

ADVANCES IN MECHANICAL CIRCULATORY SUPPORT

Venoarterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock and Cardiac Arrest

Cardinal Considerations for Initiation and Management

ABSTRACT: Venoarterial extracorporeal membrane oxygenation (VA-ECMO)—also referred to as extracorporeal life support—is a form of temporary mechanical circulatory support and simultaneous extracorporeal gas exchange. The initiation of VA-ECMO has emerged as a salvage intervention in patients with cardiogenic shock, even cardiac arrest refractory to standard therapies. Analogous to veno-venous ECMO for acute respiratory failure, VA-ECMO provides circulatory support and allows time for other treatments to promote recovery or may be a bridge to a more durable mechanical solution in the setting of acute or acute on chronic cardiopulmonary failure. In this review, we provide a brief overview of VA-ECMO, the attendant physiological considerations of peripheral VA-ECMO, and its complications, namely that of left ventricular distention, bleeding, heightened systemic inflammatory response syndrome, thrombosis and thromboembolism, and extremity ischemia or necrosis.

Prashant Rao, MD
Zain Khalpey, MD, PhD
Richard Smith, MSEE, CCE
Daniel Burkhoff, MD, PhD
Robb D. Kociol, MD

WHAT IS VA-ECMO?

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is a form of temporary mechanical circulatory support and simultaneous extracorporeal gas exchange for acute cardiorespiratory failure.^{1,2} All VA-ECMO circuits consist of a venous (inflow, drainage) cannula, a pump, an oxygenator, and an arterial (outflow, return) cannula. VA-ECMO can be established via peripheral or central access (Figure 1). Central VA-ECMO is primarily implemented in the operating room and provides short-term support, often in postcardiotomy patients unable to wean from cardiopulmonary bypass.^{3,4} Peripheral VA-ECMO can be initiated percutaneously or by surgical cut-down outside of the operating room for patients with refractory cardiogenic shock and cardiac arrest via femoral artery and femoral or internal jugular vein access. Another configuration uses the standard venous access (either via the femoral or internal jugular vein) with arterial return to a graft placed on the subclavian artery.⁵ This latter strategy has been introduced to ensure perfusion of the cerebral circulation with oxygenated blood and to allow for the possibility for patients to ambulate while on ECMO. The focus of this review will be on the hemodynamics of cardiogenic shock and the impact of percutaneously placed VA-ECMO because this is the primary approach implemented by cardiologists and cardiac surgeons in emergency settings. The hemodynamic principles are similar among approaches; significant differences will be noted when appropriate.

Since its introduction in 1972,⁶ national trends demonstrate a substantial increase in peripheral VA-ECMO use for refractory cardiogenic shock.^{7,8} Since 1990, according to the Extracorporeal Life Support Organization registry, >15 000 adult patients

Key Words: extracorporeal membrane oxygenation ■ heart arrest
■ hemorrhage ■ shock, cardiogenic
■ thrombosis

© 2018 American Heart Association, Inc.

<https://www.ahajournals.org/journal/circheartfailure>

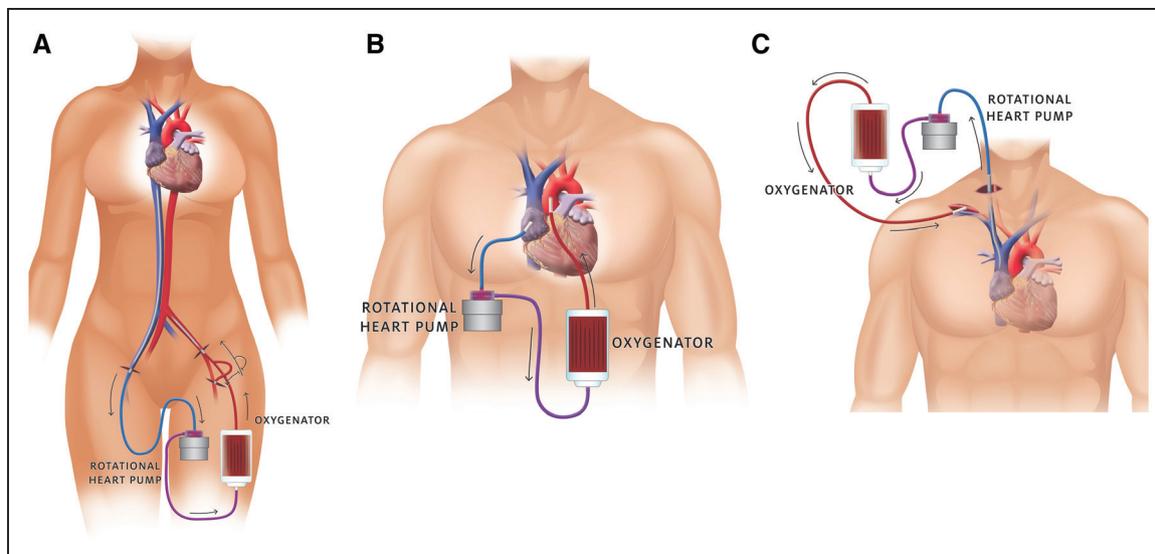


Figure 1. Central and peripheral venoarterial extracorporeal membrane oxygenation (VA-ECMO) cannulation strategies.

A, Peripheral VA-ECMO (femoro-femoral configuration). **B**, Central VA-ECMO. **C**, Peripheral VA-ECMO (sport configuration). Note although one may be cannulated peripherally through a peripheral vessel, the net effect on regional perfusion may be more akin to central cannulation (cannulation of the great vessels through a sternotomy). A good example of this is axillary cannulation as in (C).

have been supported with VA-ECMO with an $\approx 40\%$ survival rate to hospital discharge.⁹ Several single center studies support the use of VA-ECMO for refractory cardiogenic shock in carefully selected patients.^{10–14} Many centers have also assessed the role of peripheral VA-ECMO in refractory cardiac arrest (extracorporeal cardiopulmonary resuscitation). In no case, however, have randomized controlled studies been undertaken, largely because of the logistical, legal, and ethical issues involved in performing randomized studies in patients with cardiac arrest or severe cardiogenic shock. Suggestions of improved survival and neurological outcomes have been observed in select patient subgroups treated with extracorporeal cardiopulmonary resuscitation for refractory cardiac arrest. Such apparent benefit has been noted in the setting of in-hospital cardiac arrests, as well as where immediate and sufficient bystander cardiopulmonary resuscitation is performed, with minimal delay in initiating VA-ECMO.^{15–18} However, the overall survival rate using peripheral VA-ECMO in cardiac arrest and refractory cardiogenic shock remains generally reported between 29% (extracorporeal cardiopulmonary resuscitation) and 41% (refractory cardiogenic shock).^{19–21} Lack of clear evidence has resulted in the low-level recommendation for the use of VA-ECMO in current guidelines and then only for use in the setting of cardiac arrest.²²

As physicians care for an ever-increasing number of patients with profound refractory cardiogenic shock and cardiac arrest, we should better understand which patients could benefit from VA-ECMO, become increasingly familiar with its implementation, and understand how to optimize patient care while on ECMO. Overall, we should strive for better outcomes with this therapy. As such, cardiologists, cardiac surgeons, and critical care pro-

viders should familiarize themselves with the fundamental hemometabolic effects and limitations of VA-ECMO to better select the appropriate patient population and optimize device function during support and weaning. In particular, we will review 5 cardinal considerations (Figure 2) when assessing a patient for support and implanting VA-ECMO among an adult population with circulatory failure.

WHAT ARE THE BASIC HEMODYNAMIC FACTORS THAT UNDERLIE THE DEVELOPMENT OF CARDIOGENIC SHOCK?

Acute cardiogenic shock can be because of a rapid decrease in ventricular contractility in a previously normal individual as can occur with myocardial infarction or more gradually after an insult, such as acute myocarditis, where acute myocardial edema may impair ventricular filling and hence stroke volume despite an apparently mild reduction in ejection fraction. In addition, patients with chronic severe heart failure are also at risk for acute decompensation and cardiogenic shock because of either fluid overload (with consequent pulmonary edema, hypoxia, sympathetic activation, and progressive ventricular dysfunction) or progressive ventricular dysfunction independent of fluid overload, from other factors such as ongoing myonecrosis. The underlying hemodynamics of these 2 scenarios are summarized in the pressure-volume diagrams in Figure 3A and 3B, respectively. For those interested, a brief overview of the key features of ventricular pressure-volume analysis, which is critical for understanding hemodynamics and therapeutics of cardiogenic shock, is provided in the Appendix and Figure

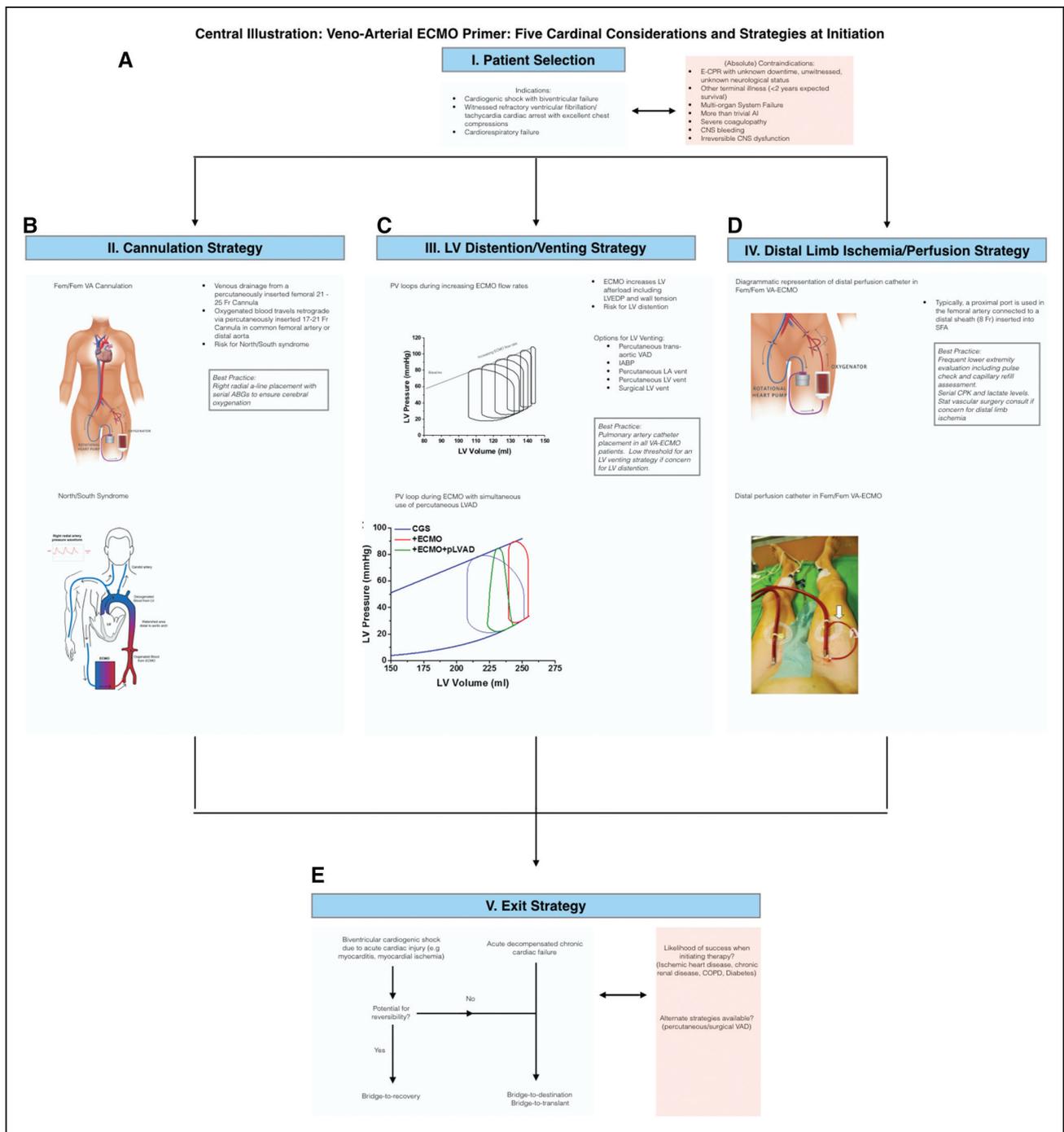


Figure 2. Cardinal considerations when implementing venoarterial extracorporeal membrane oxygenation (VA-ECMO).
A, Patient selection. **B**, Cannulation strategy. **C**, Left ventricular (LV) distention and LV venting strategy. **D**, Distal limb perfusion strategies to avoid limb ischemia.³⁶
E, Exit strategy (perhaps this should be thought of first). Does the patient have a viable exit strategy for continued survival and quality of life off of ECMO support (ie, recovery, transition to durable mechanical support, or transplant)? CNS indicates central nervous system; COPD, chronic obstructive airway disease; E-CPR, extracorporeal cardiopulmonary resuscitation; IABP, intra-aortic balloon pump; LA, left atrial; LVEDP, LV end-diastolic pressure; PV, pressure-volume; SFA, superficial femoral artery; and VAD, ventricular assist devices.

