We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

6,500 Open access books available
177,000 International authors and editors
195M Downloads

154 Countries delivered to
TOP 1% Our authors are among the most cited scientists
12.2% Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Overview of Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO) Support for the Management of Cardiac Arrest and Cardiogenic Shock

Pankaj Garg, John H. Yazji, Emad Alamouti-Fard, Ishaq Wadiwala, Mohammad Alomari, Md Walid Akram Hussain, Mohamed Samir Hassan Elawady, Saqib Masroor and Samuel Jacob

Abstract

In the United States, ~100,000 patients are hospitalized annually for cardiogenic shock with 27–51% mortality. Similarly, ~356,000 patients develop out-of-hospital cardiac arrests (OHCA) annually with 90% mortality. In the last few decades, several acute mechanical circulatory support (AMCS) devices have been developed to provide hemodynamic support and to improve outcomes in patients with cardiogenic shock and cardiac arrest. Among all the devices, venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the only AMCS device that provides immediate and complete cardiopulmonary support. With an increase in clinical experience with VA-ECMO, use of VA-ECMO has expanded beyond post-cardiotomy cardiogenic shock. In the last two decades, there has also been a rapid growth in the observational and randomized data describing the clinical and logistical considerations with successful clinical outcomes in patients with cardiogenic shock and cardiac arrest. In this review, we discuss the fundamental concepts and hemodynamic aspects of VA-ECMO, its indications, contraindications, and the complications that are encountered in the setting of VA-ECMO in patients with cardiac arrest and cardiogenic shock of various etiologies.

Keywords: cardiogenic shock, cardiac arrest, ECPR, extracorporeal membrane oxygenation, myocardial infarction, sepsis, heart failure

1. Introduction

Extra corporeal membrane oxygenator (ECMO) is a type of cardiopulmonary life support in which blood is withdrawn from the venous system, circulated outside the...
body by a mechanical pump, and oxygenated carbon dioxide is removed with the help of a membrane oxygenator and then pumped back into the arterial (VA-ECMO) or venous system [1, 2]. ECMO provides an opportunity for both heart and lungs to rest and recover while body perfusion is maintained. Also, it helps to prolong the lives of patients on the waitlist for transplants list [3].

The history of ECMO dates back to 1944 when Kloff et al. were able to oxygenate blood when it was passed through the chambers of their artificial kidney [4]. Nine years after this breakthrough accomplishment, it was clinically applied when John Gibbon in 1953 repaired an atrial septal defect in an 18-year-old female on cardiopulmonary bypass (CPB) [5, 6]. After the introduction of Mayo-Gibbon machine in 1955, oxygenator becomes an integral part of CPB machine used for repairing cardiac defects [7]. In 1972, CPB machine was used for the first time for prolonged cardiopulmonary support for shock lung in a 24-year trauma patient with tear in thoracic aorta and other orthopedic injuries. The patient was supported on CPB machine for 75 hours and subsequently recovered [8]. Other cases quickly followed where CPB was used for prolonged cardiopulmonary support called extracorporeal life support (ECLS) [9, 10]. However, consistently poor outcomes in the majority of patients led to abandonment of ECMO. In 1976, Robert Bartlett used ECMO on a neonate suffering from meconium aspiration pneumonitis as rescue therapy. The baby recovered after 3 days and was successfully weaned from ECMO. This also led to the revival of ECMO to use as ECLS [11]. Earlier ECMO circuits had many problems including large circuits, large priming volume, the presence of bladder reservoir that increased the risk of air embolism, and roller pump that increased the risk of hemolysis, air, and particle embolism. Further, earlier ECMO was highly labor-intensive requiring constant vigilance to prevent the accidents. The ECMO circuit was initially optimized by Ken Litzie in 1983 decreasing the parts and intricacy of the machine, allowing for rapid deployment in a nonhospital setting [12]. With further improvement in machine design, use of centrifugal flow pumps with magnetically levitated rotating heads and use of silicone membrane oxygenators have made ECMO circuit low profile and less labor-intensive, and support the patient on ECMO safely for days to weeks without major complications. Although the origin of both CPB and ECMO machines is from same root, there are significant differences between both as summarized in Table 1 [13].

Despite significant improvement in the ECMO circuit design, until 2009, ECMO was frequently used only for pediatric patients with good outcome. However, use of veno-venous ECMO (VV-ECMO) during the swine flu pandemic in 2009 with good outcome led to the revival of ECMO in adults. This was further boosted by successful use of ECMO in patients with COVID pneumonia during recent pandemic. Presently, ECMO circuit can be easily transported in both air and ground ambulances and instituted in a variety of cardiac and noncardiac conditions at various facilities like in the ward, operating room, cath lab, and even in the fields (mobile ECMO programs) at the site of cardiac arrest (CA) and even with ongoing cardiopulmonary resuscitation (CPR). Further, ECMO can provide robust biventricular as well as respiratory support in patients with severe refractory CS for prolonged duration with a patient being extubated and ambulant. Full VA-ECMO support offers time to perform diagnostic and therapeutic interventions while maintaining appropriate hemodynamics and gas exchange and organ perfusion.

In this chapter, we will review basics of ECMO and various indications of ECMO in patients with cardiogenic shock (CS) and cardiac arrest.
Overview of Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO) Support...

DOI: http://dx.doi.org/10.5772/intechopen.105838

1.1 Components

ECMO circuit consists of venous and arterial cannulas for drainage and return of blood, respectively, a hollow fiber membrane oxygenator for blood oxygenation and carbon dioxide (CO2) clearance, and a centrifugal pump for propelling the blood. The presence of membrane oxygenator is a critical distinguishing feature of ECMO from other acute mechanical circulatory support (AMCS) devices.

1.2 Cannulation technique

ECMO can be placed centrally or peripherally. Central VA-ECMO is usually placed in post-cardiotomy setting, when venous drainage cannula is placed in the right atrium (RA) or superior vena cava (SVC) and inferior vena cava (IVC) separately and oxygenated blood is returned directly into the ascending aorta. For the management of CS, peripheral VA-ECMO is most commonly performed and femoral artery (FA), and femoral vein (FV) is the most commonly cannulated. Alternate site of cannulation is axillary artery or subclavian artery for arterial return and internal jugular vein (IJV) for venous drainage. Artery can be cannulated percutaneously under fluoroscopic guidance or surgically with a chimney graft. The advantages of whole upper body cannulation are ambulation, lower risk of infection, limb ischemia, cannula site bleeding, and ease of maintaining sterility. However, more time-consuming needs the presence of a surgeon. On the other hand, femoral cannulation can be easily done percutaneously by an individual trained in ECMO cannulation and is rapid. Appropriate size cannula should be selected to reduce the risk of vascular injury and at the same time maintain the low negative inflow (preferably $<-50$ mmHg) and low outflow ($<300$ mmHg) pressures [14]. In our center, when femoral artery is cannulated for VA-ECMO, we always insert a 6 Fr distal reperfusion cannula into the superficial femoral artery to mitigate the risk of distal limb ischemia and splice into the arterial limb of the circuit (Figure 1).

