Case Presentation
A 28-year-old previously healthy woman was brought to the hospital after out-of-hospital resuscitated cardiac arrest attributable to ventricular fibrillation. On the evening of presentation, she was found unconscious at home by family members. Bystander cardiopulmonary resuscitation (CPR) was immediately initiated. The patient was defibrillated in the field by emergency medical response providers with return of spontaneous circulation. She aspirated during intubation in the field, and arrived to the hospital in shock, with blood pressure 88/71 mm Hg on norepinephrine 20 μg/min and vasopressin 0.04 U/min. She did not have purposeful movements, and therapeutic hypothermia was initiated in the Emergency Department. She had a metabolic acidosis and concomitant type I acute respiratory failure, with PaO₂ 66 mm Hg on volume-cycled assist/control mode with tidal volumes of 400 cc, FiO₂ 1.0, positive end-expiratory pressure 10 cm H₂O, and a respiratory rate of 26 breaths/min. Her ECG did not demonstrate stigmata of ischemia or infarction. However, a type I Brugada pattern was noted in leads V1 and V2 before cooling.

Over the ensuing several hours, vasoressor requirements escalated. A Swan-Ganz catheter demonstrated severely depressed cardiac index and elevated pulmonary capillary wedge pressure. She remained severely hypoxic despite maximal ventilator support. Chest x-ray showed diffuse bilateral pulmonary infiltrates, consistent with severe aspiration pneumonitis. PaO₂ decreased to 49 mmHg despite increased positive end-expiratory pressure and chemical paralysis, meeting Berlin criteria for severe acute respiratory distress syndrome.¹ Options for percutaneous hemodynamic support were considered (including extracorporeal membrane oxygenation [ECMO] or percutaneous ventricular assist device [VAD], such as Impella and TandemHeart), and the patient was placed on veno-arterial ECMO (VA ECMO) for both hemodynamic and respiratory rescue 6 hours after presentation.

Cardiopulmonary bypass was first developed in 1954 to facilitate open-heart surgery and used successfully 1 year later.²³ Although substantially different from early cardiopulmonary bypass systems, ECMO evolved from cardiopulmonary bypass and provides prolonged cardiopulmonary support outside of the operating suite. With increasing technological advances and safety, the uses of ECMO have expanded, with increasing interest as combined short-term circulatory and respiratory support in patients with cardiogenic shock.⁴ Although potentially life-saving, ECMO is invasive, complex, resource intensive, and can be associated with serious complications. This Clinician Update will introduce ECMO technology, review indications and contraindications, discuss management, including maintaining and weaning support, and underscore potential complications.

From Division of Cardiovascular Medicine (P.R.L., B.M.S.), Department of Anesthesiology, Perioperative and Pain Medicine (D.A.S.), Division of Cardiothoracic Surgery (G.S.C., P.C.C.), and Division of Pulmonary and Critical Care (G.L.W.), Brigham and Women’s Hospital, Harvard Medical School, Boston, MA.

Correspondence to Benjamin M. Scirica, MD, MPH, Brigham and Women’s Hospital, TIMI Trials Study Group, 350 Longwood Ave, First Floor, Boston MA, 02115. E-mail bscirica@partners.org

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Successful implementation and monitoring of ECMO require a well-trained, multidisciplinary team with expertise in this technology, typically with specialists from cardiothoracic surgery, cardiology, perfusion, intensive care medicine, anesthesiology, and respiratory care. The basic ECMO circuit comprises vascular cannulas, a pump, an external membrane oxygenator, and a blood warmer (Figure). The circuit can be configured with either 2 venous cannulas (venovenous [VV] ECMO), or with both a venous and an arterial cannula (VA ECMO). In VV ECMO, blood is typically drained from the body via an inflow (to the pump/oxygenator) cannula in the vena cava and returned via an outflow cannula in close proximity to the right atrium. VV ECMO is dependent on patients’ intrinsic cardiac output (CO) and hemodynamics for support, and as such, its application is for isolated respiratory failure. This modality was used successfully in severe cases of respiratory failure during the H1N1 influenza A pandemic.5