I in the [Data Supplement](#) and in several references.^{23,24} Typically, in common between the 2 clinical scenarios is the fact that the onset of cardiogenic shock is the result of a primary reduction of ventricular contractility (manifest as a reduced slope of the end-systolic pressure-volume relationship) compared with the respective baseline state, with secondary reflex-mediated increases in heart

rate, peripheral resistance, and venoconstriction. These primary and secondary effects conspire to increase the left ventricular (LV) end-diastolic pressure and pulmonary venous pressures; central venous pressures may also increase, even in the absence of significant right ventricular dysfunction because of redistribution of volume from the peripheral to central compartment. However,

Downloaded from <http://ahajournals.org> by on September 18, 2018

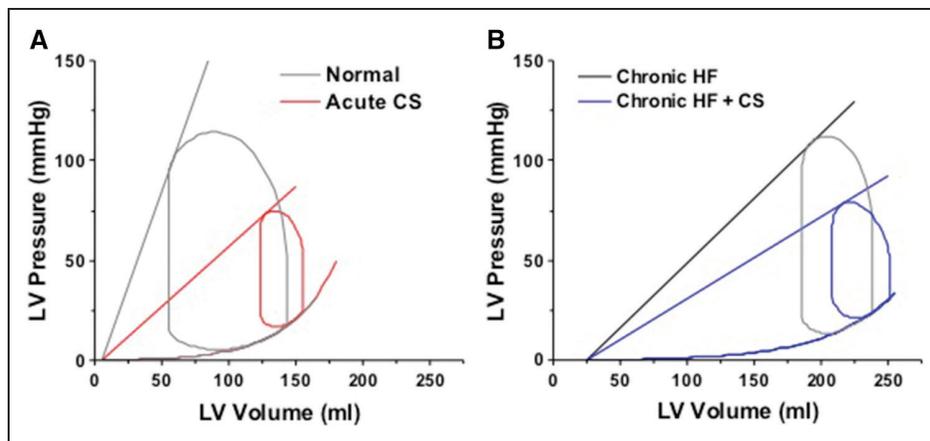


Figure 3. Pressure-volume loops illustrating the hemodynamics of acute cardiogenic shock amongst patients with previously normal heart function and prior heart dysfunction, respectively.

Pressure-volume loops during acute cardiogenic shock (red) in the setting of (A) previously normal myocardial function (black) and (B) chronic heart failure. Note in both cases (red end-systolic pressure volume relationship [ESPVR] line in the case of acute CS; blue ESPVR in the case of acute cardiogenic shock [CS] on top of chronic heart failure [HF]). The slope of the line created by the end-systolic pressure-volume relationship decreases resulting in both decreased stroke volumes and increased ventricular volumes and filling pressures. LV indicates left ventricular.

while blood pressures, wedge pressures, and cardiac outputs may be similar in these 2 scenarios, important differences include the initial and final ejection fractions and degree of compensatory LV dilatation. These differences are important to keep in mind, particularly when it comes to considering ventricular sizes and the need for triggering introduction of an LV unloading strategy during ECMO (discussed in detail below). Understanding of this pressure-volume representation of cardiogenic shock provides a strong foundation for understanding the impact of ECMO as will be illustrated below.

IN WHICH PATIENTS SHOULD VA-ECMO BE CONSIDERED? (CARDINAL CONSIDERATION I: PATIENT SELECTION)

As already noted, there are no clear society-endorsed evidence-based guidelines for the use of VA-ECMO or in the selection of patients most likely to benefit. In addition, it is important to note that the components of devices used to deliver VA-ECMO have received clearance from the US Food and Drug Administration for use up to 6 hours during procedures (eg, coronary bypass) and during patient transport. The Food and Drug Administration has approved such devices being used for respiratory support for >6 hours. Thus, information on which patients could derive benefit from ECMO relies on literature review and expert opinion. In this context, ECMO is most commonly considered in patients with profound cardiogenic shock and in the setting of cardiac arrest. Other common settings in which VA-ECMO is considered include biventricular failure and profound hypoxemia refractory to medical or other device-based interventions. In all these settings, the goal is to (mainly) take over the responsibility of providing oxygenated blood to the systemic circulation. However, understand-

ing the hemodynamics of ECMO is important for appreciating the need for appropriate patient monitoring to ensure that the LV and the lungs do not become fluid overloaded and, when present, that appropriate intervention is taken (detailed below). In this regard, one important principle is that while ECMO can unload the central veins, right atrium, and right ventricle, it does not intrinsically unload the LV, particularly when LV contractile function is severely compromised. In fact, ECMO in a poorly contractile heart can significantly increase the LV end-diastolic pressure and wall tension resulting in increased myocardial oxygen consumption and increased susceptibility to ischemia-mediated necrosis.

In patients with an acute profound but potentially reversible cardiac injury, such as myocarditis and myocardial ischemia, VA-ECMO may provide a bridge-to-recovery. In patients with acute decompensated chronic cardiac failure or massive myocardial infarction, VA-ECMO may be used as a bridge-to-destination therapy, such as a durable ventricular assist device and cardiac transplantation.²⁵

In many cases, alternative strategies, such as percutaneous or surgically implanted temporary ventricular assist devices (as a bridge to stability leading to durable support or recovery), should be considered to reduce many of the complications of ECMO, such as systemic inflammatory response syndrome, damage to platelets, and risks of bleeding, vascular damage, limb ischemia, and stroke.^{26,27} In addition, these strategies can prevent the development of pulmonary edema, increased myocardial wall stress, and the potential for cerebral hypoxemia. However, ECMO is unique among the acute mechanical circulatory support strategies in to date as providing oxygen and carbon dioxide exchange to take over for the lungs if needed. Accordingly, ECMO can be useful for patients with underlying lung disease.

As well as deciding on the need and cannulation strategy for VA-ECMO (Figure 1), clinicians should also

assess the likelihood of success when initiating this therapy. Risk factors associated with worse longer term outcomes after VA-ECMO include increasing age as well as comorbidities, such as ischemic heart disease, diabetes mellitus, chronic renal disease, and chronic obstructive pulmonary disease.^{14,28–30} Furthermore, the degree of acid/base disturbance and severity of liver/kidney dysfunction at the time of ECMO initiation are strong predictors of long-term survival.^{14,31,32} Several risk scores have been proposed for assessing the likelihood of survival to hospital discharge, such as PRESERVE (Predicting Death for Severe ARDS on VV-ECMO),³³ SAVE (Survival After Venous-Arterial ECMO),³⁴ and the simple cardiac ECMO³⁵ scores. These risk scores have modest discrimination at best. In light of the high in-hospital mortality, costs, and ethical issues, appropriate patient selection for VA-ECMO requires careful consideration of all the aforementioned factors.

HOW DOES ONE ESTABLISH PERIPHERAL VA-ECMO? (CARDINAL CONSIDERATION II: CANNULATION STRATEGY)

Peripheral VA-ECMO is established percutaneously or by vascular cut-down with dual cannulation of a peripheral vein and artery. Percutaneous insertion is performed using a modified Seldinger technique and is associated with lower bleeding and infection risk, as well as more rapid implementation. However, peripheral vascular disease, stenosis, or thrombus often limits the percutaneous approach.³⁶ Ultrasonographic evaluation of the vessels may be performed to assist in determining the optimal method for cannulation and guiding initial needle insertion.

Venous cannulas are typically 19F to 25F and drain blood from the superior vena cava, right atrium, and inferior vena cava, often via the femoral vein, right internal jugular vein, or subclavian vein.³⁷ These inflow cannulas have end and side holes to permit continued drainage in case the end of the cannula becomes obstructed, especially during higher flow conditions that would otherwise cause suction. Once blood is drained from the venous system, it passes through the pump and gas exchange circuit and is returned to the arterial system with resultant retrograde arterial flow.

Arterial cannulas are often 15F to 24F, and although multiple sites may be used, the femoral artery is typically cannulated given its size and ease of access via a percutaneous technique, with the end of the cannula terminating in the common femoral artery, common iliac artery, or distal abdominal aorta. Of note, in 1 small center study, 15F cannulas provide comparable clinical support to larger cannulas in that the larger cannulas allow for higher flows but are associated with

increased bleeding complications and limb ischemia. The smaller (15F) cannulas provided lower flow but also lower arterial complication rates.³⁸

The main advantage of peripheral VA-ECMO is the ease and speed of implementing this form of cardiopulmonary support outside of the operating room.³⁹ As such, VA-ECMO can be implemented for hemodynamic instability at the bedside, in the catheterization laboratory or even in the field. Ideally, even urgent ECMO is inserted with some type of imaging guidance—either fluoroscopy or transesophageal echocardiography, but neither are absolutely necessary.

Some benefits of a central cannulation strategy can be realized without requiring a sternotomy by using cannulation sites other than the femoral vessels. While still using a peripheral cannulation strategy, generally in the upper extremities, VA-ECMO via these other arterial cannulation sites include the axillary, innominate, or subclavian arteries.^{5,40} Although these approaches require surgical placement of an end-to-side Dacron graft and do not eliminate the potential for LV distention, they offer increased patient mobility and decrease the risk of cerebral hypoxemia and aortic root thrombosis. Unlike conventional cardiopulmonary bypass, central VA-ECMO does not use a cardiomy reservoir and is therefore associated with less inflammation and coagulopathy.⁴¹

WHAT ARE THE MAIN HEMODYNAMICS AND PHYSIOLOGICAL CONSIDERATIONS DURING VA-ECMO? (CARDINAL CONSIDERATION III: LV DISTENSION AND VENTING STRATEGY)

Using large cannulas and modern pumps, VA-ECMO flow support can be high although flows more typically run ≈ 3 to 4 L/min. By draining blood directly from the systemic venous system, VA-ECMO decreases right ventricular preload and peripheral venous congestion. Flow (Q) is driven by the pressure gradient established by the pump and is in large part determined by the radius (r) of the cannula (directly proportional to r^4) and inversely proportional to fluid viscosity (η) and cannula length (l) according to Poiseuille's law: $Q = \pi Pr^4 / 8\eta l$.