1.3 Hemodynamic aspects of VA-ECMO support

Among all the available AMCS devices, VA-ECMO has the highest capability to reduce myocardial pressure-volume area (sum of myocardial potential energy and

<table>
<thead>
<tr>
<th></th>
<th>ECMO</th>
<th>CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump</td>
<td>Centrifugal</td>
<td>Roller</td>
</tr>
<tr>
<td>Heparinization</td>
<td>50–100 units/kg</td>
<td>200–300 units/kg</td>
</tr>
<tr>
<td>Circuit type</td>
<td>Open</td>
<td>Closed</td>
</tr>
<tr>
<td>Maximal duration of circulation</td>
<td>Weeks</td>
<td>Hours</td>
</tr>
<tr>
<td>Ischemia of lower limbs</td>
<td>Common (peripheral ECMO)</td>
<td>Rare</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>Less frequent</td>
<td>More frequent</td>
</tr>
<tr>
<td>Activated clotting time (ACT) necessary</td>
<td>150–170 s</td>
<td>&gt; 400 s</td>
</tr>
<tr>
<td>Reservoir</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Open air contact</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>

Table 1. Comparison of ECMO and CPB.
myocardial stroke work) in patients with CS reducing left ventricular end-diastolic volume (LVEDV) and left ventricular end-diastolic pressure (LVEDP) while providing complete hemodynamic and respiratory support. Myocardial pressure-volume area is further reduced by the weaning of inotropes and vasopressors. All these prevent the vicious cycle of maladaptive neurohormonal and vascular mechanisms. Also, native RV function is not critical to provide systemic perfusion due to its reduced reliance on transpulmonary flow.

VA-ECMO improves systemic perfusion by increasing the MAP, reducing CVP, and increasing the systemic arteriovenous pressure gradient. This maintains the organ function and reduces the generation and accumulation of toxic metabolites. This may be particularly relevant to improving blood flow in organs with portal circulation, such as the liver and kidney. Fluid removal and reducing the venous congestion can be further enhanced by splicing a continuous veno-venous hemodialysis machine (CVVHD) into the VA-ECMO circuit [15–19].

1.4 LV distension

The Achilles heel of VA-ECMO is LV distension. The LV distension occurs when LV is unable to eject the blood returning to it. Sources for blood return to the LV are aortic regurgitation, Thebesian and bronchial veins draining in the left atrium, and systemic venous return that is not captured by the ECMO venous cannula. Uncaptured systemic venous return is the most significant source of LV blood flow, and it is directly proportional to RV function. Due to the lack of reservoir and longer and thinner peripheral venous cannulas with higher impedance, a significant amount of blood escapes drainage. To eject the blood, LV must have enough contractile function to overcome afterload due to retrograde flow of blood toward aortic valve at a higher pressure. If LV is severely dysfunctional, it may be unable to generate enough pressure and aortic valve may remain closed throughout cardiac cycle. This leads to increased LV wall stress, and myocardial oxygen demands as well as the stasis of blood in the aortic root with a potential risk of thrombus formation. Also, elevated LVEDP may result in pulmonary edema, pulmonary hemorrhage, systemic, cerebral, and myocardial hypoxia. The risk of LV and aortic thrombus formation is higher with peripheral cannulation due to a larger column of aortic root blood stasis and carries the risk of embolization down the coronary arteries, head vessels, or body. Therefore, it is important to vent the LV during VA-ECMO in patients with noncompliant LV and a competent mitral valve [20].
1.5 Diagnosis

In a patient on VA-ECMO, a dilated and hypocontractile LV with or without severe MR, stagnation of blood on echocardiography, pulmonary artery diastolic pressure >25 mmHg, and an elevated PCWP on Swan-Ganz catheter monitoring are sufficient to diagnose LV distension [19].

1.6 Indications for LV venting and unloading

On ECMO, indicators of good LV decompression are AV opening with every beat, systemic arterial pulse pressure >10 mmHg, and low PCWP. As the initial therapy inotropes, vasopressors, diuretics, and CVVHD to aid with managing volume status should be tried. Additionally, ECMO flows should be titrated to the lowest acceptable level to reduce the LV afterload. If medical management fails, one should consider LV venting [21].

Percutaneous transvenous atrial septostomy can be created under fluoroscopic and echocardiographic guidance in the catheterization lab to vent the LV. However, LV decompression through atrial septostomy is limited and dependent upon associated MR.

1.7 Percutaneous devices for LV unloading

LV can be unloaded by percutaneous devices like intra-aortic balloon pump (IABP) Impella, and TandemHeart. Impella is more robust device for LV unloading, and it also improves systemic perfusion. Impella is particularly important in patients with severely reduced LV contractility [22]. In our institute, we institute both arterial cannula and Impella 5.5 through AxA over Y chimney graft and venous cannula through IJV. Advantages of our technique are ambulation and weaning and ECMO decannulation with oversewing the Y limb of the graft can be done under local anesthesia and sedation.

1.8 Open surgical and minimally invasive LV unloading

LV unloading can be done by a surgically placed vent into the LV via the right superior pulmonary vein or via LV apex. In nonpost-cardiotomy patients, a surgical vent can still be placed into the LV apex via a left anterolateral thoracotomy and sliced into the venous limb of the ECMO cannula. Compared to ECpella, this approach perfuses the oxygenated blood into the aortic root, brain, and upper body and it unloads both the RV and LV more efficiently [19, 23].

In a patient with VA-ECMO with LV venting, patient must have a right radial arterial line for oxygenation monitoring, and a Swan-Ganz catheter in place to check mixed venous saturation, PCWP, and PAP. Daily chest X-rays should be obtained to assess degree of pulmonary edema, Impella position, and ECMO venous cannula position. Echocardiography should be performed to ensure the Impella position and LV decompression [19].

1.9 Results

Studies by Patel et al., Tepper et al., and Pappalardo et al. have shown improved survival in patients supported with ECpella with reduced all cause 30-day mortality.
compared to patients supported with VA-ECMO with inotropes or surgical LV venting. The studies attributed this improved survival to Impella as Impella was an effective means of LV unloading and prevented worsened pulmonary edema. Furthermore, the ECpella patients had a higher rate of successful bridging to either further recovery or further therapy [24–26].

1.10 Complications of VA-ECMO

Major complications are bleeding and thromboembolism (Figure 2).

1.10.1 Bleeding

Bleeding occurs in 30–50% of patients on VA-ECMO primarily due to anticoagulation and platelet dysfunction. Bleeding may occur at the cannulation site or into the body cavities (e.g., brain, abdomen, pleural and pericardial space) and may require surgical exploration to achieve hemostasis.

1.10.2 Thrombosis and thromboembolism

Systemic thromboembolism may occur due to thrombus formation in the arterial side of VA-ECMO circuit and has devastating consequences. Venous thrombosis may develop at the cannulation site with the development of deep venous thrombosis and pulmonary embolism. Arterial thrombosis may lead to limb ischemia and gangrene. To prevent complications, circuit should be regularly inspected for signs of clot.

Figure 2. Complications of VA-ECMO.
formation at the connectors site, tubing, and oxygenator, and monitoring the pressure gradient across the oxygenator. A sudden change in the pressure gradient suggests the development of thrombus. Large or mobile clots require immediate circuit or component exchange.

1.10.3 Neurological

The incidence of neurologic injury varies from 10% in adult respiratory failure patients to 50% in patients with ECPR. The types of neurological injury included coma, encephalopathy, anoxic brain injury, stroke, brain death, and myoclonus.

1.10.4 Cannulation-related

These complications are uncommon (<5%) and include vessel perforation with hemorrhage, arterial dissection, distal ischemia, and incorrect location (e.g., venous cannula within the artery).

1.10.5 Heparin-induced thrombocytopenia

Heparin-induced thrombocytopenia (HIT) can occur in patients receiving ECMO. When HIT is proven, the heparin infusion should be replaced by a nonheparin anticoagulant. We favor switching to bivalirudin in our institute.

1.11 VA ECMO-specific complications

- Pulmonary edema and hemorrhage, aortic root, and LV thrombus occur in patients who develop LV distension and stasis of blood in the LV and aortic root during VA ECMO. It is treated by venting the LA or LV.

