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REVIEW TOPIC OF THE WEEK

Hemodynamics of Mechanical Circulatory Support

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CME Objective for This Article: After reading this article, the reader should be able to: 1) describe the characteristics of the left ventricular end-systolic and end-diastolic pressure-volume relations and which of their features can be used to index contractility and diastolic properties; 2) describe how changes in preload, afterload, ventricular contractility, and heart rate impact the left ventricular pressure-volume loop (specifically end-diastolic volume and pressure, stroke volume, systolic pressure generation) and myocardial oxygen demand; and 3) describe anatomic and physiological differences between the different types of mechanical circulatory support currently in use clinically.

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Hemodynamics of Mechanical Circulatory Support

ABSTRACT

An increasing number of devices can provide mechanical circulatory support (MCS) to patients with acute hemodynamic compromise and chronic end-stage heart failure. These devices work by different pumping mechanisms, have various flow capacities, are inserted by different techniques, and have different sites from which blood is withdrawn and returned to the body. These factors result in different primary hemodynamic effects and secondary responses of the body. However, these are not generally taken into account when choosing a device for a particular patient or while managing a patient undergoing MCS. In this review, we discuss fundamental principles of cardiac, vascular, and pump mechanics and illustrate how they provide a broad foundation for understanding the complex interactions between the heart, vasculature, and device, and how they may help guide future research to improve patient outcomes.
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For patients with advanced heart failure, there are an increasing number of therapies, especially in the form of mechanical circulatory support (MCS). There are several classes of MCS devices, distinguished by hemodynamic characteristics of the pump, the sites from which blood is withdrawn and returned, the size of catheters and/or cannulas used, whether the insertion technique is percutaneous or surgical, and whether or not a gas exchange unit is used. Some devices are for short-term use, whereas others can be used for the duration of a patient's life. These characteristics contribute to determining the ease of deployment, ease of patient management while on the device, and overall safety profile, as reviewed recently in detail (1). To varying degrees, all available devices improve cardiac output and blood pressure (2–5), but their specific features result in different overall hemodynamic effects. The implications of these differences are only partially understood (6) and have not yet been researched in clinical trials.

Right heart catheterization with a pulmonary artery catheter (PAC) is the cornerstone of a standard clinical hemodynamic evaluation of patients undergoing MCS. However, widespread routine use of PAC has declined over the past decade and there is no consensus on systematic use of PAC data (7). As a result, important differences in hemodynamic effects of different forms of MCS may have gone unrecognized. A full understanding from advanced hemodynamic principles of the mechanisms of such differences has the potential to impact clinical practice and outcomes.

This review aims to provide a concise overview of advanced hemodynamic principles, including the basics of ventricular mechanics, ventricular-vascular coupling, and myocardial energetics (see [8–10] for detailed descriptions). We will then review how these principles can be applied to better understand the hemodynamic effects of MCS.

FUNDAMENTALS OF LEFT VENTRICULAR MECHANICS

Events occurring during a single cardiac cycle are depicted by ventricular pressure–volume loops (PVLs) (**Figure 1A**). Under normal conditions, the PVL is roughly trapezoidal, with a rounded top. The 4 sides of the loop denote the 4 phases of the cardiac cycle: 1) isovolumic contraction; 2) ejection; 3) isovolumic relaxation; and 4) filling. The loop falls within the boundaries of the end-systolic pressure-volume relationship (ESPVR) and the end-diastolic pressure-volume relationship (EDPVR). The ESPVR is reasonably linear, with slope Ees (end-systolic elastance) and volume-axis intercept Vo. The EDPVR is nonlinear and described by simple equations, such as: $P = \beta(e^{\alpha[V-Vo]} - 1)$ or $P = \beta V^{\alpha}$. ESPVR, and EDPVR shifts occur with changes in ventricular contractility and diastolic properties (remodeling).

The actual position and shape of the loop depend on ventricular pre-load and afterload. At the organ level, pre-load can be defined as either end-diastolic pressure (EDP) or the end-diastolic volume (EDV), which relate to average sarcomere stretch throughout the myocardium. Afterload is determined by the hemodynamic properties of the vascular system against which the ventricle contracts and is most generally characterized by its impedance spectrum (the frequency-dependent ratio and phase shift between

pressure and flow, as determined by Fourier analysis). Afterload is more simply indexed by total peripheral resistance (TPR), the ratio between mean pressure and flow. Afterload can also be depicted on the pressure-volume plane by the "effective arterial elastance" (Ea) line (**Figure 1A**) (11). The slope of the Ea line is approximately equal to TPR/T, where TPR is in units of mm Hg · s/ml and T is the duration of the heartbeat in seconds. The Ea line starts on the volume axis at the EDV and intersects the ESPVR at the ventricular end-systolic pressure-volume point of the PVL. This allows approximation of stroke volume (SV) (the width of the loop) and ventricular end-systolic pressure (Pes) (the height of the loop). Pes is closely related to mean arterial pressure (MAP): MAP ≈ 0.9·Pes. When TPR, heart rate, or pre-load volume changes, the Ea line rotates and/or shifts so that its intersection with the ESPVR occurs at a different point (**Figure 1B**). This construct can be used to understand ventricular-vascular coupling, which is the science of describing how SV, MAP, and other key cardiovascular parameters are determined by preload, afterload, and contractility (**Figure 1B**). Specifically, SV can be estimated according to: $SV \approx (EDV - Vo)/(1 + Ea/Ees)$. Cardiac output is obtained by multiplying SV by heart rate, and ejection fraction is obtained by dividing SV by EDV. Similarly, MAP can be estimated by: $MAP \approx 0.9 \cdot (EDV - Vo)/(1/Ees + 1/Ea)$.