Although such diversion of blood from the heart might be thought to also reduce LV preload and decrease pulmonary congestion, this is not often the case. This relates partially because of the fact that the increased arterial flow provided by ECMO increases blood pressure.^{42,43} Hence, despite higher flows, ECMO does not eliminate return of blood to the LV. There is residual flow through the pulmonary circuit (because some blood is not diverted into the drainage cannula but flows through right atrium and right ventricle), Thebesian drainage of coronary blood flow, aortic regurgitation (if present), and return of bronchial blood flow to the left atrium (LA).⁴⁴ Blood

returning to the LV must exit through the aortic valve. In order for this to occur, the LV must be able to generate enough pressure to overcome the ECMO-induced increase in arterial pressure. Accordingly, an equilibrium condition must be established through adjustment of LV filling pressure (and use of the Frank-Starling mechanism) such that at the arterial pressure established during ECMO, LV outflow equals the flow returning into the LV from all sources.^{23,45} In turn, pulmonary capillary wedge pressure (PCWP) is determined by LV end-diastolic filling pressure. Assuming the pulmonary artery diastolic pressure is close to the LA pressure (as a surrogate of PCWP), this is an important parameter for monitoring LV filling pressure when wedging of the pulmonary catheter is not performed.

The impact of ECMO flow on right- and left-sided parameters is depicted in Figure 4 in a setting of fixed and significantly decreased LV contractile strength. Starting from baseline conditions, with each increment of ECMO flow (from 1 to 4.75 L/min), right atrial pressure decreases and aortic pressure increases; concomitantly, however, LV volumes increase (LV distention), LV stroke volume decreases while LV end-diastolic pressure, left ventricular end-systolic pressure, LA and pulmonary artery pressures increase⁴⁶; thus, ECMO can induce or worsen pre-existent pulmonary edema. Also, as flow is increased, and arterial pressure increases, arterial pulse pressure decreases, indicating progressive decreases in LV stroke volume and shorter durations of aortic valve opening. On the pressure-volume diagram, these are manifest as rightward/upwards shifts of the pressure-

volume loop along the end-diastolic pressure-volume relationship and narrowing of the loop (ie, smaller stroke volumes). At the highest ECMO flow rate depicted here, the aortic valve barely opens, which can cause stasis of blood within the LV chamber. As described by prior investigators,⁴⁷ stasis within the LV can lead to LV, aortic, and pulmonary thrombosis, which can result in stroke, peripheral emboli, pulmonary emboli, and, in many instances, is fatal.

Another factor is that LV distention in the setting of an increased afterload and raised LV diastolic filling pressures reduces the transcortical perfusion gradient and can impair coronary perfusion (subendocardial perfusion in particular), thus creating or worsening myocardial ischemia.⁴⁸ Overall, insufficient LV unloading has been cited as the main cause of poor LV recovery and inability to wean off VA-ECMO in at least one series.⁴⁹

In summary, LV distention, pulmonary edema, and blood stasis within the LV and aortic root are highly interrelated events. As discussed below, there are at least 8 different strategies to overcome these consequences of ECMO. But, of prime importance in the management of ECMO patients is the detection of these consequences through appropriate monitoring.

Finally, among the physiological considerations of initiating VA-ECMO is its associated inflammatory reaction, akin to that observed in systemic inflammatory response syndrome. This inflammatory response arises immediately as a result of blood exposure to the non-endothelialized surface of the ECMO circuit leading to activation of the innate immune system.⁴¹ Distinguishing

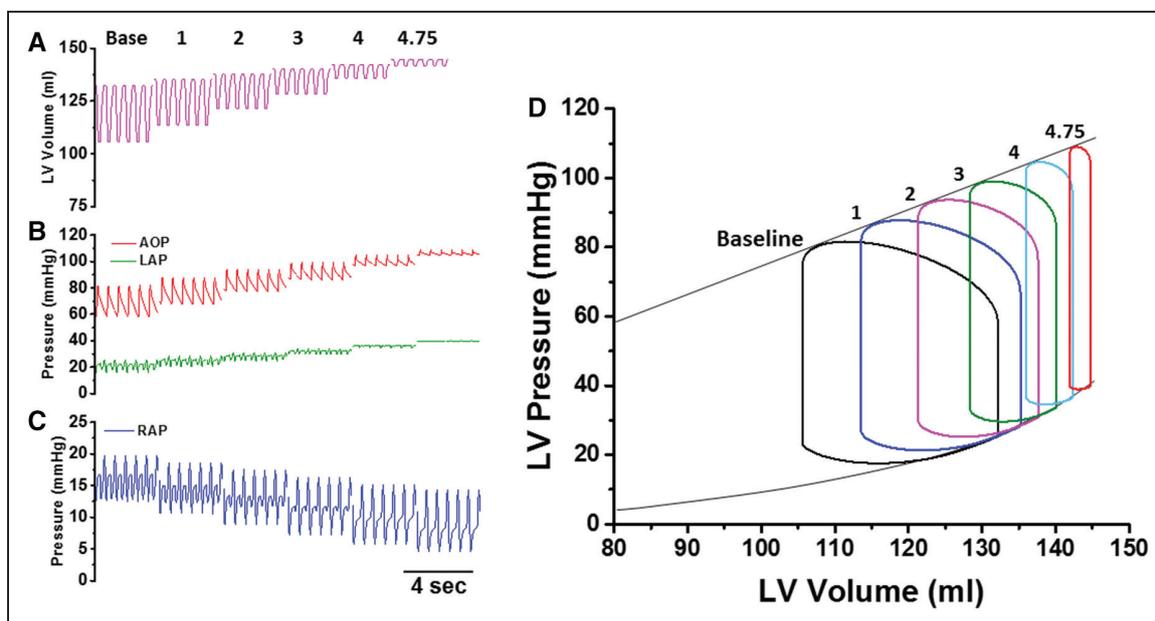


Figure 4. Hemodynamic changes that occur during acute cardiogenic shock and peripheral venoarterial extracorporeal membrane oxygenation (VA-ECMO) at increasing flow rates (1, 2, 3, 4, 4.75 L/min) with an unvented left ventricle (LV).

A, LV volume and pressure increases. **B,** Aortic pressure (AOP) and left atrial pressure (LAP) increase. **C,** Right atrial pressure (RAP) decreases. **D,** Pressure-volume loops generated during acute cardiogenic shock and VA-ECMO at increasing flow rates. With increasing ECMO flow rates, aortic pressure and afterload (slope of the arterial elastance and end-systolic pressure increase). There is a concomitant decrease in stroke volume (represented by the width of the pressure-volume loop) and an increase in LV volume (LV distention) and LAP. As stroke volume approaches zero, this would clinically correspond to the aortic valve remaining closed throughout the cardiac cycle.

post-ECMO initiation from patients with sepsis and bacteremia can, therefore, at times be challenging. Indeed, the use of VA-ECMO for septic shock is controversial.

HOW DOES ONE IDENTIFY PATIENTS AT RISK OF DEVELOPING LV DISTENTION AND PULMONARY EDEMA?

Recognition of LV distention and pulmonary edema during VA-ECMO support is important for patient care. There are several clinical indexes that can be used to monitor and identify patients at risk.⁵⁰ Most simply, the presence and degree of aortic valve opening can be detected on the arterial pulse pressure tracing. As illustrated in Figure 4, with increasing ECMO flow, mean arterial pressure increases but pulse pressure and stroke volume decrease, reflecting decreasing aortic valve opening. Second, echocardiography can be used to directly visualize the extent and duration of aortic valve opening (an M-Mode through the aortic valve is helpful to determine whether the aortic valve opens, and if so the degree and frequency of valve opening). In principle, echocardiography can also be used to assess changes in LV dimension; however, with regard to assessing LV distention, echocardiography can be particularly insensitive because the nonlinearity of the LV end-diastolic pressure-volume relationship and pericardial constraints may limit the change of LV dimension despite marked changes in LV end-diastolic pressure. In addition, because of the different premorbid condition (Figure 3), LV chamber size measured during ECMO support can be misleading as an index of ventricular distention, LV end-diastolic pressure, and PCWP. Third, progressive hypoxia in blood exiting the LV (eg, as can be measured from the right radial artery or by cerebral oximetry) can signify perfusion of the superior circulation with deoxygenated blood because of worsening pulmonary edema. Fourth, worsening pulmonary edema on a chest x-ray can signify worsening PCWP. However, this can be a late finding and is nonspecific because radiographic findings can also be because of other pathologies, such as acute respiratory distress syndrome or infection. Each of these 4 measures are straight forward for detecting aortic valve opening and LV loading but provide only indirect indexes of monitoring for increases of PCWP. The best index of LV filling pressures is to have a pulmonary artery catheter (PAC) in situ and measure either the pulmonary artery diastolic pressure or PCWP.

Accordingly, the most direct and time-sensitive means of detecting LV loading and worsening of pulmonary congestion is with the use of a PAC. Many experts advocate that all patients on VA-ECMO should be managed with a PAC, which is indeed the practice of many high-volume centers.⁵¹ Objections to the use of a PAC for the management of patients with cardiogenic shock

supported on mechanical circulatory support devices (including ECMO) are typically based on studies, such as the ESCAPE trial (Evaluation Study of Congestive Heart and Pulmonary Artery Catheter Effectiveness),⁵² and similar studies. However, patients who received inotropes and in whom the investigator believed could be helped with a PAC were excluded from such studies, and, accordingly, the conclusion that PACs are not helpful in this setting is completely unfounded.⁵³ Moreover, American Heart Association/American College of Cardiology guidelines recommend PAC use in complex cardiogenic shock.

WHAT ARE THE STRATEGIES FOR LV UNLOADING? (CARDINAL CONSIDERATION III [CONTINUED]: LV DISTENTION AND VENTING STRATEGY)

Once there is evidence of LV distention and worsening pulmonary edema (Figure 4A), some form of LV unloading or venting strategy should be introduced. It is noteworthy that at many centers, an LV unloading strategy is used early in the course of ECMO treatment not only to avoid elevations of PCWP but also to proactively unload the LV, often deploying an unloading device and ECMO sequentially during the same procedure. There are at least 8 different strategies for LV unloading, each with its own advantages and limitations. There are no studies comparing their relative effectiveness (on either hemodynamics or clinical outcomes), so clinical practice is typically guided by local expertise and experience. Developing a greater understanding of the hemodynamic principles by which each of these strategies work (Figure 5) may aid in decision making. A comparison of advantages and limitations of these approaches is provided in the Table. As we explore these options, it is important to note that the response to any strategy can vary significantly among patients because of the large number of hemodynamic factors that uniquely characterize a given patient physiological state (as detailed previously²³). Thus, the explanations provided below are based on theoretical considerations and do not provide findings that would apply to all patients, which reinforces the need for PAC monitoring to ensure desired effects are being achieved.