- Coronary or cerebral hypoxia: Patients with good ventricular function and associated pulmonary pathology may develop coronary and cerebral hypoxia due to selective perfusion of the heart, brain, and upper extremities by LV blood. Condition is managed by infusing oxygenated blood into the right atrium (called VA-V ECMO).

1.12 Contraindication to VA-ECMO

For severe PAD (percutaneous only) and moderate or severe aortic regurgitation, although ECMO provides the highest level of support, it can lead to significant complications including pump thrombosis, bleeding, ischemic limbs, and Harlequin syndrome.

2. ECMO in cardiac arrest

Cardiac arrest is defined as the sudden cessation of cardiac activity as the victim is unresponsive, has no circulation, and is unable to breathe. The sudden cessation of cardiac activity may result in the death of the victim if not identified and treated quickly. It is a major public health hazard that impacts an estimated 356,500 people out of hospital and 209,000 people in the hospitals each year. An acute coronary
syndrome is the most common cause of CA. Other common causes include pulmonary embolism, dyskalemia, acute respiratory failure, hypovolemia, sepsis, and poisoning [27]. Cardiac arrest can occur in hospital (IHCA) or outside hospital (OHCA). In a person with OHCA, cardiopulmonary resuscitation (CPR) should be initiated immediately. Mass public awareness, basic life support (BLS) training for general population, widespread availability of defibrillators, rapid response paramedic teams, and in-hospital CPR response teams, development of protocols for effective CPR have led to early and effective institution of CPR in patients with both OHCA and IHCA, especially in the developed countries; however, outcome remains dismal with <10% survival. The most important reason for high mortality after CA is the prolonged absence of blood flow to the brain and other vital organs leading to anoxic brain injury and irreversible damage to the other organs.

Till two decades back, conventional CPR (CCPR) including both basic life support and advanced cardiac life support (ACLS) was the best treatment plan for patient with CA as it would give them the best chance of survival. The purpose of doing CCPR in a patient with CA is to maintain the cerebral and coronary perfusion till the heart recovers its rhythm and contractility as the absence of cerebral blood flow for more than 3–5 minutes results in severe irreversible anoxic brain injury [28]. Studies have shown that despite effective CCPR, cerebral blood flow is only 30–40% of the resting blood flows [29]. Also, cardiac recovery with CCPR remains poor as it is unable to unload the distended LV. The distension of the heart after CA results in stretching of myofibrils beyond the physiological Frank-Starling limits. The myocardial stretching not only results in myocardial stunning but also myofibrils are unable to return to their normal resting tone unless the ventricle is empty. Therefore, despite effective BLS and ACLS, 30-day survival for a patient with OHCA is only 8–10.7%, while for IHCA the survival rate is 17–28% [30–32]. This high mortality rate led to develop new ways to treat people with CA. One of the techniques that have been developed is combining CPR with ECMO, which is known as extracorporeal cardiopulmonary resuscitation (ECPR) [33].

After the publication of few case reports about the successful use of ECMO in patients with in-hospital CA in 2008, there was renewed interest in use of ECMO in patients with out-of-hospital cardiac arrest (OHCA). Still, the use of ECMO on patients with OHCA in the United States is scarce (0.69% patients in 2014) with variable but encouraging survival (6–56%) [34–37]. A systematic review of 25 studies including patients with OHCA and IHCA showed quite variable and inconsistent outcomes with the use of ECPR. However, results of ECPR were consistently better in IHCA. This is due to difficulty in initiation of ECMO in the field. Therefore, patients with OHCA should be rapidly transported to the hospital and during transport, an automated external defibrillator (AED) should be used for automated cardioversion. Once patients arrive at the hospital, AED should be removed and ECMO is placed and initiated. Further study is needed to determine the effectiveness of the process and the survival rate [38].

3. Extracorporeal cardiopulmonary resuscitation

Extracorporeal cardiopulmonary resuscitation is an alternative method of providing cardiopulmonary resuscitation by using the ECMO device combined with CCPR in patients with CA and CS [39, 40]. ECMO takes over the function of the heart and lungs, and maintains the organ perfusion while allowing the time for heart
Overview of Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO) Support...

DOI: http://dx.doi.org/10.5772/intechopen.105838

and lung to recover and buy some time to investigate the cause of acute deterioration, to assess and treat underlying pathology to prolong the survival while minimizing complications. However, ECPR is a complex labor-intensive intervention that requires a highly trained team, specialized equipment, and multidisciplinary support within a healthcare system, and it has the risk of life-threatening complications including vessel rupture, bleeding, and thromboembolism. Therefore, physicians should carefully select patients for ECPR who can gain the most benefit, instead of applying ECPR indiscriminately.

4. Patient selection for ECPR

ECPR is a final effort employed in a patient with a deep circulatory shock after CA that is refractory to all standard treatments, and no further intervention will assuredly lead to the patient’s demise. ECMO is brought in this scenario to assist with shock state while dithering to elucidate the cause of CA and later allows reversal if possible [41]. The American heart association guidelines advised that ECPR should be instituted in a patient if ECMO is rapidly available and deployable within a facility, patient has a brief duration from collapse, and the underlying condition is reversible [42]. As ECPR is a complex technique that requires an experienced and well-trained paramedic team, careful precision, teamwork, and coordinated efforts of a lot of persons to institute ECMO with ongoing, patients with CA should be carefully selected who can potentially benefit from ECPR [43].

In patient with OHCA, prognostic factors associated with better survival and neurological outcome are patient age <70 years, shorter duration of low flow, a sustained shockable rhythm, effective CPR with a target end-tidal carbon dioxide (ETCO2) > 10 mmHg during resuscitation, lower lactate level, higher pH, and lower SOFA score [44]. While these all criteria increase the likelihood of a favorable outcome, there are no universal selection criteria. Although there are no clearly defined indications, most

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 75 years old</td>
<td>Age &gt; 75 years old</td>
</tr>
<tr>
<td>Initial shockable rhythm</td>
<td>Non shockable rhythm</td>
</tr>
<tr>
<td>Pulseless VT/VF</td>
<td>InVF</td>
</tr>
<tr>
<td>CA due to or resulting in VF</td>
<td></td>
</tr>
<tr>
<td>No ROSC within 15 mins of ACLS</td>
<td>CPR &gt; 20 mins when the heart is in asystole (exception: hypothermia, drowning, and suspected pulmonary embolism) or VF/VT with ≥120 beats/min</td>
</tr>
<tr>
<td>CA due to reversible causes</td>
<td>CA due to Trauma or unamenable cause</td>
</tr>
<tr>
<td>High-quality CPR (ETCO2 ≥10 mm Hg)</td>
<td>Low-quality CPR (ETCO2 &lt;30 mm Hg)</td>
</tr>
<tr>
<td></td>
<td>Severely acidosis (pH &lt; 6.8) or elevated lactate (≥20 mmol/L)</td>
</tr>
<tr>
<td></td>
<td>Irreversible brain damage or poor neurological prognosis</td>
</tr>
<tr>
<td></td>
<td>Severe comorbidity that would prevent independent life</td>
</tr>
<tr>
<td></td>
<td>DNR/DNI or no consent given</td>
</tr>
</tbody>
</table>

VT = ventricular tachycardia, VF = ventricular fibrillation, ROSC = return of spontaneous circulation, DNR/DNI = do not resuscitate or intubate, CA = cardiac arrest, ETCO2 = end tidal carbon dioxide.