In VA ECMO, blood is extracted from a venous inflow cannula in the vena cava and returned to the arterial system via an outflow cannula, thus bypassing the heart and lungs. VA ECMO is not dependent on native CO, and is therefore used in patients with cardiogenic shock. Cannulation for VA ECMO can be central or peripheral. In central cannulation, a venous cannula is implanted in the right atrium and an arterial cannula is implanted in the ascending aorta. Peripheral cannulation is via the femoral or internal jugular vein and the femoral or axillary artery. If femoral artery cannulation is chosen, flow from the arterial cannula is required to perfuse extracorporeally oxygenated blood retrograde up the descending aorta and into the ascending aorta to assure delivery to the coronary arteries and cerebral great vessels. If the left ventricular CO is negligible, the required extracorporeal flow will be small. However, as native cardiac function recovers and native cardiac ejection increases, anterograde aortic flow will compete with retrograde flow from the femoral cannula, and a mixing zone of anterograde deoxygenated (in patients with respiratory failure) and retrograde oxygenated blood flow will occur. The flow required to assure that this mixing zone remains in the ascending aorta will increase as native CO increases. Monitoring pulse oxygen saturation from the right upper extremity or arterial blood gases from the right radial artery will inform the critical care team whether ECMO is providing adequate cerebral (although not necessarily cardiac) oxygenation. Monitoring cerebral oximetry can also be reassuring. Given the need for large femoral arterial cannulas (size 16 to 21 Fr), distal leg ischemia can develop. This risk may be reduced by prophylactic insertion of a small (6 Fr) anterograde perfusion cannula into the superficial femoral artery, to perfuse the leg distal to the primary arterial cannula.

The extracorporeal components of the circuit include an oxygenator and a flow pump. Although commercially available oxygenators for cardiopulmonary bypass include bubble, membrane, or hollow-fiber devices, only polymethylpentene hollow fiber devices are approved for prolonged support. CO₂ is readily extracted via gradient-mediated mechanisms. The addition of oxygen is slower, owing to difference in solubility and diffusion properties, and is proportional to the concentration of oxygen provided in the sweep gas. Total gas flow through the oxygenator, or sweep, is adjusted for CO₂ clearance, and an air/oxygen blender is used to achieve desired FiO₂, starting at 1.0. Measured in L/min, sweep is generally initiated to match blood flow through the circuit, and subsequently titrated based on arterial blood gases. Blood flow through the circuit is driven by an external pump, which is either a constrained vortex centrifugal pump (most common) or a simple roller pump. These pumps can generate up to 8 to 10 L/min of flow, generally limited by venous preload and cannula size.

**Indications**

VA ECMO has a potential role in patients with refractory cardiogenic shock. Refractory cardiogenic shock is defined as organ dysfunction attributable to depressed and insufficient cardiac output, despite the administration of high doses of inotropes and vasopressors. Potential etiologies of shock include myocardial infarction, fulminating myocarditis, acute exacerbation of chronic heart failure, acute circulatory...
failure attributable to intractable arrhythmias, postcardiotomy cardiac failure, and acute heart failure attributable to drug intoxication, among others. Although the patient presented above represents an ideal candidate for VA ECMO—experiencing both refractory cardiogenic shock and severe respiratory failure—respiratory failure need not be present to consider the use of VA ECMO. When present concomitantly, frequent respiratory indications which can compel the choice of VA ECMO over pure mechanical circulatory support devices include hypoxic respiratory failure (PaO$_2$/FiO$_2$ ratio < 100), hypercapnic respiratory failure with an arterial pH < 7.20, compliance < 0.5 mL/cm H$_2$O/kg, significant or symptomatic pulmonary hypertension, and pulmonary shunt fraction > 30%. Clinical causes can include acute respiratory distress syndrome, severe bacterial or viral pneumonia or pneumonitis, status asthmaticus, decompensated end-stage pulmonary fibrosis, near drowning, and acute smoke inhalation. VA ECMO can also be considered for patients experiencing a cardiac arrest who remain refractory to initial resuscitative efforts, so called eCPR. Several working groups, including the Extracorporeal Life Support Organization (ELSO) and the European Extracorporeal Life Support Working Group, have advanced recommendations for the use of ECMO in critically ill patients.\textsuperscript{6,7} Table 1 lists common indications for VA ECMO.

Importantly, ECMO is not a long-term therapy, and should be considered as a bridge to anticipated early recovery, to heart or lung transplant, or to long-term VAD. Considering patient prognosis and expectations before ECMO implantation is critical. Patients with nonrecoverable cardiac dysfunction who are not candidates for VAD or transplantation should not be selected for ECMO.

**Contraindications**

Beyond careful patient selection guided by anticipated clinical prognosis and comorbidities, several important clinical factors should be considered when selecting patients for ECMO. The benefit of ECMO in the presence of multiorgan failure is dramatically attenuated, and ECMO is associated with poor outcomes in patients who have already been mechanically ventilated for > 10 to 14 days at the time of cannulation.\textsuperscript{5,9}

Patients on ECMO require therapeutic-dose anticoagulation to prevent thrombosis in the setting of indwelling prosthetic tubing and extracorporeal circulation. Hence, ECMO is usually contraindicated in patients with contraindications to anticoagulation, including active bleeding, recent noncardiothoracic surgery, or a hemorrhagic intracranial event. VA ECMO is also contraindicated in patients with severe aortic regurgitation or aortic dissection. Table 2 lists common contraindications to VA ECMO.