Reducing ECMO Flow

As illustrated in Figure 4, the higher the ECMO flow, the greater the degree of LV loading. Accordingly, reduction of ECMO flow rate can reduce LV loading and increase the degree of aortic valve opening. However, when ECMO flow is decreased, so too is the degree of cardiopulmonary support, which may not be possible depending on the patient's needs for arterial pressure

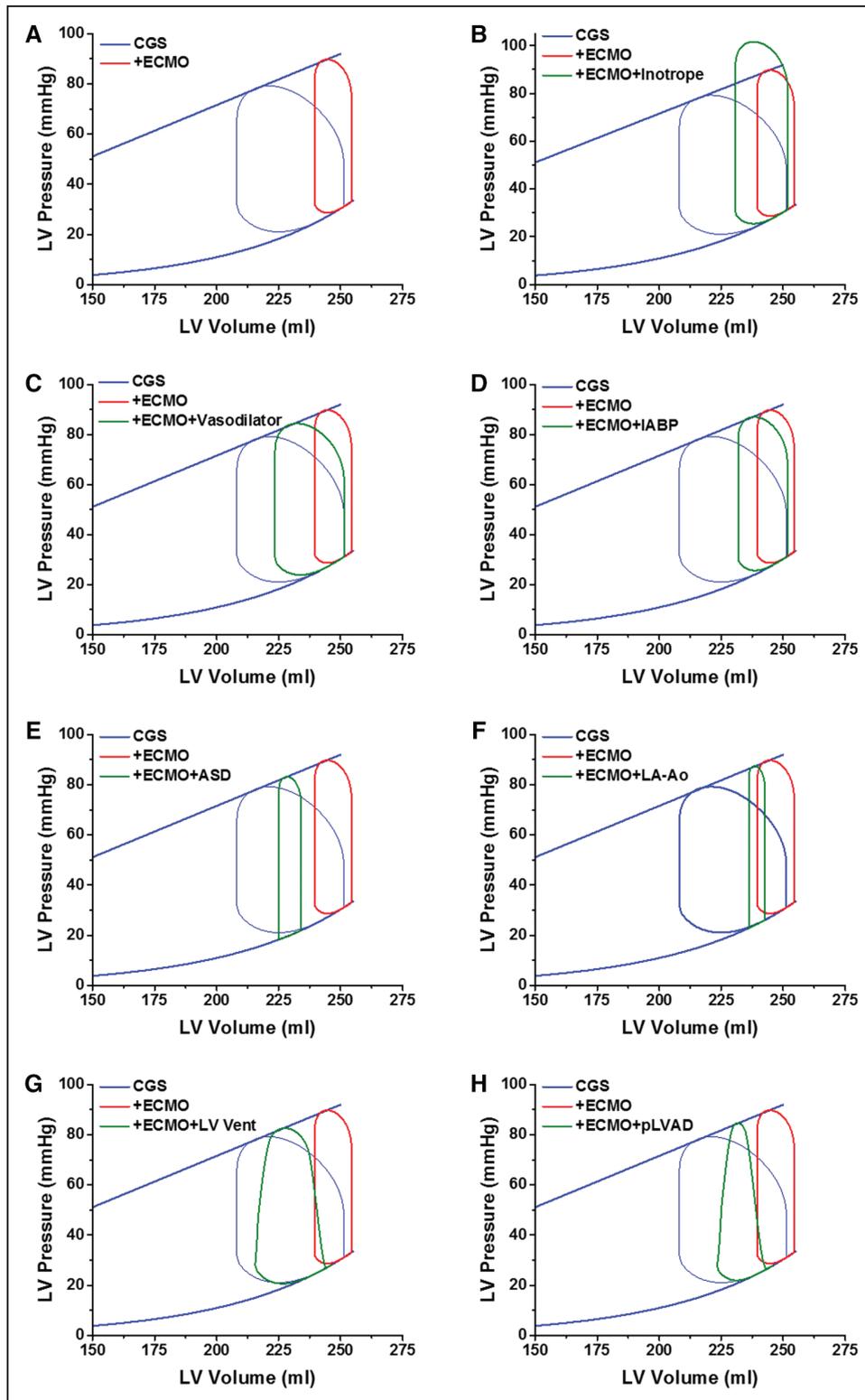


Figure 5. Hemodynamic effects of different strategies of left ventricular (LV) unloading during venoarterial extracorporeal membrane oxygenation (VA-ECMO).

Pressure-volume (PV) loops generated during acute cardiogenic shock (blue PV loops) and peripheral VA-ECMO with (A) no unloading strategy (red PV loops) and with the following venting strategies (green PV loops): (B) inotropic agent, (C) vasodilator agent, (D) intra-aortic balloon pump (IABP), (E) atrial septostomy, (F) left atrial (LA) venting via cannula connected to ECMO circuit, (G) direct LV venting via cannula connected to ECMO circuit, (H) percutaneous transaortic ventricular assist device.

and cardiac output. Yet, it is that same pressure that may load the LV (in a retrograde fashion) and be deleterious to the myocardium.^{54,55} Although this approach

will limit the degree of loading, it may not unload the ventricle or decongest the lungs compared with the patient's baseline state.

Table. LV Unloading Strategies During VA-ECMO Support

Strategy	Advantage	Disadvantage
Inotropes	Simple to implement	Limited LV unloading; increases myocardial oxygen consumption
Vasodilators	Simple to implement	Limited LV unloading; blood pressure may not be sufficient
IABP	Bedside implementation possible; increased coronary blood flow	Unreliable degree of unloading
Balloon atrial septostomy	Bedside implementation possible	Indirect LV unloading; possible need for ASD closure after decannulation
LA→Ao cannula connected to venous port of ECMO circuit	More controlled LA decompression than septostomy	Indirect LV unloading; possible need for ASD closure after decannulation
Surgical LV vent	Direct LV venting; provides reliable LV unloading	Requires surgical placement and removal; impacts apex of the heart; blood stasis in proximal aorta still possible
Percutaneous LV vent	Bedside implementation possible; direct LV unloading; provides reliable LV unloading	Limited LV unloading compared with surgical LV vent; blood stasis in proximal aorta still possible
Percutaneous ventricular support	Impella FDA approved for this indication; direct LV unloading; antegrade flow support; aortic root washing; offers the possibility for ECMO to be weaned with continued circulatory support	North-south syndrome still possible
Off-pump central VA-ECMO	Direct LV unloading; total antegrade flow support; allows for ambulation; minimizes risk of vascular injury	Requires surgical placement and removal; impacts apex of the heart

ASD indicates atrial septal defect; FDA, Food and Drug Administration; IABP, intra-aortic balloon pump; LA, left atrial; LV, left ventricle; and VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Inotropes

Inotropic support, in principle, serves to address a fundamental issue with ECMO; namely, that an LV with significant contractile dysfunction cannot overcome the increased afterload pressure created during ECMO support. Accordingly, inotropic support primarily helps enhance aortic valve opening (Figure 5B) but may provide limited LV unloading. Also, inotropes significantly increase myocardial oxygen consumption because of increased calcium cycling resulting in increased myocardial contractility, the increased total LV work, and the increased heart rate associated with their use. This may have detrimental consequences, particularly in the setting of myocardial ischemia and infarction.

Vasodilators

Reducing systemic vascular resistance with the use of vasodilators (such as nitroprusside) decreases arterial pressure and therefore allows for increased aortic valve opening and LV ejection but may provide a limited degree of LV unloading (Figure 5C). Furthermore, the use of this approach may be limited if the systemic blood pressure on support is insufficient, such as may occur during the vasoplegic phase of cardiogenic shock or the resultant systemic inflammatory response syndrome phenomena from initially being on the ECMO circuit.

Intra-Aortic Balloon Pump

As with vasodilators, intra-aortic balloon pumps (IABP) reduces blood pressure during systole and can enhance aortic valve opening and increase LV ejection (Fig-

ure 5D) with the advantage that, on balance, average arterial blood pressure can be increased because of balloon inflation during diastole. Increased arterial diastolic pressure can also enhance coronary flow. IABP in VA-ECMO patients has been shown to decrease PCWP by an average of ≈ 4 mm Hg but with variable responses among patients.⁵⁶ In one retrospective analysis, ECMO patients treated with IABP had less pulmonary congestion on chest x-ray, but the study included too small a number of patients to assess impact on outcomes.⁵⁷ However, in a relatively large meta-analysis, no survival benefit was identified with the use of IABP as an unloading strategy during ECMO.⁵⁸

Atrial Septostomy

Atrial septostomy, which permits left-to-right shunting, was among the first invasive strategies used to decompress the LV during ECMO.⁵⁹ This strategy remains commonly used among pediatric patients supported with ECMO. However, such decompression can be accompanied by decreased aortic valve opening and blood flow out of the ventricle because of the reduced LV preload (Figure 5E). Accordingly, patients should be monitored for decreased aortic valve opening and stasis within the LV because of the risk of thrombus formation. There is limited published information on the actual hemodynamic effects of this strategy.^{59,60}

LA Venting via Cannula Connected to ECMO Circuit

Similar in concept to atrial septostomy, LV decompression may also be achieved percutaneously via trans-sep-

tal placement of a LA cannula connected the venous circuit of VA-ECMO with flow regulated by a clamp if needed (Figure 5F).^{46,48,61,62} In contrast to an atrial septostomy, however, the blood is actively pumped from the LA back to the arterial system which, if total flow through the ECMO circuit is maintained constant, can better maintain arterial pressure. Accordingly, the amount of LV decompression and degree of enhancement of aortic valve opening may not be as great as with a septostomy. Thus, as with ECMO alone, appropriate monitoring should be used to ensure that the aortic valve is opening and that the PCWP is decreased sufficiently. Also, as with an atrial septal defect and standard use of a left atrial-to-femoral artery bypass, use of this approach carries the risks associated with performing a trans-septal puncture and may result in persistent interatrial shunting after decannulation.

Surgical LV Venting via Cannula Connected to ECMO Circuit

Direct LV decompression can be achieved using a cannula placed surgically via a mini-thoracotomy through the LV apex into the LV.⁶³⁻⁶⁵ The cannula is then connected to the venous port of the ECMO circuit with flow regulated by a clamp. Thus, the degree of LV unloading can be regulated and can be significant (Figure 5G). With significant unloading, the aortic valve may not open. Although stasis of blood within the LV is no longer a concern with this configuration, stasis may still occur in the proximal aorta, so that monitoring for aortic valve opening should still be performed. Surgical removal is required, and the LV apex can be compromised. Therefore, this approach is often considered when bridge-to-durable ventricular assist device or transplant is considered.

Percutaneous LV Venting via Pigtail Catheter Connected to ECMO Circuit (Transaortic Catheter Venting)

Several groups have reported use of transaortic catheter venting to provide LV decompression during VA-ECMO.⁶⁶⁻⁶⁹ Using a transfemoral approach, the procedure involves percutaneous insertion of a 5F to 8F pigtail catheter across the aortic valve with the tip lying directly in the LV cavity. The catheter drains blood directly from the LV and is connected to the venous limb of the ECMO circuit. This technique has the advantage of direct LV unloading without surgical manipulation and can be performed by bedside under echocardiographic guidance. However, the degree of flow through such a cannula, typically 8F in size, and the degree of LV unloading can be limited. Results of one study suggest that with this one can expect <100 cc/min drainage from the LV, far too small to result in significant unloading.⁷⁰ Furthermore, as with the surgical approach, sig-

nificant LV unloading may hinder aortic valve opening, leading to stasis of blood in the proximal aorta.

Percutaneous Transaortic Ventricular Assist Device (Impella)

Most recently, use of percutaneous catheter-based microaxial transaortic ventricular assist devices (pVADs) has emerged as a frequently used option for LV venting during VA-ECMO (Figure 6). Although the immediate goal is LV decompression and decreasing pulmonary venous pressure, this approach also provides additional antegrade flow support into the aortic root. Koeckert et al reported the first use of the Impella 2.5 LP (2018 Abiomed, Danvers, MA) in combination with VA-ECMO and demonstrated reductions in LV end-diastolic diameter and pulmonary edema.⁷¹ Percutaneous transaortic microaxial left ventricular assist devices providing 3.5 or 5.0 liters per minute have since been more commonly used in combination with VA-ECMO, with reports of improved outcomes compared with VA-ECMO alone.^{72,73} As with an LV vent, the LV is directly unloaded, and stasis of blood within the LV because of aortic valve closure is not a concern. Unlike an LV vent, implantation and explantation of a pVAD are percutaneous procedures. As noted above, blood flow from a pVAD adds to that of the ECMO circuit to further improve total blood flow to the body if needed. This may allow for initiation of ECMO weaning (provided blood is adequately oxygenated), which will result in further unloading of the LV and pulmonary veins. Finally, pVADs capable of 3.5 or 5.0 liters per minute generally provide sufficient flow so that ECMO can be fully weaned to these devices should longer term support be required in the setting of persistent profound LV dysfunction once the lungs are decongested and adequate blood oxygenation achieved. Implantation of pVADs via an axillary artery approach (either by percutaneous or surgical techniques), in combination with appropriate ECMO configurations, allows for patient mobility and ambulation while on support.⁷⁴⁻⁷⁷ Data provided in these reports also provide initial evidence suggest that the combination of ECMO and Impella can improve survival over the use of ECMO alone.

ARE THERE LESS INVASIVE, EMERGING SURGICAL MEANS OF INITIATING CENTRAL VA-ECMO?