Table 2. Positive and negative predictors of ECPR.
centers perform ECPR for young patients with an initial shockable rhythm or presumed correctable cause and those with a witnessed collapse and bystander CPR without ROSC within 10–20 minutes of CCPR. In patients with IHCA, ECPR is useful in patients with CA in the cardiac surgical ICU, medical cardiac ICU, cardiac catheterization laboratory, and CA before or after cardiac surgery or intervention. When a cardiac diagnosis is irreversible pathology, cardiac replacement therapy, such as heart transplantation or artificial heart, should be considered [45, 46]. Poor prognostic factors after ECPR are patients with poor physical activity levels such as those confined to bed; severe permanent neurologic injury; noncardiopulmonary cause of arrest, such as severe sepsis; prolonged CCPR without ROSC; inadequate ACLS, such as failed advanced airway or ineffective chest compression due to severe hypovolemia or unfavorable chest wall anatomy (e.g., aortic rupture or severe pectus excavatum); and pre-existing severe multiple organ failure. However, no single one can be considered an absolute contraindication for ECPR; the physician in charge of a patient’s care should discuss resuscitation with leaders of the CPR and ECLS teams if the situation arises. Prognostic factors can be broken down into positive/negative factors influencing outcomes explained in Table 2 [46].

5. Implementation of ECPR

Institution of ECMO in adult patient with CA is challenging and should be performed by an expert specialized in percutaneous ECMO cannulation [47, 48]. Cannulation can be done in various locations including femoral vessel, internal Jugular vein (IJV)-femoral artery, femoral vein-subclavian artery, or IJV-subclavian artery [49]. The femoral vessels are most common and most appropriate for cannulation as it is easiest to locate the femoral vessels blindly with the pulse guidance, under Doppler ultrasound guidance as well as surgically even in the absence of pulse and also with ongoing CPR as groins are away from site of resuscitation and more
space is available to work compared to subclavian artery and axillary arteries that are very close to the site of CPR and always crowded. Percutaneous technique is easier and quicker and does not require surgical skills. However, percutaneous technique is fraught with the risk of inability to puncture or cannulate the vessel [50]. With open surgical cannulation, it is easier to locate and cannulate the vessel of interest, but it significantly impacts procedure time [51]. Further, availability of cardiac or vascular surgeons for the exposure of femoral vessels and need for appropriate setup and instruments are additional hurdles for open surgical cannulation. Although, in pediatric patients with ECPR, open surgical cannulation of carotid artery and internal Jugular vein is the standard of care, in adults with CA, percutaneous cannulation of femoral vessels is preferred as time is the essence. But, if this fails, then an open surgical technique must be used [52]. In ECPR, selection of appropriate size cannulas is especially important as the size of cannula determines how efficiently the ECMO will work. The largest possible venous and arterial cannula appropriate to provide >2.5 L/m² flow with injuring the vessels should be selected. For an adult patient, 23–25 Fr venous drainage cannula and 17–19 Fr arterial cannula are sufficient for adequate flow [41, 53]. The venous cannula is extended up to the right atrium or inferior vena cava and right atrial junction, and the arterial cannula is brought to the descending thoracic aorta (Figure 3).

6. Steps of institution of ECPR

With continued CPR, femoral artery and vein are cannulated percutaneously. After proper timeout, cannulas are connected to ECMO circuit and ECMO is initiated. After the achievement of adequate ECMO flows, CPR is stopped. Mild therapeutic hypothermia is achieved for 24–48 hours by cooling the patient to 33–34°C through integrated heat exchanger in the ECMO circuit. Permissive hypothermia reduces the tissue metabolism including cerebral metabolism, giving a better chance of survival of the patient, and reducing the progressive cerebral injury [54–56]. The patient is
Management of Shock - Recent Advances

connected to the ventilator to reduce the work of breathing. IV heparin is infused for anticoagulation and routine arterial blood gas (ABGs) and lactate monitoring are done to measure the success of ECMO, and mean arterial pressure (MAP) is aimed at 70 mmHg. As soon as a patient is stabilized on ECPR, he should be wheeled to the cath lab for angiography for coronary angiography with or without stenting. To prevent the ischemia in the limb with arterial cannula, 6–7 Fr, arterial cannula is inserted distally and sliced into the arterial cannula allowing perfusion of the distal limb. However, insertion of distal limb perfusion cannula may be extremely challenging in patients with peripheral vascular disease, profound shock with collapsed and constricted arteries, or obesity. The alternative in such patients may be to use retrograde limb perfusion through dorsalis pedis, anterior tibial, or posterior tibial artery. Reports have shown favorable results with retrograde limb perfusion with decreased incidence of leg ischemia and fasciotomy [57, 58]. In patients with small femoral vessels, an alternate technique may be to insert 12 Fr or 14 Fr bilateral femoral arterial cannula instead of a single 17 Fr or 19 Fr arterial cannula. The steps of ECPR are shown in Figure 4.

7. Complications of ECPR

ECPR, like other forms of ECLS, is used as a potential lifesaving approach. But it has the potential for adverse consequences ranging from minor to fatal complications. Observational studies show that 1 in 4 patients ends up having complications [59]. Complications include limb ischemia, vascular damage leading to inability to cannulate the vessel or profound intracorporeal or extracorporeal bleeding, tamponade, failure to maintain adequate ECMO flow resulting in inadequate support, and intracranial hemorrhage with grave consequences and dismal survival. Other issues such as multiple organ failure, sepsis, and hypoxic brain injury (cerebral stroke or cerebral stroke and hemorrhage, coma, diffuse axonic brain injury, and brain death) can also occur in the absence of adequate perfusion of the organs with oxygenated blood [50, 60].

8. Results

8.1 In-hospital cardiac arrest

Patients who have IHCA are usually witnessed and have high likelihood of a good outcome with CCPR. A considerable proportion of these patients are candidates for ECPR. However, of all patients who had an in-hospital cardiac arrest (IHCA), only less than 1% were treated with ECPR in the United States [61]. With widespread availability and increasing familiarity of physician with ECMO, ECPR is gradually increasing in the past 20 years in a hospital setting. Encouraging results of ECPR for IHCA include renewed interest in research in this field with the development of automated CPR tools, percutaneous cannula, and localization of vessels under ultrasound guidance. Even with this limited research, there have been promising results of ECPR on patients who had IHCA with survival rates between 17 and 28% [31, 32]. These survival rates have led to great optimism in ECPR as a treatment for CA. Chen et al. conducted a 3-year prospective observational study using ECLS. The inclusion criteria were patients aged 18–75 years old who had an IHCA of cardiac origin having CPR >10 min compared to patients with CCPR. The prognostic factors in both groups
were balanced by propensity score resulting in a comparable cohort, 113 with CCPR, and 59 in the ECPR group. Patients with ECPR had superior 1-year survival and survival to discharge rate, which was also the primary endpoint [62]. Shin et al. from Korea conducted a single-center, retrospective observational study from January 2003 to June 2009. A total of 406 patients had IHCA, broken down into a population getting CCPR (n = 321) vs. ECPR (n = 85). Propensity matching was used to balance the groups, and discharge with minimal neurologic impairment was used as the primary endpoint. ECPR group was superior in the primary endpoint. In addition, survival rates at 6-month survival were statistically significant in ECPR group [63].

8.2 Out-of-hospital cardiac arrest

Encouraging results with IABP in patients with coronary artery disease, cardiogenic shock, and postcardiotomy shock led to use of IABP for resuscitation of patients with CA. However, subsequent studies performed to review the results of IABP in patients with CA failed to show any survival benefit [64]. In a study by Iqbal et al. comparing the effects of IABP in patients with CA (55 patients with IABP vs. 174 without IABP), authors found no difference in favorable functional status at discharge (49.1% in IAPB group vs. 57.1% in without IABP group) and mortality rate at one year (45.5% in IABP group vs. 35.5% in without IABP group) [65]. In a randomized clinical trial by Firdaus et al. including 60 patients with CA due to acute coronary syndrome patients (ACS) (30 patients received IABP after CA vs. 30 patients without IABP), there was no difference between the groups in terms of hospital mortality, hospital stay, cell death marker, or improvement in lactate clearance [66].