The ESPVR shifts with changes in ventricular contractility (**Figure 1C**) (8,12). Increases and decreases in contractility are associated with leftward and rightward shifts of the ESPVR, respectively, which are generally manifested as changes in Ees. In reality, Vo can also shift with changes in contractility. It is therefore necessary to account for changes of both Ees and Vo when using ESPVR to index contractility. This can be achieved through use of an index that integrates changes in both Ees and Vo, such as V_{120}, the volume at which the ESPVR reaches 120 mm Hg: $V_{120} = 120/Ees + Vo$. Higher values of V_{120} are associated with decreased contractility and vice versa.

The EDPVR is nonlinear and defines the passive diastolic properties of the ventricle (**Figure 2A**). This nonlinearity introduces complexity when indexing diastolic properties, specifically diastolic stiffness. Stiffness is the change in pressure for a given change in volume (dP/dV). Accordingly, diastolic stiffness varies with filling pressure, increasing as EDP increases, even in normal hearts. Some reports incorrectly quantify stiffness by the ratio of EDP to EDV (P/V), which also varies with filling pressure (**Figure 2A**). From an engineering perspective, diastolic material properties of the heart can be more appropriately indexed by its dimensionless stiffness constant, defined as (dP/dV)/(P/V) (8). For the case when the EDPVR is fit to the equation $P = \beta V^{\alpha}$, it can be shown that α is the stiffness constant. Because it requires measuring EDP and EDV over a range of volumes, quantification of the stiffness constant can be difficult in practice, especially when EDP is low and the nonlinear portion is not readily apparent.

Another index of diastolic properties is ventricular capacitance (**Figure 2B**), the volume at a specified filling pressure. Capacitance indexes the degree to which the EDPVR is either dilated (as with ventricular remodeling in chronic heart failure with reduced ejection fraction) or smaller than appropriate (as occurs in hypertrophic cardiomyopathy and other forms of diastolic heart failure). We and others have used V_{30}, the volume at an EDP of 30 mm Hg, as the index of ventricular capacitance.

In addition to providing a platform for explaining ventricular mechanics, the pressure-volume diagram also provides a platform for understanding the determinants of myocardial oxygen consumption (MVO_2) (**Figure 3A**) (13). MVO_2 is linearly related to ventricular pressure-volume area (PVA), which is the sum of the external stroke work (the area inside the PVL) and the potential energy. Potential energy is the area bounded by the ESPVR, the EDPVR, and the diastolic portion of the PVL, and represents the residual energy stored in the myofilaments at the end of systole that was not converted to external work.

APPLICATION TO MCS

Current modes of left ventricular (LV) MCS can be characterized by 1 of 3 different circuit configurations (**Central Illustration**): 1) pumping from the right atrium (RA) or central vein to a systemic artery; 2) pumping from the left atrium (LA) to a systemic artery; or 3) pumping from the LV to a systemic artery (generally the aorta). Peak flow rates achievable by different systems range from approximately 2.5 to 7.0 l/min. Flow rates and circuit configurations both have a major impact on their overall cardiac and systemic effects. Many other factors also affect the response to MCS, including: 1) the cardiovascular substrate (i.e., whether the patient has a prior history of chronic heart failure with a dilated, remodeled LV and/or