Recently, case reports have emerged of central VA-ECMO performed using an inferior vena cava-superior vena cava drainage cannula in conjunction with a centrifugal flow pump and oxygenator.²⁵ The pump connected transapically off-cardiopulmonary bypass via a left mini-thoracotomy approach using a dual lumen 31F cannula with the inflow portion located within the left

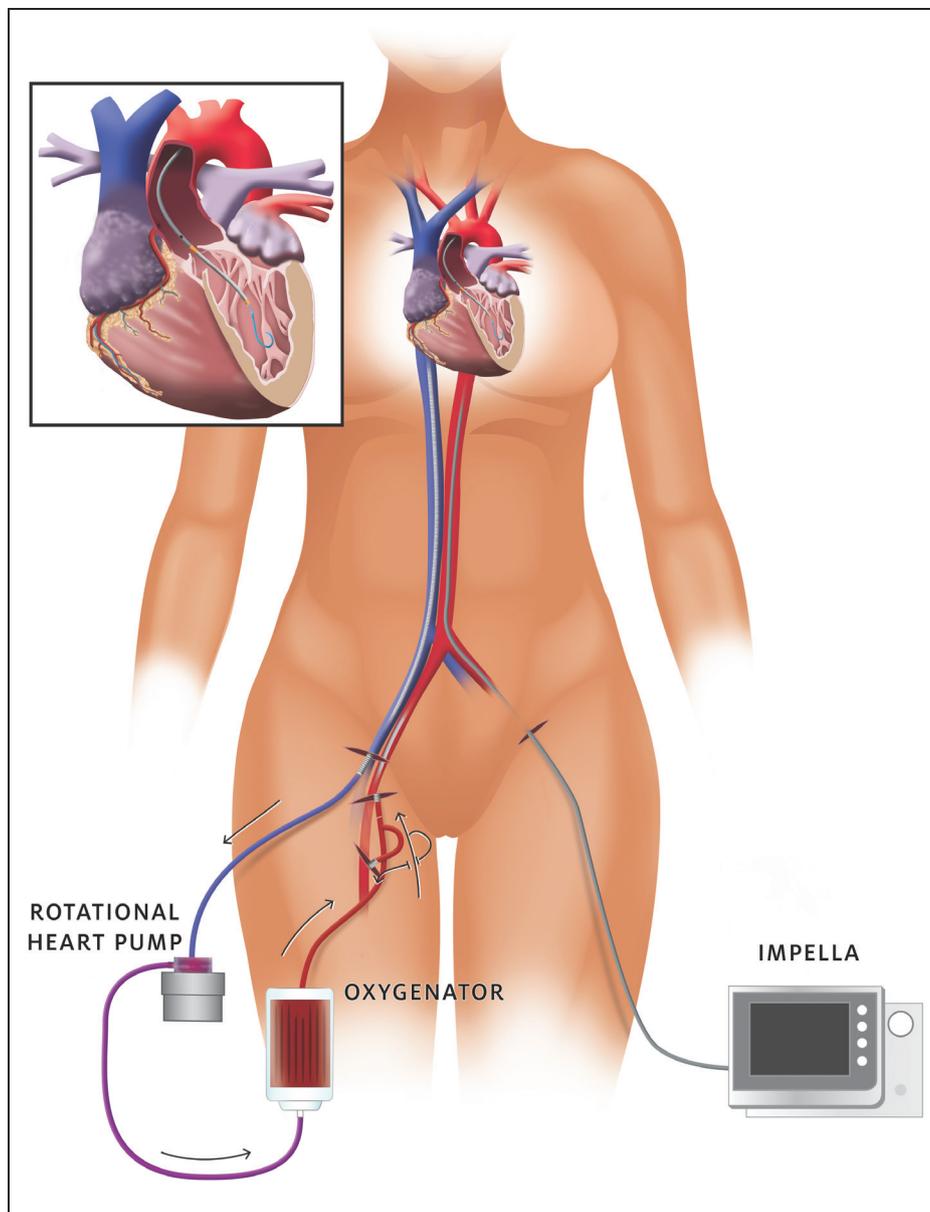


Figure 6. Peripheral venoarterial extracorporeal membrane oxygenation with a percutaneously inserted transaortic valve ventricular assist device that directly unloads the left ventricle.

The arterial access site for the percutaneous left ventricular assist device may be in the femoral artery (shown) or axillary/subclavian artery (not shown).

ventricle, and the outflow port and cannula tip situated 2 to 3 cm above the aortic valve. In this circuit, blood is drained from both the inferior vena cava-superior vena cava cannula and directly from the LV (1 of 2 lumens of the 31F dual lumen cannula). Oxygenated blood is then ejected into the proximal aorta. It should be noted that this approach, although described in a few case reports, is relatively novel and untested. This strategy is physiologically similar to simultaneous VA-ECMO with pVAD as described above. Ambulatory VA-ECMO has also been reported using venous drainage from the right internal jugular vein with return of blood into the axillary, subclavian, or innominate artery,^{5,40} with an Impella pVAD placed via a subclavian arterial graft.

WHAT ARE THE HARLEQUIN SYNDROME, NORTH-SOUTH SYNDROME, AND THE WATERSHED REGION?

Because of the retrograde flow support in the setting of peripheral VA-ECMO, blood travels in the direction opposite to normal; retrograde from the femoral or iliac artery back toward the thoracic aorta. Therefore, in patients receiving peripheral VA-ECMO, there is an area of watershed, which is the region within the aorta where the 2 blood streams meet (Figure 7).^{78,79} This watershed region can lie anywhere between the aortic root and diaphragm depending on the output of the LV relative to ECMO flow.

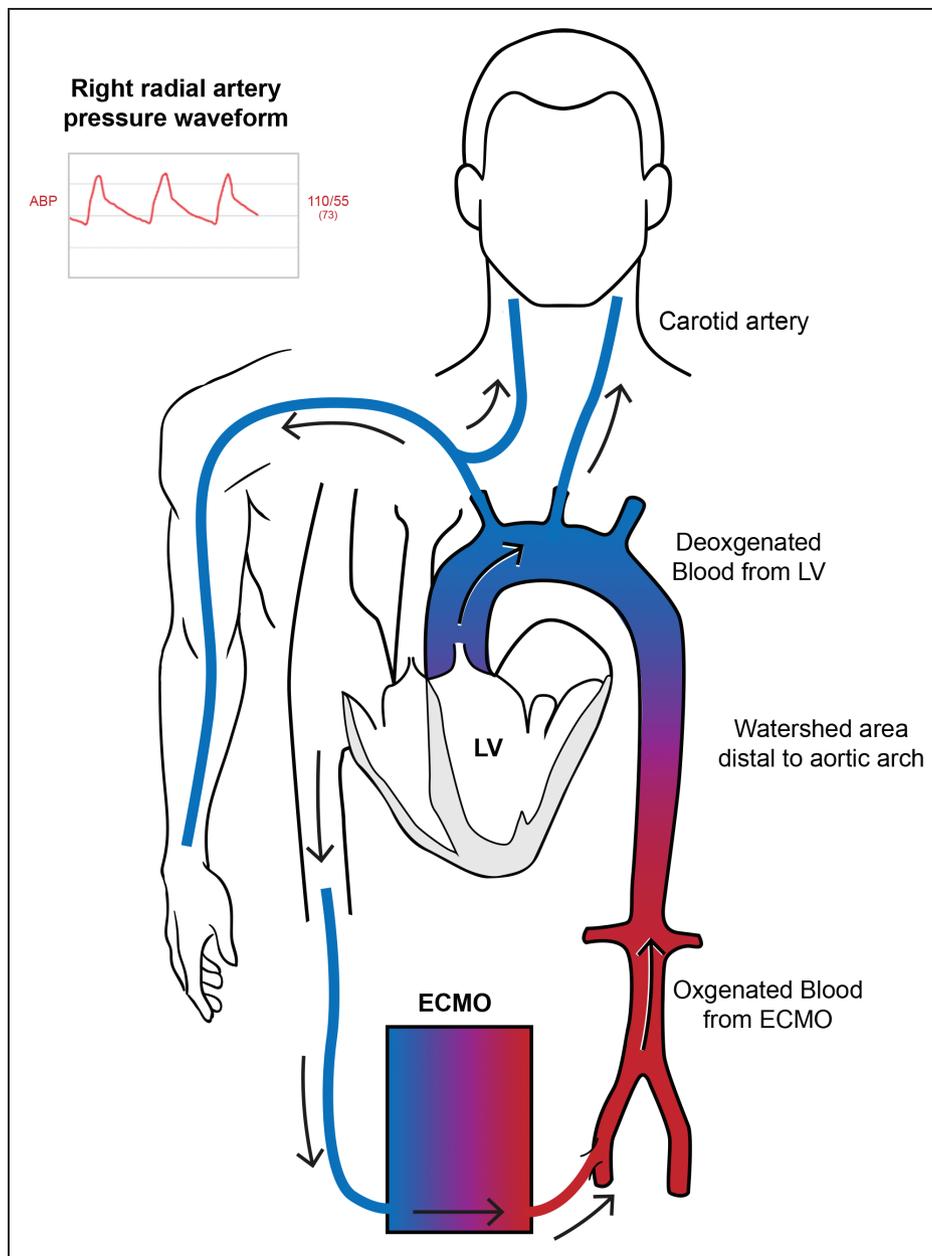


Figure 7. North-south (Harlequin) syndrome: a common consideration with femoral artery cannulation and when the lungs are not adequately oxygenating blood.

Relatively deoxygenated (blue) blood enters the left atrium and is ejected antegrade by the left ventricle (LV). This hinders oxygenated (red) extracorporeal membrane oxygenation (ECMO) blood from making it retrograde to the aortic arch resulting in cerebral hypoxemia. Arterial line monitoring in the right arm is mandatory to assess the location of the watershed region and monitor for cerebral hypoxemia. Because ECMO flow is nonpulsatile, a wide pulse pressure at the right radial artery indicates an ejecting LV or LV recovery (as shown) and a watershed region distal to the arch. If there is concern for cerebral hypoxemia, alternative cannulation strategies must be considered. ABP indicates arterial blood pressure.

When antegrade LV output is high relative to retrograde ECMO flow, the area of watershed lies more distal (ie, closer to the diaphragm). When LV output is low relative to ECMO flow, the area of watershed is more proximal (ie, closer to the aortic root). Recognition of the location of the watershed zone is important because oxygenation of the ECMO flow and LV output may be markedly different. Although blood derived from the ECMO circuit is typically well oxygenated, blood exiting the LV is dependent on adequate pulmonary gas exchange, which is

often impaired in the setting of acute cardiogenic shock and pulmonary edema. Therefore, if the watershed region is located distal to the left subclavian artery, there may be considerable risk of profound hypoxemia to the brain, heart, and upper extremities. In extreme circumstances, this may lead to Harlequin syndrome, also known as north-south syndrome. This is when venous blood (ie, blue blood) passing through lungs with impaired oxygen diffusion capacity (eg, because of pulmonary edema, infection, intrinsic disease, etc) is poorly oxygenated and is ejected

by the LV into the ascending aorta to perfuse the upper body and brain.⁸⁰ Meanwhile, venous blood drained by the venous cannula passes through the ECMO circuit and perfuses the lower body with well-oxygenated blood (ie, red blood). This leads to differential cyanosis with upper body hypoxemia and lower body hyperoxia, resulting in a Harlequin-like appearance. Treating pulmonary pathology and increasing ventilator support (to improve blood oxygenation) may help in overcoming this phenomenon. When alveolar gas exchange is impaired because of cardiogenic pulmonary edema, using an LV venting strategy may be helpful. Although some clinicians advocate increasing ECMO flow to reduce flow to the lungs, this will typically worsen pulmonary edema, thus worsening blood oxygenation. It is also worth noting that in some cases, such as massive PE with a hyperdynamic LV, decreasing cardiac contractility, for example, with an esmolol drip may allow for red blood to make it to the arch.