8.3 Comparison between in-hospital and out-of-hospital cardiac arrest

The length of CA, which is more relevant than the site of CA, is an important variable for the disparity in outcomes. IHCA patients are more likely to witnessed with a shorter time to initiate BLS and ACLS and a shorter period until the initiation of ECMO, as well as that their comorbidities are known to the treating physician, implying a bias in the choice to implant an ECMO. The key element in determining the success of ECPR in a patient with CA is the amount of time elapsed between the occurrence of the CA and initiation of ECMO. In most cases, IHCA would have a shorter time in achieving the ECMO flow as the tools and equipment are more readily available than OHCA. Still, survival to discharge in patients managed with ECPR for OHCA was reported to be significantly higher compared to patients managed with CCPR (56.9% vs. 43.1%, respectively; OR: 1.16, 95% CI: 1.11–1.21, p < 0.001) [67, 68].

The CHEER trial (mechanical CPR, Hypothermia, ECMO, and Early Reperfusion), a single center, prospective, observational study done in The Alfred Hospital Australia, included 24 patients with IHCA and OHCA who were eventually put on ECMO. ROSC was seen in all the patients, and more than half could be taken off ECMO, eventually making the survival rate above fifty percent. Neurological recovery was seen in over half of the patients who were discharged from the hospital in similar numbers [54]. Another retrospective review from Canada by Sun et al. in patients who received ECMO for cardiac arrest (8 IHCA, 1 OHCA) or cardiogenic shock (13 patients) from April 2009 to July 2015 at Vancouver General Hospital in Canada reported that ECMO was successfully weaned off in 18 patients and 16 could be discharged. Fifteen patients had satisfactory neurologic outcomes [69]. Aforesaid studies demonstrate that in appropriately selected patients, ECPR provides survival benefits and more
positive neurological outcomes. In a meta-analysis including 2260 patients from six studies comparing ECPR or CCPR in patients with CA since 2000, Wang et al. reviewed the survival rates and neurological outcomes at discharge and at 3–6 months as well as 1 year after CA. The survival rate to discharge (RR 2.37, 95% CI 1.63–3.45, P < 0.001) and good long-term neurological outcome (RR 2.79, 95% CI 1.96–3.97, P < 0.001) were significantly better in ECPR group. In subgroup analysis, survival to discharge was significantly better with ECPR over CCPR in OHCA patients (RR 2.69, 95% CI 1.48–4.91, P = 0.001), while no significant difference was found in IHCA patients (RR 1.84, 95% CI 0.91–3.73, P = 0.09). The patient’s survival rate to discharge was 25.5% in patients who received ECPR, and 19.4% of them had good long-term neurological outcomes [70]. Authors concluded that with the availability of facilities using ECPR for IHCA, more patients would survive and have an active life with little neurological deficiency.

8.4 Limitations

ECPR remains a niche procedure that requires trained staff and resources, both of which are only available in tertiary centers with vital ECMO programs. Another problem is deciding which patients should receive ECPR, as the etiology alone is insufficient to foretell survival using ECPR. More multi-institutional studies are necessary to develop better guidelines for ECPR [71]. Presently, ECPR use is mainly limited to the pediatric population as most of the etiology is linked to congenital pathologies and may see better outcomes if ECMO buys enough time for recovery from postcardiotomy myocardial stunning, a transplant, or corrective procedure [72, 73].

9. Conclusion

Over the last several decades, healthcare results for this demographic procedure have improved significantly due to increased expertise and experience in patient care. ECMO remains an invaluable tool in the armamentarium of cardiac surgery, and its use combined with CPR has promising results, but it is hindered by nonavailability and high capital usage from the hospital. ECPR must be judicially used in the context of CA as every case will not lead to successful resuscitation. Surgical and medical management of CA patients continues to be difficult. Despite gains, various learning opportunities remain as we try to make even more progress.

9.1 Role of ECMO in cardiogenic shock due to acute myocardial infarction and nonacute myocardial infarction cardiogenic shock

Acute myocardial infarction (AMI) remains the leading cause of CS. However, non-AMI-related CS is on the rise. Etiologies of cardiogenic shock are enumerated in Table 3 [74]. The management and response to the intervention vary based on etiology. Despite optimal management, CS continues to be associated with significant morbidity and 30–60% mortality [75]. Various AMCS devices that are available for the management of these patients are IABP, Impella, Protec Duo cannula, CentriMag pump, TandemHeart, and VA-ECMO to provide left- and/or right-heart support [76]. Among all AMCS devices, IABP remains the most widely used, although the use of other more robust devices is increasing [76–78]. Among all the available devices, ECMO provides the highest level of cardiopulmonary support.
Overview of Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO) Support...
DOI: http://dx.doi.org/10.5772/intechopen.105838

In the subsequent sections, we will discuss the role of ECMO in CS due to AMI (AMICS) and in the subsequent section, we will discuss the role of ECMO in non-AMI CS including septic shock.

9.2 Role of ECMO in post-acute myocardial infarction cardiogenic shock

Shock is a condition of cellular and tissue hypoxia due to decreased oxygen delivery, increased oxygen demand, or inefficient oxygen utilization, or a combination of these [79]. Acute shock is reversible for a short duration, but it quickly becomes irreversible, leading to multi-organ failure (MOF) and death [80]. Cardiogenic shock (CS) occurs due to cardiac pump failure and defined as a primary cardiac disorder that results in both clinical and biochemical evidences of tissue hypoperfusion including altered mental status, oliguria, and respiratory failure. Clinical criteria include systolic blood pressure (SBP) ≤90 mmHg for ≥30 minutes or need for support to maintain systolic blood pressure ≥90 mmHg and urine output less ≤ 30 mL/h or cool extremities. Hemodynamic criteria include a depressed cardiac index (≤2.2 L/min/m²

<table>
<thead>
<tr>
<th>Acute myocardial infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical complications related to acute myocardial infarction</td>
</tr>
<tr>
<td>• Ventricular septal defect</td>
</tr>
<tr>
<td>• Ischemic mitral regurgitation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute on chronic heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute right ventricular failure</td>
</tr>
<tr>
<td>• Right ventricular myocardial infarction</td>
</tr>
<tr>
<td>• Right ventricular failure after left ventricular assist device</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute myocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory cardiac arrest</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-cardiomyopathy shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe valvular heart disease</td>
</tr>
<tr>
<td>Post-heart transplant primary graft dysfunction</td>
</tr>
<tr>
<td>Stress cardiomyopathy (Takotsubo cardiomyopathy)</td>
</tr>
<tr>
<td>Peripartum cardiomyopathy</td>
</tr>
<tr>
<td>Cardiac trauma with or without cardiac tamponade</td>
</tr>
<tr>
<td>Acute pulmonary embolism</td>
</tr>
<tr>
<td>Severe pulmonary hypertension</td>
</tr>
<tr>
<td>Drug intoxication</td>
</tr>
<tr>
<td>High-risk interventions</td>
</tr>
<tr>
<td>• Percutaneous coronary intervention</td>
</tr>
<tr>
<td>• Ventricular tachycardia ablation</td>
</tr>
</tbody>
</table>

| Septic shock |

Table 3. Potential indications for acute mechanical circulatory support device in cardiogenic shock.