ABBREVIATIONS AND ACRONYMS

CVP = central venous pressure

Ea = effective arterial elastance

ECMO = extracorporeal membrane oxygenation

EDP = end-diastolic pressure

EDPVR = end-diastolic pressure-volume relationship

EDV = end-diastolic volume

Ees = end-systolic elastance

ESPVR = end-systolic pressure-volume relationship

LA = left atrial/atrium

LV = left ventricle/ventricular

LVAD = left ventricular assist device

MAP = mean arterial pressure

MCS = mechanical circulatory support

MVO_2 = myocardial oxygen consumption

PAC = pulmonary artery catheter

PCWP = pulmonary capillary wedge pressure

Pes = ventricular end-systolic pressure

PVA = pressure-volume area

RA = right atrial/atrium

RPM = rotations per minute

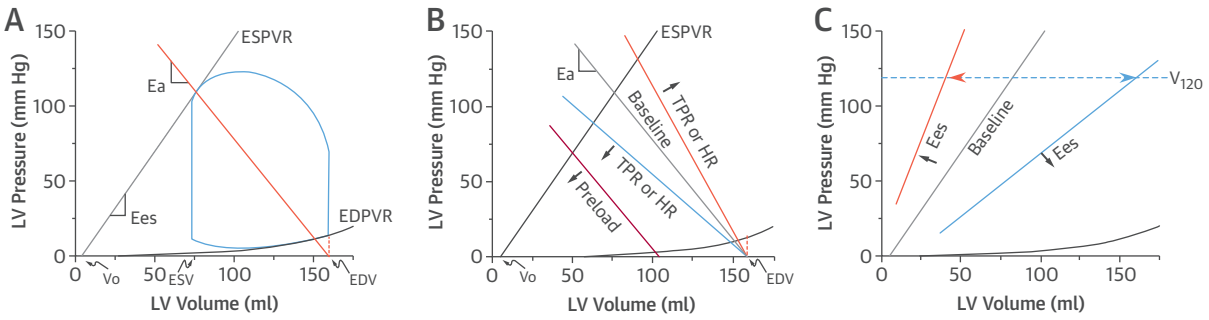
RV = right ventricle/ventricular

SV = stroke volume

TPR = total peripheral resistance

Vo = volume-axis intercept

FIGURE 1 Overview of PVLs and Relations

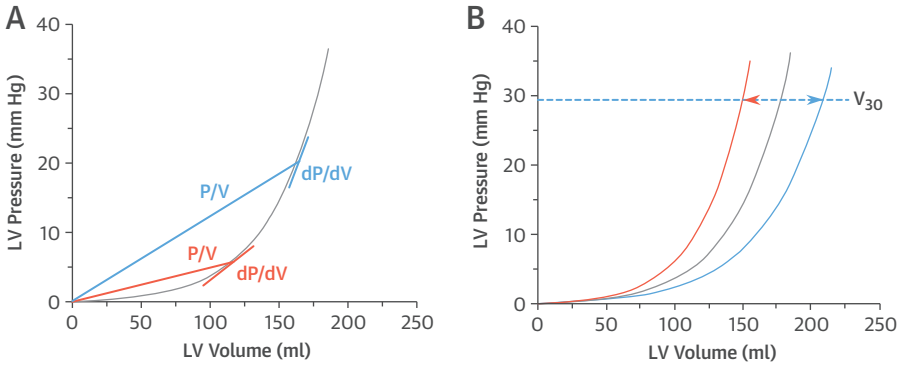


(A) Normal pressure–volume loop (PVL), is bounded by the end-systolic pressure–volume relationship (ESPVR) and end-diastolic pressure–volume relationship (EDPVR). ESPVR is approximately linear with slope end-systolic elastance (Ees) and volume-axis intercept (Vo). Effective arterial elastance (Ea) is the slope of the line extending from the end-diastolic volume (EDV) point on the volume axis through the end-systolic pressure–volume point of the loop. **(B)** Slope of the Ea line depends on total peripheral resistance (TPR) and heart rate (HR), and its position depends on EDV. **(C)** The ESPVR shifts with changes in ventricular contractility, which can be a combination of changes in Ees and Vo. Changes in contractility can be indexed by V_{120}, the volume at which the ESPVR intersects 120 mm Hg. ESV = end-systolic volume; LV = left ventricular.

right ventricle [RV], or whether it is a first event, with previously normal heart structure); 2) the degree of acute LV recovery following initiation of MCS (e.g., potentially recoverable in some forms of acute coronary syndrome, but less likely recoverable with idiopathic cardiomyopathy); 3) right-sided factors, such as RV systolic and diastolic function and pulmonary vascular resistance; 4) the degree to which baroreflexes are intact and can modulate vascular and ventricular properties; 5) concomitant medications; and 6) metabolic factors, such as pH and pO_2, which, if corrected, could result in improved ventricular and vascular function. Finally, the characteristics of the pump (e.g., pulsatile, axial, or centrifugal flow) can also have an impact on several aspects of the hemodynamic responses to MCS (14).

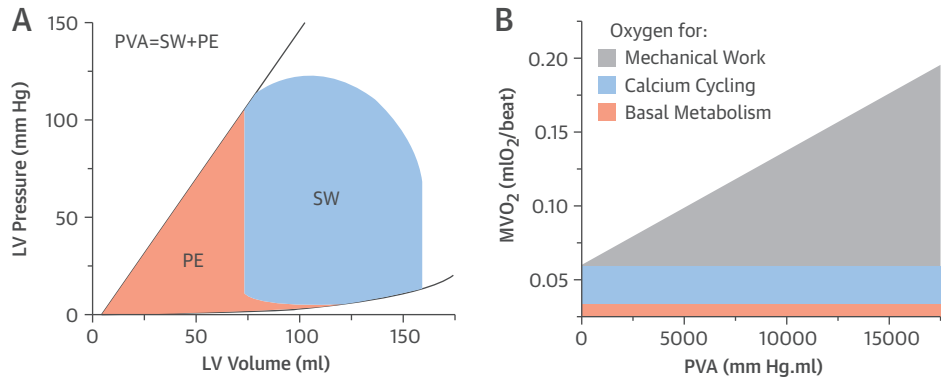
It is therefore important to understand and distinguish between the primary hemodynamic effects of a device (i.e., the expected effects on pressures and flow in the absence of any change in native heart or vascular properties) and the net hemodynamic effects observed after accounting for the impact of secondary modulating factors invoked

FIGURE 2 Characteristics of the EDPVR



(A) The EDPVR is nonlinear. Stiffness is indexed by the change in pressure divided by the change in volume (dP/dV), varies with pressure. P/V, the ratio of end-diastolic pressure to volume, also varies with pressure. The myocardial stiffness constant, (dP/dV)/(P/V), is considered a valid measure of myocardial diastolic material properties. **(B)** One clinically useful index of diastolic properties is ventricular capacitance, which is the volume at a specified pressure such as V_{30}, the volume at 30 mm Hg. Abbreviations as in Figure 1.

FIGURE 3 Myocardial Energetics Assessed on the Pressure-Volume Diagram



(A) Pressure-volume area (PVA) is the sum of the stroke work (SW) and potential energy (PE). **(B)** Myocardial oxygen consumption (MVO_2) is linearly correlated with PVA and is divided into 3 major components, as indicated in the figure. LV = left ventricular.

following initiation of MCS. Both components of device effects will be discussed later.