Failing the above measures, splitting the arterial outflow with a Y connector to deliver well-oxygenated blood into the venous system and pulmonary circulation will increase the oxygen content delivered by the LV output. This configuration of ECMO is referred to as veno-arterio-venous ECMO.⁸¹ A right upper extremity arterial line with serial monitoring of blood gases is considered standard for monitoring for potential cerebral hypoxemia and helps guide the need for veno-arterio-venous-ECMO.

Assessment of the pulse pressure at the right radial artery is helpful in locating the watershed region. ECMO flow is nonpulsatile, and as such, a narrow pulse pressure at the right radial artery indicates a watershed in the aortic root. By contrast, a wide pulse pressure at the right radial artery suggests a watershed region distal to the innominate artery.

PATIENT MANAGEMENT ISSUES

How Does One Ensure Perfusion of the Cannulated Leg? Cardinal Consideration IV: Distal Limb Ischemia and Distal Limb Perfusion Strategies

Lower extremity ischemia occurs in 12% to 22% of patients with peripheral VA-ECMO for refractory cardiogenic shock, and many require fasciotomy for compartment syndrome or amputation.²⁶ Typically, a 6F to 8F vascular introducer is placed distal to the arterial cannula in the common femoral artery or superficial femoral artery to provide antegrade femoral blood flow to the cannulated leg and prevent ischemic insult. Its proximal connection is to a port near the insertion site on the arterial cannula.^{82,83} Alternatively, a distal perfusion cannula can be inserted into the posterior tibial artery⁸⁴ or dorsalis pedis artery⁸⁵ and provide retrograde perfusion. Early percutaneous placement of a distal per-

fusion cannula is associated with a lower risk of ischemic limb injury⁸⁴ although most centers standardize timing of placement of a distal perfusion cannula at the time of ECMO initiation.⁸⁶

What Is the Optimal Anticoagulation Strategy for Peripheral VA-ECMO?

VA-ECMO and its attendant prothrombotic inflammatory environment increase the risk of thrombosis, which may cause pump malfunction, oxygenator failure, and thromboembolic events.⁸⁷ However, major bleeding is reported to occur in roughly one quarter of all VA-ECMO patients⁸⁸ and can happen in patients without anticoagulation therapy.⁸⁹ Data on the optimal strategy for anticoagulation are limited, and guidelines, largely based on expert opinion, currently recommend using unfractionated heparin targeting an activated clotting time of 180 to 220 seconds.⁹⁰ Increasingly, centers have found little correlation between activated clotting time and partial thromboplastin time and bleeding events. The standard of care is moving toward use of the anti-Xa assay (goal, 0.3–0.7). Little evidence exists to support the use of anti-Xa, which essentially monitors heparin levels, but it has become the gold standard because there are few interfering conditions with its accuracy (other than hemolysis). Because of consumption, antithrombin III (ATIII), which must bind heparin for its anticoagulant activity to work, often becomes depleted, at which point apparent heparin resistance develops. When this happens, an ATIII functional assay should be checked, and if <70% along with clinical heparin resistance, it should be repleted for a goal functional activity of 80% to 120%. Although many centers use plasma to replete ATIII, there is little ATIII for the volume administered. It is preferable to use one of the concentrated forms of ATIII—pooled human ATIII or recombinant human antithrombin.⁹⁰

What Are the Alternatives to the Use of VA-ECMO? (Cardinal Considerations I and V: Patient Selection and Exit Strategy)

Other forms of mechanical circulatory support should be considered for patients with cardiogenic shock. Use of IABP for this purpose is waning as results indicate lack of hemodynamic and clinical benefit,^{91,92} and recommendations for its use are downgraded in treatment guidelines in United States and Europe. LA femoral artery bypass is one alternative option but requires a trans-septal puncture.^{93,94} However, because of ease of implantation and use, and range of flows offered across the spectrum of available devices, percutaneous transaortic microaxial flow pump is currently the main alternative option. In many institutions, these are first-line therapy, especially when blood oxygenation is not a factor. Even then, their support can markedly and rapidly improve oxygenation

by reducing PCWP and decongesting the lung; in such cases, ECMO can be avoided.

SUMMARY AND CONCLUSIONS

Peripheral VA-ECMO is a potential option for refractory cardiogenic shock and cardiac arrest because it quickly improves hemodynamics and can be initiated rapidly. However, VA-ECMO is associated with several complications and high mortality rates. Carefully thinking through the main cardinal considerations (Figure 2) we have discussed in this article will allow one to make the best strategic choices, including appropriate patient selection, cannulation strategies, venting strategies for LV distension, and distal extremity perfusion. The purpose of this document was to give the reader a jumping off point from which to carefully strategize around these important considerations at the time of decision and cannulation instead of requiring reactionary decision making further into the patient's clinical course (Figure 2).

For example, one of the most significant major limitations of VA-ECMO is LV distention and pulmonary edema, which lead to a plethora of other adverse events, including aortic root thrombosis. There are a variety of LV decompression strategies that can be used after initiation of emergent peripheral VA-ECMO. However, the optimal method and timing for LV decompression are not well established. Recent reports describe techniques that directly decompress the LV, provide antegrade flow support, and allow for patient mobility. With availability of these strategies, we enter a new era of combined VA-ECMO and mechanical circulatory support and provide new options for patients with refractory cardiogenic shock and cardiac arrest. As adoption of VA-ECMO increases and the number of clinical sites able to deliver this therapy grows, we should not lose sight of the attendant profound hemodynamic effects. With more careful patient selection, greater experience in its implementation, and innovative therapies for LV decompression, we can expect significant improvements in outcomes for cardiogenic shock and cardiac arrest.

ARTICLE INFORMATION

The online-only Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/CIRCHEARTFAILURE.118.004905>.

Correspondence

Robb D. Kociol, MD, Advanced Heart Failure and Mechanical Circulatory Support Program, University of Massachusetts Memorial Medical Center, MA. Email robb.kociol@umassmemorial.org

Affiliations

Sarver Heart Center (P.R.) and Division of Cardiothoracic Surgery, Department of Surgery (Z.K.), University of Arizona, Tucson. Artificial Heart and Perfusion Programs, Banner University Medical Center, Tucson, AZ (R.S.). Cardiovascular Research Foundation, Columbia University Medical Center, New York, NY (D.B.). Advanced Heart Failure and Mechanical Circulatory Support Program, University of Massachusetts Memorial Medical Center, Worcester (R.D.K.).

Disclosures

Dr Kociol received a research grant from the Extracorporeal Life Support Organization to fund a study to identify those most at risk for bleeding or thrombotic events while on ECMO support and the associated mortality risk.

REFERENCES

1. Keebler ME, Haddad EV, Choi CW, McGrane S, Zalawadiya S, Schlendorf KH, Brinkley DM, Danter MR, Wigger M, Menachem JN, Shah A, Lindenfeld J. Venoarterial extracorporeal membrane oxygenation in cardiogenic shock. *JACC Heart Fail*. 2018;6:503–516. doi: 10.1016/j.jchf.2017.11.017
2. McRae K, de Perrot M. Principles and indications of extracorporeal life support in general thoracic surgery. *J Thorac Dis*. 2018;10(suppl 8):S931–S946. doi: 10.21037/jtd.2018.03.116
3. Wang L, Wang H, Hou X. Clinical outcomes of adult patients who receive extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock: a systematic review and meta-analysis [published online March 12, 2018]. *J Cardiothorac Vasc Anesth*. doi: 10.1053/j.jvca.2018.03.016. <https://doi.org/10.1053/j.jvca.2018.03.016>
4. Biancari F, Perrotti A, Dalén M, Guerrieri M, Fiore A, Reichart D, Dell'Aquila AM, Gatti G, Ala-Kokko T, Kinnunen EM, Tauriainen T, Chocron S, Airaksinen JKE, Ruggieri VG, Brascia D. Meta-analysis of the outcome after postcardiotomy venoarterial extracorporeal membrane oxygenation in adult patients. *J Cardiothorac Vasc Anesth*. 2018;32:1175–1182. doi: 10.1053/j.jvca.2017.08.048
5. Biscotti M, Bacchetta M. The “sport model”: extracorporeal membrane oxygenation using the subclavian artery. *Ann Thorac Surg*. 2014;98:1487–1489. doi: 10.1016/j.athoracsur.2014.02.069
6. Hill JD, O'Brien TG, Murray JJ, Dontigny L, Bramson ML, Osborn JJ, Gerbode F. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. *N Engl J Med*. 1972;286:629–634. doi: 10.1056/NEJM197203232861204
7. Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. *J Am Coll Cardiol*. 2014;64:1407–1415. doi: 10.1016/j.jacc.2014.07.958
8. Cavarocchi NC. Introduction to extracorporeal membrane oxygenation. *Crit Care Clin*. 2017;33:763–766. doi: 10.1016/j.ccc.2017.06.001
9. Extracorporeal Life Support Organization. ECLS Registry Report, International Summary. 2018. <https://www.else.org/Registry/Statistics.aspx> Accessed August 2, 2018.
10. Pagani FD, Lynch W, Swaniker F, Dyke DB, Bartlett R, Koelling T, Moscucci M, Deeb GM, Bolling S, Monaghan H, Aaronson KD. Extracorporeal life support to left ventricular assist device bridge to heart transplant: a strategy to optimize survival and resource utilization. *Circulation*. 1999;100(19 suppl):II206–II210.
11. Hoefler D, Ruttman E, Poelzl G, Kilo J, Hoermann C, Margreiter R, Laufer G, Antretter H. Outcome evaluation of the bridge-to-bridge concept in patients with cardiogenic shock. *Ann Thorac Surg*. 2006;82:28–33. doi: 10.1016/j.athoracsur.2006.02.056
12. Bermudez CA, Rocha R V, Zaladonis D, Bhama JK, Crespo MM, Shigemura N, Pilewski JM, Sappington PL, Boujoukos AJ, Toyoda Y. Extracorporeal membrane oxygenation as a bridge to lung transplant: midterm outcomes. *Ann Thorac Surg*. 2011;92:1222–1226. doi: 10.1016/j.athoracsur.2010.11.078
13. Lorusso R, Centofanti P, Gelsomino S, Barili F, Di Mauro M, Orlando P, Botta L, Milazzo F, Actis Dato G, Casabona R, Casali G, Musumeci F, De Bonis M, Zangrillo A, Alfieri O, Pellegrini C, Mazzola S, Coletti G, Vizzardi E, Bianco R, Gerosa G, Massetti M, Caldaroni F, Pilato E, Pacini D, Di Bartolomeo R, Marinelli G, Sponga S, Livi U, Mauro R, Mariscalco G, Beghi C, Miceli A, Glauber M, Pappalardo F, Russo CF; GIROC Investigators. Venoarterial extracorporeal membrane oxygenation for acute fulminant myocarditis in adult patients: a 5-year multi-institutional experience. *Ann Thorac Surg*. 2016;101:919–926. doi: 10.1016/j.athoracsur.2015.08.014
14. Burrell AJ, Pellegrino VA, Wolfe R, Wong WK, Cooper DJ, Kaye DM, Pilcher DV. Long-term survival of adults with cardiogenic shock after venoarterial extracorporeal membrane oxygenation. *J Crit Care*. 2015;30:949–956. doi: 10.1016/j.jccr.2015.05.022
15. Chen YS, Chao A, Yu HY, Ko WJ, Wu IH, Chen JJC, Huang SC, Lin FY, Wang SS. Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. *J Am Coll Cardiol*. 2003;41:197–203. doi: 10.1016/S0735-1097(02)02716-X
16. Le Guen M, Nicolas-Robin A, Carreira S, Raux M, LePrince P, Riou B, Langeron O. Extracorporeal life support following out-of-hospital refractory cardiac arrest. *Crit Care*. 2011;15:R29. doi: 10.1186/cc9976