In the subsequent sections, we will discuss the role of ECMO in CS due to AMI (AMICS) and in the subsequent section, we will discuss the role of ECMO in non-AMI CS including septic shock.

9.2 Role of ECMO in post-acute myocardial infarction cardiogenic shock

Shock is a condition of cellular and tissue hypoxia due to decreased oxygen delivery, increased oxygen demand, or inefficient oxygen utilization, or a combination of these [79]. Acute shock is reversible for a short duration, but it quickly becomes irreversible, leading to multi-organ failure (MOF) and death [80]. Cardiogenic shock (CS) occurs due to cardiac pump failure and defined as a primary cardiac disorder that results in both clinical and biochemical evidences of tissue hypoperfusion including altered mental status, oliguria, and respiratory failure. Clinical criteria include systolic blood pressure (SBP) ≤90 mmHg for ≥30 minutes or need for support to maintain systolic blood pressure ≥90 mmHg and urine output less ≤ 30 mL/h or cool extremities. Hemodynamic criteria include a depressed cardiac index (≤2.2 L/min/m²

15
of body surface area) and an elevated pulmonary-capillary wedge pressure (PCWP) >15 mmHg [81, 82].

Acute myocardial infarction complicated by cardiogenic shock (AMICS) is a grievous condition associated with significant morbidity and mortality. In several observational studies in patients with AMI, conservative therapy has >80% mortality [83]. Despite primary percutaneous intervention (PCI) with coronary artery angioplasty has significantly improved the survival and has become standard of care for the management of AMI, no definitive management is available for the patients with AMICS [84]. In patients with AMI, 3–10% patients develop CS. Emergency revascularization does not significantly reduce 30-day mortality but significantly improves the six-month survival and long-term outcome in patients with AMICS [83]. In patients with AMICS, mortality rate is 30–50% with primary PCI and >80% in patients without primary PCI [85–87].

Acute myocardial infarction due to acute myocardial ischemia results in severe systolic and diastolic dysfunction of the heart with elevation in left ventricular end-diastolic pressure (LVEDP), PCWP, pulmonary edema, decrease in stroke volume, and low cardiac output [88]. Therefore, the aim of treating AMICS patients is to alleviate myocardial ischemia, reduce ventricular loading, support cardiac and respiratory function, and improve end-organ perfusion [89].

Given the high early mortality rate associated with AMICS despite revascularization therapies, physicians have sought out other therapies to improve results. Advancement in the technology has expanded the availability of acute mechanical circulatory support (AMCS) devices such as intra-aortic balloon pump (IABP), Impella, and ECMO. IABP was the earliest available AMCS device. Positive impact in improving coronary and systemic perfusion and reducing the myocardial oxygen demand in the setting of heart failure reported in various animal and human studies in the late 1990s and early 2000s led to widespread use of IABP in patients with AMI [90, 91]. The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) registry also showed >15% reduction in in-hospital mortality with use of IABP in patients with AMI who underwent thrombolysis (46.5% in thrombolysis and IABP vs. 62.9% in thrombolysis alone, \( P < 0.005 \)). However, when the SHOCK Trial and Registry established the significant impact of early revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) on the survival in patients with AMI, use of IABP went into disrepute [83, 92]. Subsequent IABP-SHOCK II (Intra-aortic Balloon Support for Myocardial Infarction with Cardiogenic Shock) trial in 2012 that included 600 patients failed to demonstrate any benefit of IABP over medical therapy alone immediately prior to coronary revascularization in terms of reduced 30-day mortality, achieving hemodynamic stability, ICU stay, organ perfusion, dose of catecholamine, rate of stroke, bleeding, peripheral ischemic complications, recurrent AMI, and stent thrombosis [93]. Further 12-month and 6-year follow-ups of SHOCK-IABP II trial patients also did not show any mortality benefit [94, 95]. All of these led to downgradation of IABP use in patients with AMI-CS to class IIIB in the European Society of Cardiology and class IIb recommendation in the American College of Cardiology/American Heart Association guidelines [96, 97]. Subsequently, use of other AMCS devices has increased for the management of AMICS. In last decade, Impella has become the most commonly used device after IABP in patients with AMICS with LV dysfunction for periprocedural management. However, in patients with biventricular
failure, associated respiratory distress or acute respiratory distress syndrome (ARDS), and mechanical complications of AMI such as mitral regurgitation or ventricular septal defect, ECMO is preferred over other devices. In resource-limited countries where other AMCS devices are not available apart from IABP and ECMO, ECMO can be used for periprocedural management. Further, ECMO is the only AMCS device that provides complete cardiopulmonary support and improves end-organ perfusion. Studies have also supported the role of ECMO in the management of AMICS patients. A study by Sheu et al. including patients with AMICS who underwent primary PCI without the ECMO (115 patients) and primary PCI with ECMO (219 patients) found significantly reduced 30-day mortality (30.1% for ECMO group vs. 41.7% for non-ECMO group) with the use of ECMO [98]. Another study by Tsao et al. also evaluated the role of ECMO in patients with AMICS and managed with primary PCI. The first group managed with IABP (25 patients), and the second group managed with ECMO (33 patients). Baseline characteristics and disease severity including age, gender, coronary risk factors, TIMI risk scores for STEMI and NSTEMI, euro SCORE, APACHE score, and SYNTAX score (including the number of coronary vessels that were involved) were comparable in both the groups. Patients in the ECMO group had significantly increased survival compared to IABP group (44% in IABP group vs. 81.82% in ECMO group), and this trend continued through the 1-year follow-up (survival in IABP group 24% vs. survival in ECMO group 63.64%) [99]. A retrospective single-center study done by Esper et al. included 18 patients who received VA-ECMO for AMICS, after the revascularization therapy. ECMO run lasted for an average of 3.2 ± 2.5 days with a mean hospital stay of 23.4 days, and 67% of patients survived to discharge [100].

Another study by Negi et al. included 15 patients with AMI and refractory CS who were placed on VA-ECMO. One-third of these patients had OHCA and 60% had ST elevated AMI. In 60% of patients, IABP was inserted in addition to VA-ECMO. Median duration of VA-ECMO support was 45 hours, and 50% of patients were successfully weaned off VA-ECMO. The survival to discharge was 47%, and all survivors were alive 30 days after discharge. In total, 53% of patients experienced vascular complications [101]. Another observational study by Vallabhajosyula et al. utilizing the National Inpatient Sample database also reported 40.8% survival with use of VA-ECMO in patients with AMICS. The study analyzed 2962 patients over a period of 14 years. There was a notable trend toward improving survival over the course of time, and 12% of patients were bridged to a left ventricular assist device (LVAD) or heart transplantation [102]. A systematic review of nine studies of patients with acute myocardial infection-induced cardiac shock concluded that using venoarterial extracorporeal membrane oxygenation provides temporary support has more benefits compared to standards of care and can assure a higher survival rate [103].