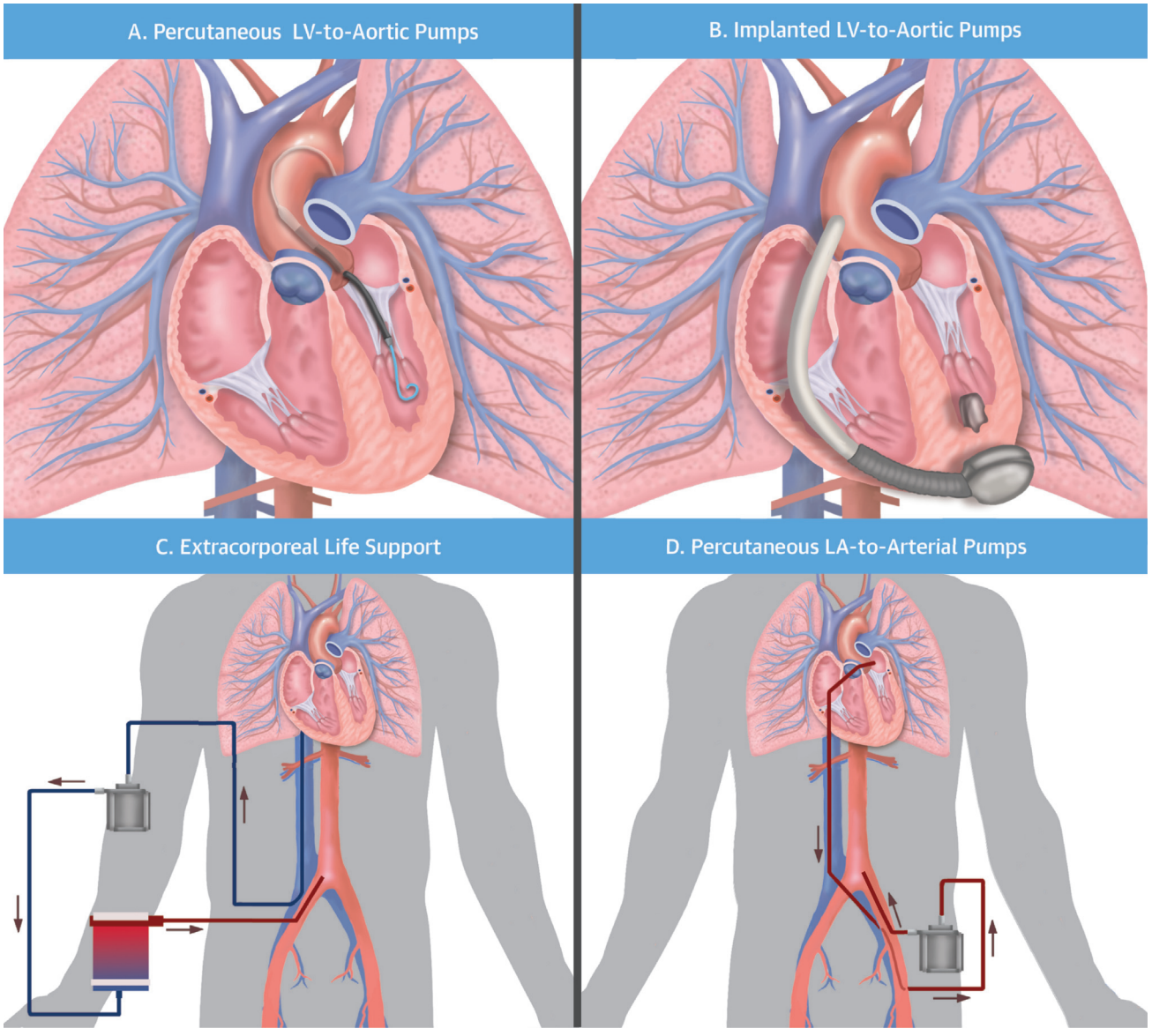
Finally, use of the theories of ventricular mechanics detailed earlier within the context of a comprehensive cardiovascular simulation (9,10) facilitates illustration and comparison of the hemodynamic effects of different forms of MCS. The simulation we used has been detailed, can be used to understand the physiology of MCS, and has been validated to a certain degree pre-clinically (15). Other aspects of validation and limitations of the simulation have also been detailed previously (15–17). Note that the response of a given patient to MCS must account for baseline pre-load, afterload LV contractility, and the flow rate of the MCS pump. For simplicity, subsequent comparisons keep these factors constant. Importantly, the basic principles to be discussed apply across a wide range of conditions.

RA-TO-ARTERIAL CIRCULATORY SUPPORT. Extracorporeal venoarterial membrane oxygenation (ECMO), also referred to as extracorporeal life support, utilizes a pump with the capacity to assume responsibility for the entire cardiac output and a gas exchange unit for normalizing pCO_2, pO_2, and pH. However, strictly on a hemodynamic basis, the use of this circuit configuration can cause significant increases in LV pre-load and, in some cases, pulmonary edema. This is illustrated in **Figure 4A**, which depicts PVLs in a case of cardiogenic shock due to profound, irreversible LV dysfunction. Baseline cardiogenic shock conditions (PVL in black) have a high LV EDP, low pressure generation, low SV, and low ejection fraction. As ECMO flow is initiated and increased stepwise from 1.5 to 3.0 to 4.5 l/min, the primary hemodynamic effect is increased LV afterload pressure and effective Ea. If TPR and LV contractility are fixed, the only way for the LV to overcome the increased afterload is via the Starling mechanism, and blood accumulates in the LV. Consequently, LV EDP, LA pressure, and pulmonary capillary wedge pressure (PCWP) increase, and the PVL becomes increasingly narrow (decreased native LV SV) and taller (increased afterload pressure), and shifts rightward and upward along the EDPVR. Because the EDPVR is nonlinear, large increases in LV EDP may cause only subtle increases in LV EDV. An echocardiogram showing a persistently closed aortic valve during ECMO would also signify a state of maximal LV loading and high PCWP. These increases in LV pre-load and PCWP are detrimental to blood oxygen saturation coming from the lung and markedly increase myocardial oxygen demand (increased PVA), which can worsen LV function, especially in the setting of acute myocardial ischemia or infarction.