17. Kagawa E, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Kurisu S, Nakama Y, Dai K, Takayuki O, Ikenaga H, Morimoto Y, Ejiri K, Oda N. Assessment of outcomes and differences between in- and out-of-hospital cardiac arrest patients treated with cardiopulmonary resuscitation using extracorporeal life support. *Resuscitation*. 2010;81:968–973. doi: 10.1016/j.resuscitation.2010.03.037
18. Chen YS, Lin JW, Yu HY, Ko WJ, Jerng JS, Chang WT, Chen WJ, Huang SC, Chi NH, Wang CH, Chen LC, Tsai PR, Wang SS, Hwang JJ, Lin FY. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet*. 2008;372:554–561. doi: 10.1016/S0140-6736(08)60958-7
19. Massetti M, Tasle M, Le Page O, Deredec R, Babatasi G, Buklas D, Thuau-det S, Charbonneau P, Hamon M, Grollier G, Gerard JL, Khayat A. Back from irreversibility: extracorporeal life support for prolonged cardiac arrest. *Ann Thorac Surg*. 2005;79:174–178.
20. de Waha S, Fuernau G, Eitel I, Desch S, Thiele H. Long-term prognosis after extracorporeal life support in refractory cardiogenic shock—results from a real-world cohort. *EuroIntervention*. 2016;12:414. doi: 10.4244/EIJV12I3A71
21. Pavasini R, Cirillo C, Campo G, Nobre Menezes M, Biscaglia S, Tonet E, Ferrari R, Patel BV, Price S. Extracorporeal circulatory support in acute coronary syndromes: a systematic review and meta-analysis. *Crit Care Med*. 2017;45:e1173–e1183. doi: 10.1097/CCM.0000000000002692
22. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, Neumar RW, O'Neil BJ, Paxton JH, Silvers SM, White RD, Yannopoulos D, Donnino MW. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(18 suppl 2):S444–S464. doi: 10.1161/CIR.0000000000000261
23. Burkhoff D, Sayer G, Doshi D, Uriel N. Hemodynamics of mechanical circulatory support. *J Am Coll Cardiol*. 2015;66:2663–2674. doi: 10.1016/j.jacc.2015.10.017
24. Burkhoff D, Dickstein M, Schleicher T. Harvi - Online. 2017. <https://harvi.online> Accessed August 2, 2018.
25. Rao P, Alouidor B, Smith R, Khalpey Z. Ambulatory central VA-ECMO with biventricular decompression for acute cardiogenic shock [published online December 4, 2017]. *Catheter Cardiovasc Interv*. doi: 10.1002/ccd.27428.
26. Cheng R, Hachamovitch R, Kittleson M, Patel J, Arabia F, Moriguchi J, Esmailian F, Azarbal B. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. *Ann Thorac Surg*. 2014;97:610–616. doi: 10.1016/j.athoracsur.2013.09.008
27. Baran DA. Extracorporeal membrane oxygenation (ECMO) and the critical cardiac patient. *Curr Transplant Rep*. 2017;4:218–225. doi: 10.1007/s40472-017-0158-5
28. Lee SH, Chung CH, Lee JW, Jung SH, Choo SJ. Factors predicting early- and long-term survival in patients undergoing extracorporeal membrane oxygenation (ECMO). *J Card Surg*. 2012;27:255–263. doi: 10.1111/j.1540-8191.2011.01400.x
29. Chang WW, Tsai FC, Tsai TY, Chang CH, Jenq CC, Chang MY, Tian YC, Hung CC, Fang JT, Yang CW, Chen YC. Predictors of mortality in patients successfully weaned from extracorporeal membrane oxygenation. *PLoS One*. 2012;7:e42687. doi: 10.1371/journal.pone.0042687
30. Distelmaier K, Niessner A, Haider D, Lang IM, Heinz G, Maurer G, Koinig H, Steinlechner B, Gollasch G. Long-term mortality in patients with chronic obstructive pulmonary disease following extracorporeal membrane oxygenation for cardiac assist after cardiovascular surgery. *Intensive Care Med*. 2013;39:1444–1451. doi: 10.1007/s00134-013-2931-y
31. Aubron C, Cheng AC, Pilcher D, Leong T, Magrin G, Cooper DJ, Scheinkestel C, Pellegrino V. Factors associated with outcomes of patients on extracorporeal membrane oxygenation support: a 5-year cohort study. *Crit Care*. 2013;17:R73. doi: 10.1186/cc12681
32. Bakhtiari F, Keller H, Dogan S, Dzemali O, Oezaslan F, Meininger D, Ackermann H, Zwissler B, Kleine P, Moritz A. Venoarterial extracorporeal membrane oxygenation for treatment of cardiogenic shock: clinical experiences in 45 adult patients. *J Thorac Cardiovasc Surg*. 2008;135:382–388. doi: 10.1016/j.jtcvs.2007.08.007
33. Schmidt M, Zogheib E, Rozé H, Repesse X, Lebreton G, Luyt CE, Trouillet JL, Bréchet N, Nieszkowska A, Dupont H, Ouattara A, Leprince P, Chastre J, Combes A. The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Intensive Care Med*. 2013;39:1704–1713. doi: 10.1007/s00134-013-3037-2
34. Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT, Hodgson V, Scheinkestel C, Cooper DJ, Thiagarajan RR, Brodie D, Pellegrino V, Pilcher D. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J*. 2015;36:2246–2256. doi: 10.1093/eurheartj/ehv194
35. Peigh G, Cavarocchi N, Keith SW, Hirose H. Simple new risk score model for adult cardiac extracorporeal membrane oxygenation: simple cardiac ECMO score. *J Surg Res*. 2015;198:273–279. doi: 10.1016/j.jss.2015.04.044
36. Rupperecht L, Lunz D, Philipp A, Lubnow M, Schmid C. Pitfalls in percutaneous ECMO cannulation. *Heart Lung Vessel*. 2015;7:320–326.
37. Jayaraman AL, Cormican D, Shah P, Ramakrishna H. Cannulation strategies in adult veno-arterial and veno-venous extracorporeal membrane oxygenation: techniques, limitations, and special considerations. *Ann Card Anaesth*. 2017;20(suppl):S11–S18. doi: 10.4103/0971-9784.197791
38. Takayama H, Landes E, Truby L, Fujita K, Kirtane AJ, Mongero L, Yuze-fpolskaya M, Colombo PC, Jorde UP, Kurlansky PA, Takeda K, Naka Y. Feasibility of smaller arterial cannulas in venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2015;149:1428–1433. doi: 10.1016/j.jtcvs.2015.01.042
39. Camp PC. Short-term mechanical circulatory support. *Oper Tech Thorac Cardiovasc Surg*. 2013;18:239–251. doi: 10.1053/j.optechstcvs.2013.11.004
40. Chicotka S, Rosenzweig EB, Brodie D, Bacchetta M. The “Central Sport Model”: extracorporeal membrane oxygenation using the innominate artery for smaller patients as bridge to lung transplantation. *ASAIO J*. 2017;63:e39–e44. doi: 10.1097/MAT.0000000000000427
41. Millar JE, Fanning JP, McDonald CI, McAuley DF, Fraser JF. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. *Crit Care*. 2016;20:387. doi: 10.1186/s13054-016-1570-4
42. Napp LC, Kühn C, Hoepfer MM, Vogel-Claussen J, Haverich A, Schäfer A, Bauersachs J. Cannulation strategies for percutaneous extracorporeal membrane oxygenation in adults. *Clin Res Cardiol*. 2016;105:283–296. doi: 10.1007/s00392-015-0941-1
43. Hála P, Mlček M, Ošťádal P, Janák D, Popková M, Bouček T, Lacko S, Kudlíčka J, Neuzil P, Kittnar O. Regional tissue oximetry reflects changes in arterial flow in porcine chronic heart failure treated with venoarterial extracorporeal membrane oxygenation. *Physiol Res*. 2016;65(suppl 5):S621–S631.
44. Chocron S, Perrotti A, Durst C, Aupècle B. Left ventricular venting through the right subclavian artery access during peripheral extracorporeal life support. *Interact Cardiovasc Thorac Surg*. 2013;17:187–189. doi: 10.1093/icvts/ivt119
45. Dickstein ML. The starling relationship and veno-arterial ECMO: ventricular distension explained. *ASAIO J*. 2018;64:497–501. doi: 10.1097/MAT.0000000000000660
46. Aiyagari RM, Rocchini AP, Remenapp RT, Graziano JN. Decompression of the left atrium during extracorporeal membrane oxygenation using a transeptal cannula incorporated into the circuit. *Crit Care Med*. 2006;34:2603–2606. doi: 10.1097/01.CCM.0000239113.02836.F1
47. Weber C, Deppe AC, Sabashnikov A, Slottoch I, Kuhn E, Eghbalzadeh K, Scherner M, Choi YH, Madershahian N, Wahlers T. Left ventricular thrombus formation in patients undergoing femoral veno-arterial extracorporeal membrane oxygenation. *Perfusion*. 2018;33:283–288. doi: 10.1177/0267659117745369
48. Hlavacek AM, Atz AM, Bradley SM, Bandisod VM. Left atrial decompression by percutaneous cannula placement while on extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2005;130:595–596. doi: 10.1016/j.jtcvs.2004.12.029
49. Kurihara H, Kitamura M, Shibuya M, Tsuda Y, Endo M, Koyangi H. Effect of transaortic catheter venting on left ventricular function during venoarterial bypass. *ASAIO J*. 1997;43:M838–M841.
50. Ong CS, Hibino N. Left heart decompression in patients supported with extracorporeal membrane oxygenation for cardiac disease. *Postepy Kardiol Interwencyjne*. 2017;13:1–2.
51. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, Kern M, Garratt KN, Goldstein JA, Dimas V, Tu T; Society for Cardiovascular Angiography and Interventions (SCAI); Heart Failure Society of America (HFSA); Society of Thoracic Surgeons (STS); American Heart Association (AHA), and American College of Cardiology (ACC). 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiología Intervención; affirmation of value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. *J Am Coll Cardiol*. 2015;65:e7–e26. doi: 10.1016/j.jacc.2015.03.036