Although various retrospective observational studies support the role of ECMO in the management of patients with AMICS, there have been no randomized controlled trials (RCTs) assessing the use of ECMO in AMICS. Currently, two European RCTs, EURO-SHOCK, and ECLS-SHOCK, are enrolling the patients. EURO-SHOCK will randomly assign 428 patients to ECMO or conventional therapy and evaluate 30-day mortality as the primary result; the study is anticipated to conclude in February 2024 [104]. ECLS SHOCK will also randomize 420 patients with AMICS undergoing revascularization to ECMO or medical treatment alone. The primary outcome is 30-day mortality, and the trial is anticipated to conclude in August 2023 [105].
9.3 Role of ECMO in nonacute myocardial infarction cardiogenic shock

Patients with acute heart failure (HF) who present in CS have high mortality. Conventional HF therapies including optimal medical management, inotropes, vasopressors, and IABP are the initial line of management. However, patients who fail to respond to medical management may benefit from VA-ECMO. It is indicated in patients with medically refractory CS and in patients at high risk of cardiogenic shock as determined by scoring systems such as CardShock risk score and IABP-SHOCK II risk scores. ECMO is also AMCS of choice in patients with CS who have biventricular failure, respiratory failure, life-threatening arrhythmias, or cardiac arrest. There is often an overlap between indications for ECMO and AMCS devices. However, patients with CS who have associated respiratory failure are best managed by ECMO [106, 107]. The outcome of ECMO in patients with HF varies significantly depending on the etiology. The survival after hospital discharge for patients managed with ECMO is 71.9% for myocarditis [108], 74.3% for patients with primary graft failure post-heart transplant [109], and 42% one-year survival for patients with acute decompensation of chronic cardiomyopathy. However, patients aged >75 years, patients with severe neurological injury, multiple organ failure, and multiple comorbidities are risk factors for adverse outcomes. Dangers et al. also reported poor outcomes of ECMO in patients with SOFA scores >13 prior to ECMO cannulation [110].

The role of ECMO in these patients varies depending upon the etiology and can be a bridge to recovery, bridge to transplant, bridge to left ventricular assist device (VAD), or bridge to decision [111].

1. Bridge to recovery (BTR): ECMO weaning rates are reported as 75.5% in patients with acute myocarditis, 87% for patients with primary graft failure after heart transplant, and 55% for AMICS. In most cases, recovery occurs within a week, and if recovery does not occur, the strategy must be changed to bridge to bridge (BTB) or Bridge to transplant (BTT) [108, 109, 112].

2. Bridge to bridge (BTB): Patients with CS due to acute on chronic heart failure are often bridged to durable VAD (the durable VAD itself may serve as bridge to transplantation). It is important to make the decision early to bridge to VAD after patient stabilizes on ECMO if there is no recovery of cardiac function [113, 114].

3. Bridge to transplant (BTT): With the availability of other robust percutaneous AMCS devices, it has become rare to use ECMO as a bridge to transplant, especially in adult patients as other AMCS devices are easier to manage and can be kept for longer duration without significant complications compared to ECMO.

4. Bridge to decision: Patients having acute decompensation with CS, especially with unknown neurological status, can be acutely managed with ECMO. This provides sufficient time for evaluation, intervention, and decision for further management while the heart and rest of the body are supported with ECMO. The decision of further management can be taken based on the recovery of organ function and neurological status.
9.4 Advantages of ECMO in cardiogenic shock

1. Easy and rapid insertion: Time is of essence for a patient rapidly deteriorating due to CS. ECMO can be placed rapidly percutaneously with Seldinger technique using ultrasound at the patient’s bedside, in the cath lab, in the operating room, and in the field. Even nonsurgeon medical personnel can insert an ECMO in the prehospital setting without compromising safety [115].

2. Provides complete cardiac support: With flow rates of up to 6 L/min, ECMO can completely replace native heart function in patients with profound CS [116].

3. Biventricular support: Almost 38–45% patients with AMICS develop acute RV failure and patients with chronic cardiomyopathy, post-cardiotomy also develop acute heart failure. Among all the available AMCS devices, only ECMO can provide complete biventricular support [117].

4. Respiratory support: In patients with ARDS with secondary Takotsubo syndrome and patients with CS having associated respiratory failure, increased pulmonary airway pressure can adversely affect the failing right heart. ECMO by providing complete cardiorespiratory support provide an opportunity to keep the ventilator at rest setting allowing the lungs to recover without barotrauma and preventing the adverse effect of high positive end-expiratory pressure on the right ventricle.

5. Effective in life-threatening arrhythmias: Uncontrollable arrhythmias, such as incessant ventricular tachycardia (VT storm), can be managed with ECMO by reducing myocardial stroke work and improving coronary perfusion, and patient can undergo ablation of VT focus in the cath lab on ECMO support [81].

6. Cardiogenic shock complicated by refractory cardiac arrest: CardShock study showed that 28% of patients with CS suffer from cardiac arrest. The use of ECMO in patients with witnessed refractory CA has been shown to improve survival [118].

7. Portable: Miniaturized ECMO machine is easy to transport on the ground as well as air ambulance.

9.5 Disadvantages of ECMO in cardiogenic shock

1. Left ventricular (LV) distension: ECMO drains the blood from the right atrial, but, has no direct effect on the left side of the heart. Due to the absence of reservoir, smaller size of venous cannula, significantly amount of blood escapes the venous drainage and reaches the left heart. Further, blood returning to the left atrium vis. Thèbesian veins, bronchial veins draining into the pulmonary veins, and blood returning to the LV due to aortic regurgitation also reach the left ventricle. Further, ECMO increases LV afterload by retrogradely flowing the blood into the ascending aorta. The heart with severely reduced contractility is unable to overcome this afterload, and the aortic valve remains closed. These patients are at risk of left ventricular distention, left atrial hypertension, and pulmonary edema [119].
2. Complications: Due to the large size of arterial and venous cannula, patients are at risk of vascular injury and injury to the heart. A meta-analysis reported 40.8% incidence of bleeding, 30.4% incidence of infection, 5.8% incidence of stroke, and 4.7% incidence of lower limb amputation [60]. The cannulation site is the most common site for bleeding [109, 120]. In a Japanese study, use of smaller cannula in small caliber vessels was associated with reduced risk of bleeding without compromising the outcome [121]. A meta-analysis of 22 cohort studies also found that distal perfusion cannulas reduced the limb ischemia by 15.7% [122]. Another devastating complication of ECMO is intracranial hemorrhage as patients on VA-ECMO are anticoagulated with heparin or bivalirudin. In a large study of adult patients with intracranial bleeds after ECMO, low platelets were independently associated with an increased risk of bleeding [123]. The risk of inter-cranial bleeding increased significantly at platelet counts below 50,000/cc. Therefore, it is recommended to maintain the platelet counts ≥100,000/cc while a patient is on ECMO [124].

The outcome of ECMO can be improved by using smaller cannula in small vessels, more liberal use of LV venting, routine use of distal limb perfusion cannula, and maintaining adequate platelet counts. SAVE and EN COURAGE score systems, which are used in pre-ECMO patient variables to predict outcomes, may help in better patient selection for this risky but life-saving intervention [125].

9.6 Sepsis-induced cardiomyopathy and Use of ECMO

Sepsis is a potentially life-threatening condition that occurs due to systemic dysregulated inflammation secondary to overwhelming infection, which affects various organs [125]. An important complication of severe sepsis is sepsis-induced cardiomyopathy (SIC), which is reversible depression of myocardium [126]. This occurs due to structural damage and dysfunction of the myocardium caused by widespread inflammatory cytokine release and mitochondrial dysfunction [127]. There are three characteristics of SIC: dilation of the left ventricle (LV), reduced EF (ejection fraction), and reversibility of cardiomyopathy in 7–10 days after the resolution of sepsis [128]. With improvement in the understanding of molecular biology, our understanding of SIC has significantly improved in last few decades. Although the use of ECMO is increasing in the treatment of various cardiac and noncardiac conditions, it has not been treated as standard practice protocol for adult patients with septic shock, unlike pediatric and neonatal patients [129–132]. Despite the ECMO has gained wide acceptance for the treatment of adult respiratory distress syndrome (ARDS), the effectiveness of ECMO in treating septic shock still remains controversial [129, 133]. In this section, we will discuss SIC and the viability of ECMO as a treatment option.