These responses to ECMO can be modulated by secondary regulatory factors that influence either TPR or LV contractility. TPR can be reduced naturally by the baroreceptors, pharmacologically (e.g., nitroprusside), or mechanically (e.g., by intra-aortic balloon pumping). As illustrated in **Figure 4B**, a 50% reduction in TPR during ECMO markedly blunts the rise in LV EDP.

Short-term improvements in LV function can also modulate the rise in PCWP. LV function can be improved during ECMO due to increased central aortic pressure, the improved coronary perfusion, normalization of blood oxygen content (improved oxygen delivery to the myocardium), and normalization of

CENTRAL ILLUSTRATION **Mechanical Circulatory Support: 4 Options to Pump Blood Within the Cardiovascular System**

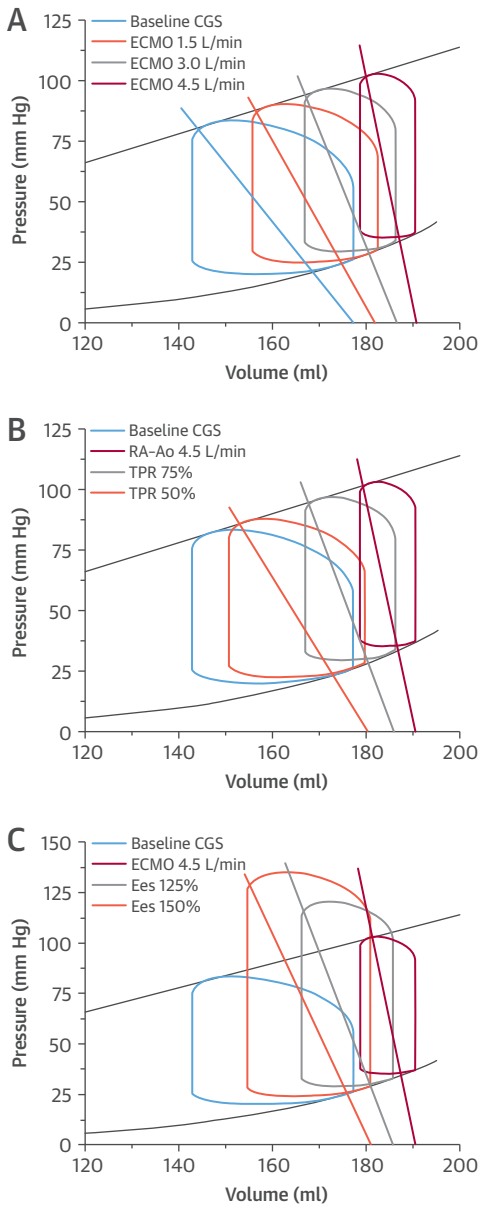


Burkhoff, D. et al. J Am Coll Cardiol. 2015; 66(23):2663-74.

Although all forms of mechanical circulatory support return blood to the arterial system, they differ with respect to the site from which they draw blood. These differences underlie differences in their hemodynamic effects. Percutaneous **(A)** and durable ventricular devices **(B)** that take blood from the LV have similar physiology. Extracorporeal membrane oxygenation (ECMO) withdraws blood from the right atrium or venous system and utilizes a blood gas exchange unit **(C)**. Percutaneous devices can also achieve LA sourcing of blood (without need for a gas exchange unit) **(D)**. LA = left atrium/atrial; LV = left ventricle/ventricular.

acid-base and other metabolic abnormalities. Pharmacological enhancement of contractility (e.g., by β-agonists or phosphodiesterase inhibitors) is also possible, but may not be beneficial in cardiogenic shock due to their independent effects to increase MVO_2 and potential effects on heart rate and arrhythmias. As illustrated in **Figure 4B**, a 50% increase in LV Ees during ECMO also blunts the primary rise in LV EDP.

FIGURE 4 Ventricular Effects of ECMO



(A) Impact of extracorporeal membrane oxygenation (ECMO) on pressure-volume loops, showing flow-dependent increases of end-diastolic pressures (EDPs), increases of effective arterial elastance, and decreases in LV stroke volume. ECMO-dependent increases in EDP can be partially mitigated by decreases in TPR **(B)**, and/or improvements in Ees **(C)**. CGS = cardiogenic shock; RA-Ao = right atrium to aorta; other abbreviations as in Figure 1.

When secondary factors are insufficient to self-mitigate a rise in LV EDP, other strategies can be utilized to reduce possible increases in afterload pressure and allow for LV decompression. These include atrial septostomy (to allow left-to-right shunting), a surgically placed LV vent, an intraaortic balloon pump, or use of a percutaneous LV-to-aorta ventricular-assist device (described in later text) (1,18).

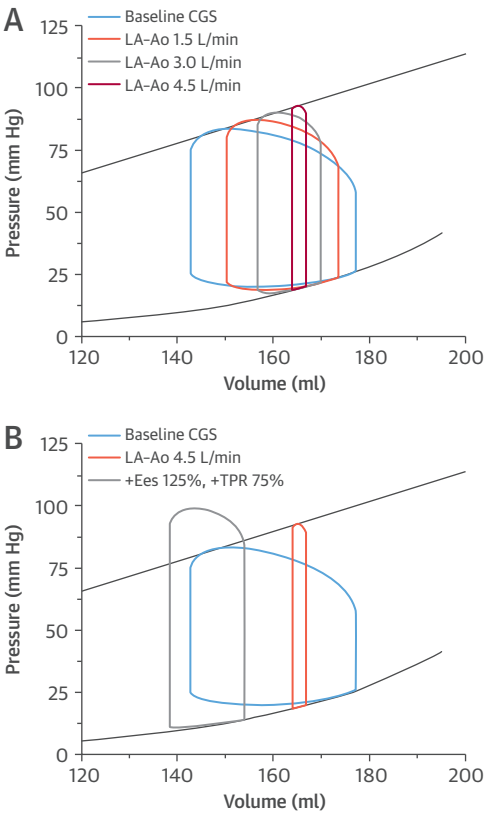
Incorporation of a gas exchange unit that normalizes blood gases is a key feature of ECMO, compared with other forms of MCS. It is important to note that blood gases measured near the site of blood return do not necessarily reflect blood gases throughout the body. If, for example, blood is returned to the femoral or iliac artery and pulmonary edema compromises native lung function, oxygen delivery to the lower extremities may be normal, although oxygen delivery to the head and upper extremities may be significantly compromised.