52. Binanay C, Califf RM, Hasselblad V, O'Connor CM, Shah MR, Sopko G, Stevenson LW, Francis GS, Leier CV, Miller LW; ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA*. 2005;294:1625–1633. doi: 10.1001/jama.294.13.1625
53. Hadian M, Pinsky MR. Evidence-based review of the use of the pulmonary artery catheter: impact data and complications. *Crit Care*. 2006;10(suppl 3):S8. doi: 10.1186/cc4834
54. Fincke R, Hochman JS, Lowe AM, Menon V, Slater JN, Webb JG, LeJemtel TH, Cotter G; SHOCK Investigators. Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock: a report from the SHOCK trial registry. *J Am Coll Cardiol*. 2004;44:340–348. doi: 10.1016/j.jacc.2004.03.060
55. Mendoza DD, Cooper HA, Panza JA. Cardiac power output predicts mortality across a broad spectrum of patients with acute cardiac disease. *Am Heart J*. 2007;153:366–370. doi: 10.1016/j.ahj.2006.11.014
56. Petroni T, Harrois A, Amour J, Lebreton G, Brechot N, Tanaka S, Luyt CE, Trouillet JL, Chastre J, Leprince P, Duranteau J, Combes A. Intra-aortic balloon pump effects on macrocirculation and microcirculation in cardiogenic shock patients supported by venoarterial extracorporeal membrane oxygenation. *Crit Care Med*. 2014;42:2075–2082. doi: 10.1097/CCM.0000000000000410
57. Gass A, Palaniswamy C, Aronow WS, Kolte D, Khara S, Ahmad H, Cuomo LJ, Timmermans R, Cohen M, Tang GH, Kai M, Lansman SL, Lanier GM, Malekan R, Panza JA, Spielvogel D. Peripheral venoarterial extracorporeal membrane oxygenation in combination with intra-aortic balloon counterpulsation in patients with cardiovascular compromise. *Cardiology*. 2014;129:137–143. doi: 10.1159/000365138
58. Cheng R, Hachamovitch R, Makkar R, Ramzy D, Moriguchi JD, Arabia FA, Esmailian F, Azarbal B. Lack of survival benefit found with use of intra-aortic balloon pump in extracorporeal membrane oxygenation: a pooled experience of 1517 patients. *J Invasive Cardiol*. 2015;27:453–458.
59. Koenig PR, Ralston KA, Kimball TR, Meyer RA, Daniels SR, Schwartz DC. Balloon atrial septostomy for left ventricular decompression in patients receiving extracorporeal membrane oxygenation for myocardial failure. *J Pediatr*. 1993;122:S95–S99.
60. Alhussain M, Osten M, Horlick E, Ross H, Fan E, Rao V, Billia F. Percutaneous left atrial decompression in adults with refractory cardiogenic shock supported with veno-arterial extracorporeal membrane oxygenation. *J Card Surg*. 2017;32:396–401. doi: 10.1111/jocs.13146
61. Kang MH, Hahn JY, Gwon HC, Song YB, Choi JO, Choi JH, Choi SH, Lee SH, Jeon ES. Percutaneous transseptal left atrial drainage for decompression of the left heart in an adult patient during percutaneous cardiopulmonary support. *Korean Circ J*. 2011;41:402–404. doi: 10.4070/kcj.2011.41.7.402
62. Bernhardt AM, Hillebrand M, Yildirim Y, Hakmi S, Wagner FM, Blankenberg S, Reichenspurner H, Lubos E. Percutaneous left atrial unloading to prevent pulmonary oedema and to facilitate ventricular recovery under extracorporeal membrane oxygenation therapy. *Interact Cardiovasc Thorac Surg*. 2018;26:4–7. doi: 10.1093/icvts/ivx266
63. Takeda K, Garan AR, Topkara VK, Kirtane AJ, Karpaliotis D, Kurlansky P, Yuzefpolskaya M, Colombo PC, Naka Y, Takayama H. Novel minimally invasive surgical approach using an external ventricular assist device and extracorporeal membrane oxygenation in refractory cardiogenic shock. *Eur J Cardiothorac Surg*. 2017;51:591–596. doi: 10.1093/ejcts/ezw349
64. Eudailey KW, Yi SY, Mongero LB, Wagener G, Guarrera JV, George I. Transdiaphragmatic left ventricular venting during peripheral venous-arterial extracorporeal membrane oxygenation. *Perfusion*. 2015;30:701–703. doi: 10.1177/0267659115592468
65. Rao P, Mosier J, Malo J, Dotson V, Mogan C, Smith R, Keller R, Slepian M, Khalpey Z. Peripheral VA-ECMO with direct biventricular decompression for refractory cardiogenic shock. *Perfusion*. 2018;33:493–495. doi: 10.1177/0267659118761558
66. Fumagalli R, Bombino M, Borelli M, Rossi F, Colombo V, Osculati G, Ferrazzi P, Pesenti A, Gattinoni L. Percutaneous bridge to heart transplantation by venoarterial ECMO and transaortic left ventricular venting. *Int J Artif Organs*. 2004;27:410–413.
67. Hong TH, Byun JH, Yoo BH, Hwang SW, Kim HY, Park JH. Successful left-heart decompression during extracorporeal membrane oxygenation in an adult patient by percutaneous transaortic catheter venting. *Korean J Thorac Cardiovasc Surg*. 2015;48:210–213. doi: 10.5090/kjtcs.2015.48.3.210
68. Barbone A, Malvindi PG, Ferrara P, Tarelli G. Left ventricle unloading by percutaneous pigtail during extracorporeal membrane oxygenation. *Interact Cardiovasc Thorac Surg*. 2011;13:293–295. doi: 10.1510/icvts.2011.269795
69. Hong TH, Byun JH, Lee HM, Kim YH, Kang GH, Oh JH, Hwang SW, Kim HY, Park JH, Jung JJ. Initial experience of transaortic catheter venting in patients with venoarterial extracorporeal membrane oxygenation for cardiogenic shock. *ASAIO J*. 2016;62:117–122. doi: 10.1097/MAT.0000000000000327
70. Kim WH, Hong TH, Byun JH, Kim JW, Kim SH, Moon SH, Park HO, Choi JY, Yang JH, Jang IS, Lee CE, Yun JH. Flow rate through pigtail catheter used for left heart decompression in an artificial model of extracorporeal membrane oxygenation circuit. *ASAIO J*. 2017;63:346–350. doi: 10.1097/MAT.0000000000000472
71. Koeckert MS, Jorde UP, Naka Y, Moses JW, Takayama H. Impella LP 2.5 for left ventricular unloading during venoarterial extracorporeal membrane oxygenation support. *J Card Surg*. 2011;26:666–668. doi: 10.1111/j.1540-8191.2011.01338.x
72. Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G, Greco T, Lembo R, Müllerleile K, Colombo A, Sydow K, De Bonis M, Wagner F, Reichenspurner H, Blankenberg S, Zangrillo A, Westermann D. Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. *Eur J Heart Fail*. 2017;19:404–412. doi: 10.1002/ehf.668
73. Patel SM, Lipinski J, Al-Kindi SG, Patel T, Saric P, Li J, Nadeem F, Ladas T, Alaiti A, Phillips A, Medalion B, Deo S, Elgudin Y, Costa MA, Osman MN, Attizzani GF, Oliveira GH, Sareyyupoglu B, Bezerra HG. Simultaneous veno-arterial extracorporeal membrane oxygenation and percutaneous left ventricular decompression therapy with impella is associated with improved outcomes in refractory cardiogenic shock [published online February 27, 2018]. *ASAIO J*. doi: 10.1097/MAT.0000000000000767. https://doi.org/10.1097/MAT.0000000000000076
74. Moazzami K, Dolmatova EV, Cocke TP, Elmann E, Vaidya P, Ng AF, Satya K, Narayan RL. Left ventricular mechanical support with the Impella during extracorporeal membrane oxygenation. *J Tehran Heart Cent*. 2017;12:11–14.
75. Nakamura K, Krishnan S, Mahr C, McCabe JM. First-in-man percutaneous transaxillary artery placement and removal of the Impella 5.0 mechanical circulatory support device. *J Invasive Cardiol*. 2017;29:E53–E59.
76. Tayal R, Barvalia M, Rana Z, LeSar B, Iftikhar H, Kotev S, Cohen M, Wasty N. Totally percutaneous insertion and removal of impella device using axillary artery in the setting of advanced peripheral artery disease. *J Invasive Cardiol*. 2016;28:374–380.
77. Pozzi M, Quessard A, Nguyen A, Mastroianni C, Niculescu M, Pavie A, Leprince P. Using the Impella 5.0 with a right axillary artery approach as bridge to long-term mechanical circulatory assistance. *Int J Artif Organs*. 2013;36:605–611. doi: 10.5301/ijao.5000237
78. Hoepfer MM, Tudorache I, Kühn C, Marsch G, Hartung D, Wiesner O, Boenisch O, Haverich A, Hinrichs J. Extracorporeal membrane oxygenation watershed. *Circulation*. 2014;130:864–865. doi: 10.1161/CIRCULATIONAHA.114.011677
79. Napp LC, Brehm M, Kühn C, Schäfer A, Bauersachs J. Heart against veno-arterial ECMO: competition visualized. *Int J Cardiol*. 2015;187:164–165. doi: 10.1016/j.ijcard.2015.03.311
80. Choi JH, Kim SW, Kim YU, Kim SY, Kim KS, Joo SJ, Lee JS. Application of veno-arterial-venous extracorporeal membrane oxygenation in differential hypoxia. *Multidiscip Respir Med*. 2014;9:55. doi: 10.1186/2049-6958-9-55
81. Cakici M, Gumus F, Ozcinar E, Baran C, Bermede O, Inan MB, Durdu MS, Sirlak M, Akar AR. Controlled flow diversion in hybrid venoarterial-venous extracorporeal membrane oxygenation. *Interact Cardiovasc Thorac Surg*. 2018;26:112–118. doi: 10.1093/icvts/ivx259
82. Madershahian N, Nagib R, Wippermann J, Strauch J, Wahlers T. A simple technique of distal limb perfusion during prolonged femoro-femoral cannulation. *J Card Surg*. 2006;21:168–169. doi: 10.1111/j.1540-8191.2006.00201.x
83. Lamb KM, Hirose H, Cavarocchi NC. Preparation and technical considerations for percutaneous cannulation for veno-arterial extracorporeal membrane oxygenation. *J Card Surg*. 2013;28:190–192. doi: 10.1111/jocs.12058
84. Spurlock DJ, Toomasian JM, Romano MA, Cooley E, Bartlett RH, Haft JW. A simple technique to prevent limb ischemia during veno-arterial ECMO using the femoral artery: the posterior tibial approach. *Perfusion*. 2012;27:141–145. doi: 10.1177/0267659111430760
85. Kimura N, Kawahito K, Ito S, Murata S, Yamaguchi A, Adachi H, Ino T. Perfusion through the dorsalis pedis artery for acute limb ischemia secondary to an occlusive arterial cannula during percutaneous cardiopulmonary support. *J Artif Organs*. 2005;8:206–209. doi: 10.1007/s10047-005-0300-5
86. Makdisi G, Makdisi T, Wang IW. Use of distal perfusion in peripheral extracorporeal membrane oxygenation. *Ann Transl Med*. 2017;5:103. doi: 10.21037/atm.2017.03.01

87. Esper SA, Levy JH, Waters JH, Welsby IJ. Extracorporeal membrane oxygenation in the adult: a review of anticoagulation monitoring and transfusion. *Anesth Analg*. 2014;118:731–743. doi: 10.1213/ANE.000000000000115
88. Sy E, Sklar MC, Lequier L, Fan E, Kanji HD. Anticoagulation practices and the prevalence of major bleeding, thromboembolic events, and mortality in venoarterial extracorporeal membrane oxygenation: a systematic review and meta-analysis. *J Crit Care*. 2017;39:87–96. doi: 10.1016/j.jcrc.2017.02.014
89. Lazzara RR, Magovern JA, Benckart DH, Maher TD Jr, Sakert T, Magovern GJ Jr. Extracorporeal membrane oxygenation for adult post cardiomyotomy cardiogenic shock using a heparin bonded system. *ASAIO J*. 1993;39:M444–M447.
90. Lequier L, Annich G, Al-Ibrahim O, Bembea M, Brodie D, Brogan T, Buckvold S, Chicoine L, Conrad S, Cooper D, Dalton H, Frischer J, Harris B, Mazor R, Paden M, Rintoul N, Ryerson L, Wong T, Masicotte P. ELSO Anticoagulation Guideline. 2014; 1–17. <https://www.else.org/portals/0/files/elseanticoagulationguideline8-2014-table-contents.pdf> Accessed August 2, 2018.
91. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebel H, Schneider S, Schuler G, Werdan K; IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296. doi: 10.1056/NEJMoa1208410
92. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, Schuler G. Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. *Eur Heart J*. 2005;26:1276–1283. doi: 10.1093/eurheartj/ehi161
93. Kar B, Adkins LE, Civitello AB, Loyalka P, Palanichamy N, Gemmato CJ, Myers TJ, Gregoric ID, Delgado RM III. Clinical experience with the TandemHeart percutaneous ventricular assist device. *Tex Heart Inst J*. 2006;33:111–115.
94. Kar B, Gregoric ID, Basra SS, Idelchik GM, Loyalka P. The percutaneous ventricular assist device in severe refractory cardiogenic shock. *J Am Coll Cardiol*. 2011;57:688–696. doi: 10.1016/j.jacc.2010.08.613