9.7 Mechanism of sepsis-induced cardiomyopathy

There are two different mechanisms proposed for the etiopathogenesis of SIC. First, based on animal studies, insufficient coronary blood flow is supposed to cause myocardial ischemia [134]. Second, due to the surge of chemical mediators such as cytokines, endotoxins, and nitric oxide (NO) that are released during the dysregulated inflammation may cause SIC. However, in a study done by Cunnion et al., measuring coronary blood flow and myocardial metabolism using coronary sinus thermodilution catheters in seven patients with septic shock to determine whether
myocardial depression was associated with reduced coronary flow [135]; the authors found that coronary blood flow was similar or higher in the patients with septic shock compared to the controls despite the presence of myocardial depression. A recent study by Rudiger and Singer has also shown that SIC cannot be attributed to the disruption in coronary circulation [128].

The role of chemical mediators has also been studied extensively in the pathophysiology of SIC. Studies have implicated the role of endotoxins, interleukin-1β (IL-1β), and tumor necrosis factor-alpha (TNF-α) in the pathogenesis of SIC [136–138]. Endotoxins induce NO synthase and increase the production and release of NO [136]. Similarly, cytokines such as TNF-α and IL-1β also increase the activity of cyclic guanosine monophosphate (cGMP) and NO [138]. It has been hypothesized that excess NO production causes cardiac dysfunction by reducing the myofibril response to calcium, dysfunction of the mitochondria, and downregulation of β-adrenergic receptors [128, 139, 140]. Several studies have also suggested that NO overproduction and mitochondrial dysfunction may contribute to cardiac dysfunction and mortality [141–144]. Interestingly, using methylene blue an inhibitor of NO production pathway has demonstrated improvement in myocardial depression, maintenance of oxygen transportation, and reduction in the requirement for concurrent adrenergic support [145].

9.8 Diagnosis, treatment options and use of ECMO

There is a range of tests that are available for diagnosing SIC. These include blood tests such as brain natriuretic peptide (BNP) assay and Troponin Assay as well as use of echocardiogram to check for ventricular dysfunction. While BNP and troponin I, both rise in SIC, their rise is mainly dependent on the severity of illness rather than markers for cardiomyopathy [146–148]. The gold standard for the diagnosis of SIC is echocardiography. Echocardiogram may show normal or reduced ejection fraction, LV diastolic dysfunction, and RV systolic dysfunction, as well as global longitudinal strain (GLS) on myocardial speckle tracking [149–152].

9.9 Improved outcome of patients with sepsis-induced cardiomyopathy and use of ECMO

While the management of SIC has been previously limited to vasopressors, inotropes, and fluid management, the use of ECMO has recently been explored. A low cardiac output due to SIC can impair the organ perfusion and precipitate multi-organ failure. Thus, it appears reasonable to identify and restore the cardiac output in these patients. Patients deteriorating despite maximal pharmacological support should be promptly transitioned to acute mechanical circulatory support (AMCS) device including VA-ECMO. Studies have found that VA-ECMO significantly improves the survival in patients with SIC with LV dysfunction compared to patients with preserved LV function [153, 154].

An important multicenter retrospective study performed by Bréchot et al. and published in 2020 investigated the role of VA-ECMO in patients with SIC. In this study, 82 patients with a sepsis-induced refractory shock treated with VA-ECMO were compared to 130 patients treated with conventional therapy for 90 days. Despite a propensity-weighted analysis, survival in the treatment group was higher than that in the control group (51% vs. 14%, relative risk for mortality 0.57, p = 0.003). The study also concluded that survival with VA-ECMO was better in younger patients and
the strong initial protective effect of VA-ECMO waned over time [(0 to 7 days: HR 0.14; 95% CI: 0.05 to 0.41) vs. (7 to 14 days: HR 0.79; 95% CI: 0.13 to 4.64)] [155]. The findings of the study emphasized that patients with SIC should be identified and supported with VA-ECMO as early as possible.

9.10 Patient selection for ECMO

In patients with sepsis, 13–65% develop SCM, but not all patients in septic shock will benefit from VA-ECMO [153, 156–158]. Patients with sepsis who are refractory to standard therapy, including adequate fluid resuscitation, antibiotics, and stress dose steroids, have increasing requirement of vasopressors and inotropes, and echocardiography findings are consistent with SCM, and they should be considered for prompt VA-ECMO support. A positive blood culture alone is not a contraindication for VA-ECMO, especially when source control and antibiotic therapy have already been initiated [159]. The early introduction of VA-ECMO and other types of MCS can prevent adverse effects of an escalating dose of inotropes and vasopressors and the mechanical ventilation, the effect termed as “metabolic rest” [160]. Any situation in which incremental escalation of standard therapies results in disproportionately lower hemodynamic improvement should warrant the use of ECMO and other AMCS devices. However, use of ECMO in patients with SCM who had CA remains controversial with poor outcomes [161, 162].

9.11 Concurrent management along with ECMO

In a patient with SCM supported by VA-ECMO, apart from managing ECMO, other important goals are augmentation of cardiac output, ventilator management, anticoagulation, and hemodynamic support [163]. Ventilation parameters should promote “lung rest” by offloading the mechanical power required for oxygenation and ventilation by the lungs [164]. Peak inspiratory pressure should be maintained <25 cmH2O and minimizes FiO2 while maintaining 5–12 cmH2O of positive end expiratory pressure (PEEP) to prevent atelectasis [165]. For anticoagulation, heparin is most commonly used and recommended by ELSO [166]; however, use of bivalirudin has been found to be associated with reduced mortality in adult patients [167]. For hemodynamic management, these patients are usually vasoplegic due to both septic shock and VA-ECMO and need vasopressors such as norepinephrine, phenylephrine, and the like.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fully restores cardiac output [167].</td>
<td>1. Resource and personnel intensive to manage ECMO.</td>
</tr>
<tr>
<td>2. Decompresses right ventricle [170].</td>
<td>2. Risk of LV distension due to increased systemic afterload especially in peripheral configuration [19].</td>
</tr>
<tr>
<td>3. Provide adequate pulmonary support [164].</td>
<td>3. Risk of ischemia of lower extremity (distal perfusion cannulation may alleviate this) [171].</td>
</tr>
<tr>
<td></td>
<td>4. The risk of cerebral hypoxemia (North-South Syndrome) [172].</td>
</tr>
<tr>
<td></td>
<td>5. Risk of heparin-induced thrombo-cytopenia (HIT) in patients receiving heparin as anticoagulant [173].</td>
</tr>
</tbody>
</table>

**Table 4.**
Pros and cons of using VA-ECMO in patients with septic cardiomyopathy.
vasopressin, and epinephrine to counteract vasoplegia. In case of suboptimal effect, agents such as methylene blue, hydroxycobalamin, and angiotensin II should be considered [168, 169].

**Pros and Cons of VA-ECMO in sepsis-induced cardiomyopathy:** While it has been established that ECMO is a viable option for management of SCM, **Table 4** presents the pros and cons of ECMO in patients with septic cardiomyopathy.
References


[56] Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. The


[104] Gershlick A. EURO SHOCK testing the value of novel strategy and its cost efficacy in order to improve the poor outcomes in cardiogenic shock. ClinicalTrials.gov identifier: NCT03813134

[105] Thiele H. Prospective randomized multicenter study comparing
extracorporeal life support plus optimal medical care versus optimal medical care alone in patients with acute myocardial infarction complicated by cardiogenic shock undergoing revascularization. ClinicalTrials.gov identifier: NCT03637205


registry. Journal of Cardiac Failure. 2018;24(3):148-156


Management of Shock - Recent Advances