In summary, hemodynamic responses to ECMO are complex and variable among patients due to a host of clinical factors. In some patients, it becomes readily apparent that afterload reduction or mechanical LV unloading is required, either when pulmonary edema appears on a chest x-ray or PCWP is noted to be elevated. Variable secondary effects of ECMO on TPR and LV contractility can explain the variability of responses among patients. However, even in the presence of relatively large secondary effects, ECMO by itself may not lead to significant LV unloading.

LA-TO-ARTERIAL CIRCULATORY SUPPORT. Temporary LA-to-arterial MCS can be achieved with extracorporeal devices, such as TandemHeart (CardiacAssist, Pittsburgh, Pennsylvania), which has a flow capacity up to ~5 l/min. LA-to-arterial MCS has also been investigated for long-term use in patients with severe, but stable (INTERMACS ≥4) chronic heart failure (19). The site of blood return is typically 1 or both femoral arteries for the percutaneous approach, and the right subclavian or axillary artery for the chronic application. Given that blood is withdrawn directly from the LA, PCWP and LV EDP decrease with this approach. In the case that the patient has pulmonary edema, blood oxygenation can be improved due to the reduction in PCWP. As for ECMO, blood must exit the LV through the aortic valve with LA-to-arterial MCS. Therefore, if arterial pressure is increased during MCS, LV pressure generation must also increase. In contrast to ECMO, the necessary increase in LV pressure generation can be achieved by an isolated increase in end-systolic volume (Figure 5A). Thus, PVA and MVO_2 can be unchanged or decreased by this approach.

These primary effects are modified when secondary factors result in decreases in TPR and increases of Ees. In such cases, end-systolic and end-diastolic volumes can both decrease, along with PVA and

FIGURE 5 Ventricular Effects of LA-to-Arterial MCS



(A) Flow-dependent changes in pressure–volume loops with left atrial-to-aortic (LA-Ao) pumping, showing reducing end-diastolic pressures, increasing end-systolic volume, and decreasing LV stroke volume. **(B)** Effects on end-diastolic and end-systolic volumes and pressure are modified by changes in TPR and Ees. MCS = mechanical circulatory support; other abbreviations as in Figures 1 and 4.

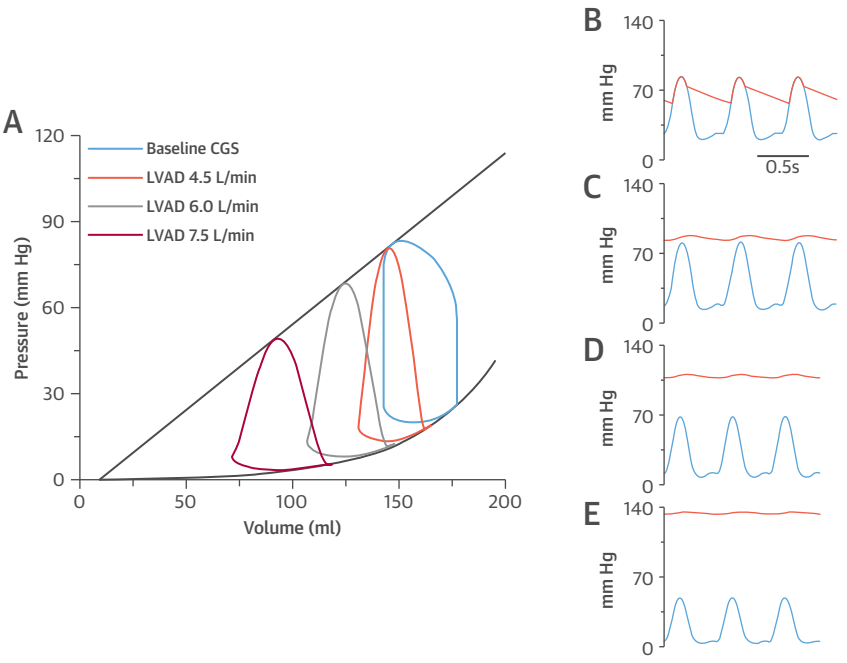
MVO_2 (Figure 5B). Because these responses can vary significantly between patients, the net impact of LA-to-arterial MCS, like ECMO, can vary between patients.

LV-TO-AORTA CIRCULATORY SUPPORT. Several devices pump blood from the LV to the arterial system, including percutaneous catheter-based transvalvular devices for temporary use and fully implantable, durable, LV assist devices (LVADs), intended for long-term or permanent support. Percutaneous transvalvular devices include the commercially available Impella 2.5, Impella CP, Impella 5.0, and Impella LD family of devices (Abiomed, Danvers, Massachusetts) and the Percutaneous Heart Pump (PHP, Thoratec, Pleasanton, California, which has received CE Mark and is under clinical investigation in the United States). These devices can, in principle, reach mean flows of ~5 l/min. Durable devices include the HeartMate II (St. Jude Medical, St. Paul, Minnesota) and the HVAD (HeartWare, Framingham Massachusetts), and a number of other devices currently under clinical evaluation (e.g., HeartMate III and MVAD). These devices can reach mean flows over 7 l/min. Although these devices employ different mechanisms to pump blood (e.g., axial, centrifugal, and mixed-flow pump technologies), are implanted with different techniques, and have different flow capacities, the same principles govern their hemodynamic effects.