### Table 1. Potential Indications for Veno-Arterial Extracorporeal Membrane Oxygenation*

<table>
<thead>
<tr>
<th>Cardiogenic shock</th>
<th>Acute MI</th>
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<tbody>
<tr>
<td>Fulminant myocarditis</td>
<td>Acute exacerbation of chronic severe HF</td>
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<tr>
<td>Acute circulatory failure attributable to intractable arrhythmias</td>
<td>Postcardiomyocardial failure</td>
</tr>
<tr>
<td>Postcardiomyocardial failure</td>
<td>Acute HF attributable to drug toxicity</td>
</tr>
<tr>
<td>Severe concomitant respiratory failure†</td>
<td>Hypercapnic respiratory failure (arterial pH &lt; 7.20)</td>
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</tbody>
</table>
| Severe ARDS‡              | ARDS indicates acute respiratory distress syndrome; HF, heart failure; and MI, myocardial infarction;  
|                           | *Partial list of potential indications.  
|                           | †Concomitant respiratory failure is not required for selection of veno-arterial extracorporeal membrane oxygenation, but compels consideration of this mode of life support over other modalities of mechanical circulatory support.  
|                           | ‡Defined as PaO$_2$/FiO$_2$ is ≤ 100 mm Hg on ventilators setting that include positive end-expiratory pressure ≥ 5 cm H$_2$O, with supportive clinical features including compliance < 0.5 mL/cm H$_2$O/kg. |

### Table 2. Frequent Contraindications for Veno-Arterial Extracorporeal Membrane Oxygenation*

<table>
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<tr>
<th>Absolute contraindication</th>
<th>Patients with nonrecoverable cardiac dysfunction who are not candidates for LVAD or transplantation</th>
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| Relative contraindications | Contraindications to therapeutic-dose anticoagulation†  
|                           | Severe aortic regurgitation  
|                           | Aortic dissection  
|                           | Existent multiorgan failure  
| Mechanical ventilation > 7–10 days | LVAD indicates left ventricular assist device.  
|                           | *Partial list of potential contraindications.  
|                           | †Contraindications to anticoagulation including active bleeding, certain recent surgeries, or hemorrhagic intracranial event. |

**Titration and Maintenance of ECMO**

Once VA ECMO support is initiated, clinical targets for titration include arterial oxyhemoglobin saturation of > 90%, venous oxyhemoglobin saturation of > 70% to 80%, and adequate tissue perfusion (including monitoring of end-organ function and blood lactate levels). Close surveillance by a trained ECMO specialist is essential for establishing and monitoring circuit function. If the venous oxyhemoglobin saturation is below target, blood flow rate can be increased, intravascular volume expansion may be undertaken, hemoglobin concentration may be increased via blood transfusion, and fever/pyrexia may be treated to decrease oxygen uptake. Unfractionated heparin infusion is maintained for an activated clotting time (ACT) of 180 to 210 seconds, or a plasma partial thromboplastin time (PTT) of ≥ 1.5 times normal. Low-tidal volume, lung protective, ventilatory strategies should be used to minimize barotrauma and volutrauma. These include using positive end-expiratory pressure to maintain alveolar recruitment, limiting tidal volumes to no more than 6cc/kg ideal body weight, and airway plateau pressures to ≤ 30 cm H$_2$O, and minimizing FiO$_2$. A lung rest strategy that ECMO makes possible...
generally results in further reduction of ventilator settings to tidal volumes of 1 to 2 cc/kg and plateau pressures of around 20 cm H₂O, until weaning from ECMO is contemplated. Reduction of ventilator support is often accompanied by increased venous return and cardiac output. The effects of changes in positive end-expiratory pressure on hemodynamics should be monitored closely. One unique aspect of VA ECMO is the need to assure that the left atrium and ventricle do not become distended, a complication which can lead to myocardial injury. Serial echocardiograms can monitor cardiac filling, and occasionally addition of a vent cannula or alternative support modalities (such as percutaneous VAD, including Impella) has been used to decompress the ventricle. Pending projected ventilator dependence, tracheostomy can be performed to improve patient comfort and reduce ventilatory dead space. Patients on ECMO do not necessarily require sedation once on ECMO, but VA ECMO circuitry is extensive, and ambulation on VA ECMO is generally not possible. Ultrafiltration or other modalities of renal replacement therapy may be added in series to ECMO circuits, decreasing the risk of infection associated with placement of additional percutaneous cannulas, but increasing the risk of thrombosis, air embolus, or other disruption of the circuit.

