patient Recovery and Weaning of Support

The final area in which echocardiography plays an important role is the determination of recovery and readiness for weaning from ECMO support. For VA ECMO, this is may be performed under direct transesophageal echocardiographic visualization and guidance with or without a pulmonary artery catheter. The decision to wean ECMO support and its timing are complex. Cardiac recovery is often

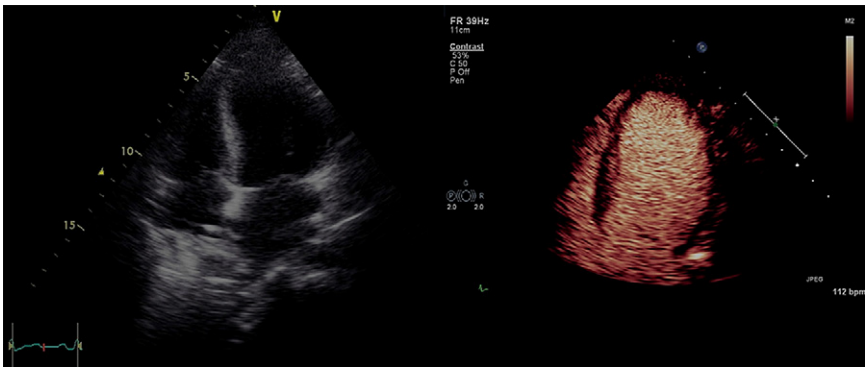

Figure 12 Precontrast and postcontrast imaging to determine LV function in a supine, ventilated patient in cardiogenic shock on VA ECMO. Note the improved endocardial definition after contrast administration.

marked by increasing pulsatility seen on the patient's arterial line tracing. For VA ECMO, it would be unusual to attempt to wean ECMO in the first 72 hours.[45] Although there are no specific echocardiographic protocols developed for ECMO weaning, an approach similar to weaning from a VAD may be used for VA ECMO.[46-49] The level of recovery and likelihood of weaning ECMO support are based on a multitude of clinical, hemodynamic, and echocardiographic variables. Echocardiographic parameters that may suggest an attempt to cease ECMO support include an LV ejection fraction > 35% to 40%, an LV outflow tract velocity-time integral > 10 cm, absence of LV dilatation, and no cardiac tamponade.[25,50]

Invasive calculation of the cardiac index using a right-heart catheter may be misleading during weaning from VA ECMO because a significant proportion of the circulating blood flow actually bypasses the pulmonary artery. When weaning VA ECMO, a common approach is to reduce the VA ECMO flows in 0.5 to 1.0 L/min increments and assess the clinical and hemodynamic parameters (including heart rate, blood pressure, arterial waveform pulsatility, oxygen tension level in a right radial arterial line, and changes in central venous pressure and pulmonary artery pressure) and echocardiographic parameters (stroke volume, ventricular dimensions, ventricular volumes, and ejection fraction).[50,51] ECMO flows are usually not reduced below 1 to 2 L/min, because of the increased risk for circuit thrombosis at low flow rates. Weaning from VV ECMO relies primarily on the assessment of oxygenation and pulmonary compliance, by decreasing the gas flow through the ECMO circuit and resuming conventional lung protective ventilation rather than decreasing ECMO circuit blood flow. Consequently, echocardiography is usually not required for weaning from VV ECMO. There are few published data outlining methods and findings during ECMO weaning. In a study by Konishi *et al.*,[52] Doppler evaluation of flow in the descending aorta was used to help determine cardiac recovery after viral myocarditis treated with peripheral VA ECMO. The authors commented that the level at which the two flows mix may be of benefit in determining whether adequate cardiac output is being generated by the native heart.

Contrast-Enhanced TTE and ECMO

The critical care setting frequently limits satisfactory transthoracic imaging, and contrast echocardiography has been shown to improve image quality, as well as altering patient diagnosis and management.[53-61] However, the role of echocardiographic contrast agent use in patients supported with VADs or ECMO is not well documented. It is in these patients that accurate determination of ventricular function and monitoring its change over time are of key importance. Additionally, assessment for ECMO complications, such as ventricular thrombus formation, is also important and may be enhanced by contrast echocardiography.

TEE is typically required for patients in the critical care setting who have nondiagnostic images. However, patients supported on ECMO are systemically anticoagulated, may have multiple-organ failure with generalized edema, or are thrombocytopenic, all of which increase the risk associated with performing TEE. In this scenario, contrast-enhanced TTE could be considered. In conventional contrast imaging situations, the signal persistence after a bolus dose of diluted contrast is approximately 3 to 5 min. Because these microspheres are small (with a mean diameter of 3 μm) and made of a shell and gaseous core, they are also hydrodynamically labile. As such, increased bubble destruction will occur if they are administered through the "side arm" of intravenous access, forcibly injected into a narrow lumen, or passed through mechanical pumps (such as VADs or ECMO pumps). Passage of these hydrodynamically labile microspheres through the ECMO circuit increases bubble destruction, occurring primarily within the rotor housing, where hydrodynamic pressure changes, contact with the impeller blades, and propulsion in a rotary motion at several thousand revolutions per minute would increase the destruction of the microspheres. This increased bubble destruction, when coupled with natural attrition, will result in reduced signal persistence and hence reduced diagnostic imaging time with each bolus dose. Despite passage of the microbubbles through the rotary flow circuit and an anticipated increased rate of destruction, transthoracic image quality can be significantly improved using contrast-specific imaging.[62,63] Consequently, depending on the indication, sufficient diagnostic imaging could be obtained with contrast-enhanced TTE, reducing the need for more invasive TEE. Figure 12, and Videos 11 and 12 (view video clips online) demonstrate pre- and post-contrast TTE images of a patient on VA ECMO. Note the improved endocardial definition with contrast imaging.

CONCLUSIONS

ECMO is a specialized form of extracorporeal support for critically ill patients who require short-term respiratory and/or cardiac support. ECMO can be applied as either a VA circuit or a VV circuit, through either peripheral or central cannulation. Echocardiography has a fundamental role in managing patients supported with ECMO. It provides information that determines appropriate patient selection, guides the insertion of cannulas, monitors progress, detects

complications, and helps in determining recovery and weaning of support. TEE is the primary form of imaging required during insertion and commencement of ECMO, monitoring patient response, and detecting complications. In those patients with nondiagnostic transthoracic echocardiographic images, the addition of contrast-specific imaging may also result in diagnostic images for assessment of wall motion, LV ejection fraction, LV thrombus, and LV morphology. Institutions that perform ECMO require an echocardiography service that is readily available and experienced in the evaluation of these critically unwell patients.

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