Continuous pumping of blood directly from the LV, independent of the phase of the cardiac cycle, results in loss of the normal isovolumic periods. This transforms the PVL from its normal trapezoidal shape to a triangular shape (Figure 6). Unlike the other forms of support, removal of blood from the LV is not dependent on ejection through the aortic valve. As pump flow rate increases, the LV becomes increasingly unloaded (progressive leftward shifted PVL), peak LV pressure generation decreases, and there are marked decreases in PVA and MVO_2. At the same time, arterial pressure increases, such that peak LV pressure and arterial pressure are increasingly dissociated (Figure 6B to 6E). This direct unloading also results in decreased LA and wedge pressures. As illustrated in the cases described earlier, improved blood oxygenation, systemic pressures, and perfusion may improve the metabolic milieu and invoke beneficial secondary changes in LV contractility and TPR. For the case of LV-to-arterial pumping, these secondary changes result in even greater degrees of LV unloading (Figure 7). Also note that for this particular case of increased LV Ees and decreased TPR, LV pressure is sufficient to overcome aortic pressure, and LV ejection occurs; nevertheless, the more triangular shape of the PVL is still present.

Another consideration for durable LV-to-arterial MCS is the difference in characteristics between axial and centrifugal flow pumps, typified by the HVAD and HeartMate II, respectively, the 2 pumps in most common use today. Some authors argue that the differences are significant, largely on the basis of theoretical considerations (14). However, in a recent study in experimental heart failure in which these types of pumps were compared (20), the authors concluded that there were no pronounced acute differences. This is consistent with our own recent clinical data showing no significant differences in overall hemodynamic effects of these 2 pumps (7). Further work on this topic is needed because new pumps of both types are currently being introduced into the clinic.

FIGURE 6 Ventricular Effects of LV-to-Arterial MCS



(A) Flow-dependent changes of the pressure-volume loop with LV-to-aortic pumping. The loop becomes triangular and shifts progressively leftward (indicating increasing degrees of LV unloading). Corresponding LV and aortic pressure waveforms at baseline **(B)**, 4.5 l/min **(C)**, 6.0 l/min **(D)** and 7.5 l/min **(E)**. With increased flow, there are greater degrees of LV unloading and uncoupling between aortic and peak LV pressure generation. LVAD = left ventricular assist device; other abbreviations as in Figures 1, 4, and 5.

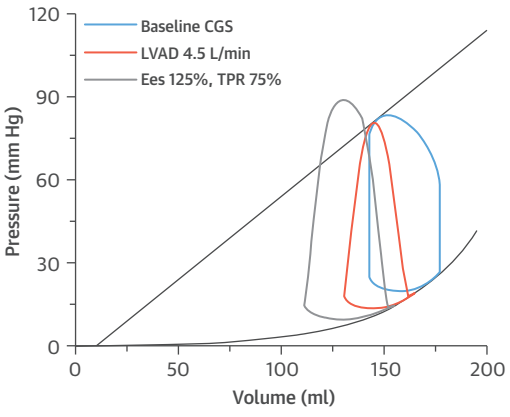
RIGHT HEART CATHETERIZATION

Descriptions in the preceding sections focused on theoretical characterizations of primary and secondary effects of different forms of acute and chronic MCS through the window of the pressure-volume diagram. Because measurements of continuous volume signals are mainly restricted to the clinical research setting, direct application in everyday clinical practice is not feasible. Nevertheless, these theories help to inform which data to collect and how to interpret it, not only on a general population basis, but also potentially on a patient-by-patient basis (17).

In this regard, information from standard PAC is central for evaluating patients potentially in need of MCS, for the definitive assessment of patient volume status, adequacy of ventricular support, and for diagnosis of potential MCS complications, including pump thrombosis. A sound understanding of the underlying theories reviewed earlier have helped guide our own development of patient evaluation and management strategies that aim to make maximal use of PAC-derived measures.

As a first step towards that end, the theories and simulations described earlier led us to propose a means of evaluating the adequacy of MCS and medical therapy by simultaneous evaluation of central