**Weaning ECMO**

Potential recovery of left ventricular systolic function should be monitored closely by examining for pulsatility in the arterial line waveform and by echocardiography for patients on VA ECMO. In parallel, improvements in arterial oxyhemoglobin saturation, pulmonary compliance measures, and chest radiography can suggest respiratory recovery for patients on VV ECMO. Once there is durable evidence of cardiac or respiratory recovery, trials of discontinuation of ECMO may be undertaken. A trial of discontinuation of VA ECMO may be undertaken by temporarily clamping the arterial and venous cannulas, and allowing blood to continue to circulate through an external tubing bridge between the inflow and outflow limbs. If a bridge is not present in the circuit for clamping, flow through the circuit can be decreased to a minimal volume with a reduction in the sweep gas, with close monitoring of blood pressure, oxygen saturation, and arterial blood gases. Such trials should only be undertaken when therapeutic anticoagulation is achieved, and the duration of these minimized, as the risk of thrombosis during this time is high, even on full-dose anticoagulation.

Weaning VV ECMO requires eliminating all countercurrent sweep gas through the oxygenator, so that blood flow remains constant but no gas exchange occurs. Ventilatory parameters are adjusted to maintain adequate oxygenation and ventilation off ECMO for several hours, and assessment of likelihood of successful decannulation determined. If respiratory failure persists but cardiac function begins to recover, care must be undertaken to assure that the mixing of oxygenated and deoxygenated blood remains adequately saturated in the ascending aorta; alternatively, such patients may be converted to VV ECMO.

**Complications of ECMO**

The most common complications of ECMO are bleeding (up to 34%) and thrombosis (up to 17%). The need for systemic anticoagulation to prevent thrombosis at the blood-catheter interface needs to be counterbalanced with an elevated risk of bleeding. Disseminated intravascular coagulation, shearing hemolysis, and thrombocytopenia can develop insidiously or abruptly, and coagulation factors and platelet count should be closely followed. Patients are at elevated risk of embolic, hypoxic, and hemorrhagic stroke. Case series of VA ECMO have reported stroke rates of ≈8%.10

**Clinical Evidence**

Evidence supporting the application of VA ECMO as short-term life support in critically ill patients is limited, and is primarily from case series, cohort studies, and registry data, with a paucity of randomized, controlled trials. In 1 case series, patients were treated with ECMO for acute myocardial infarction (20%), fulminant myocarditis (20%), dilated cardiomyopathy (22%), postcardiotomy shock (20%), post-transplantation (12%), and for miscellaneous reasons (6%). The majority of patients were treated via femoral cannulation. Fifteen patients had ECMO placed for eCPR (only 1 of whom survived). Fifteen percent of patients had been treated with intra-aortic balloon counterpulsation before ECMO initiation. More than half of patients on ECMO experienced a major complication, including major bleeding (32% of all patients), femoral vein thrombosis (10%), arterial ischemia (19%), vena cava thrombosis (7%), surgical wound infection (17%), or overt pulmonary edema (6%). Stroke occurred in 8% of patients on ECMO. Of the initial 81 patients enrolled, 34 (42%) survived to discharge from intensive care unit, and 29 (36%) survived long-term.

Rastan et al11 reported their experience with ECMO as salvage therapy in patients with refractory postcardiotomy cardiogenic shock. Of this critically ill population (almost three-quarters of whom were still in shock despite intra-aortic balloon counterpulsation before ECMO implantation), ECMO was successfully weaned in 63%, and 25% of patients survived to discharge. Stroke occurred in 17%, gastrointestinal complications in 19%, and renal replacement therapy in 65%.

Using data from the multicenter ELSO registry, Thiagarajan et al12 reported that survival to hospital discharge was 27% among patients in whom ECMO was used to support CPR in cardiac arrest. Conversely, in patients with an out-of-hospital witnessed cardiac arrest who remain in refractory arrest, a single-center study reported extremely poor outcomes, even when ECMO was initiated very early (median time, 120 minutes), with only 4% of patients surviving to hospital discharge with a favorable neurological prognosis.13
Conclusions
VA ECMO is a potential therapy for patients with refractory cardiogenic shock, particularly in those with severe cardiogenic shock and combined respiratory failure. VA ECMO for cardiogenic shock is a bridge to recovery, durable VAD implantation, or transplantation, and clinical trajectory and prognosis must enter centrally into the judgment of a patient’s candidacy for ECMO. The use of VA ECMO in critically ill patients requires a multi-specialty team of practitioners.

The patient presented above remained on VA ECMO for 8 days, but was successfully decannulated after adequate cardiopulmonary recovery. On the 6th day on ECMO, she complained of homonymous hemianopia and was diagnosed with an occipital stroke, but fortunately had full neurological recovery. A secondary prevention implantable cardioverter defibrillator was placed. Genetic testing was undertaken which demonstrated a mutation in the cardiac sodium channel gene SCN5A, corroborating the finding of a Brugada pattern on ECG. Appropriate counseling and family screening was undertaken, and the patient has done well in follow-up.

Disclosures
None.

References