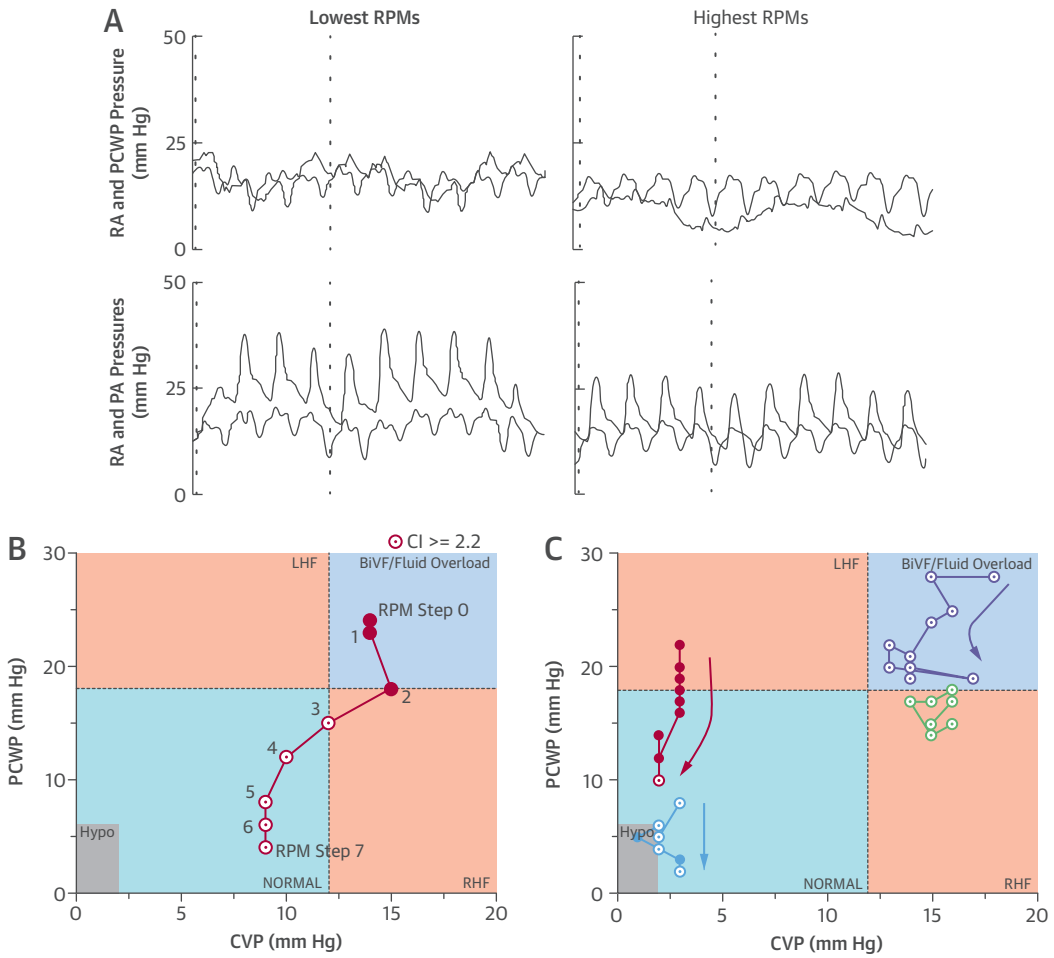
FIGURE 7 Secondary Increases in Ees and Decreases in TPR Enhance Unloading Effects of LV-to-Aortic Pumping



Abbreviations as in Figures 1 and 4.

venous pressure (CVP), PCWP, and cardiac index over a range of device speeds (7). To achieve this, patients undergo a standardized speed ramp test in which device rotations per minute (RPM) are initially decreased to the lowest recommended value and are then increased stepwise by a standardized amount. At each RPM, hemodynamic parameters are recorded after steady-state conditions are re-established (generally 2 to 5 min). Maximal RPM for the test is determined either by the maximal recommended speed for the device, or the occurrence of hypertension, suction events, or arrhythmias. CVP and PCWP are plotted as a function of each other, and the individual data points can be coded, depending on the adequacy of cardiac index (e.g., cardiac index >2.0 l/min/m^2). **Figure 8A** shows examples of original tracings of RA, PA, and PCWP tracings obtained at the highest and lowest speeds of a typical durable-LVAD patient (7). As shown, the increase in RPM is associated with significant decreases in PA pressures and PCWP; RA pressure is influenced significantly less. Note normal respiratory variations; it is important for proper results that readings be made at end-expiration which, during spontaneous respiration, is during the phase at which pressures are highest (note that automated computer analyses of these tracings generally

FIGURE 8 Impact of Rotational Speed Variations of Durable LVADs on Standard PAC-Derived Hemodynamics



(A) Original tracings of right atrial (RA), pulmonary artery (PA), and pulmonary capillary wedge pressures (PCWP) at lowest and highest speeds measured during a ramp test. Note normal respiratory variations. **(B)** Simultaneous changes in central venous pressure (CVP) and PCWP as speed of a ventricular assist device is increased. Five zones of this domain are detailed in the text. Symbols further code for whether cardiac index (CI) is ≥2.0 l/min/m^2. **(C)** Data from 4 different patients showing variability of responses to speed changes. **B and C** were modified from Uriel et al. (7). BiVF = biventricular failure; LHF = left heart failure; LVAD = left ventricular assist device; PAC = pulmonary artery catheter; RHF = right heart failure; RPM = rotations per minute.

do not account for the phase of respiration and can provide misleading results). As illustrated in **Figure 8B**, the CVP-PCWP diagram can be divided into 5 zones on the basis of proposed (though arbitrary) clinically acceptable ranges of CVP (3 to 12 mm Hg) and PCWP (8 to 18 mm Hg): 1) normal; 2) right heart failure; 3) left heart failure; 4) biventricular failure and/or fluid overload; and 5) hypovolemic zones. The test shown consisted of 8 different RPMs (steps 0 to 7). This particular patient starts with high values of CVP and PCWP. As RPMs are increased, the CVP-PCWP point moves into the normal range, including achievement of an adequate cardiac index. Although pump speed adjustments on the basis of ramp test results have not yet been correlated with improved clinical outcomes, it is suggested that the optimal speed can be determined by identifying the speed that provides normal values for CVP, PCWP, and cardiac index. In this example, the speed at steps 4 and 5 would satisfy this condition.

An individual patient's response depends on many factors, such as volume status, intrinsic RV contractility, systemic and pulmonary vascular properties, and any coexisting valvular lesions. Thus, not every patient can be brought into the normal ranges for all measured values. Such deviations suggest the need for additional evaluations for definitive diagnosis and medical therapies. CVP-PCWP relations measured during ramp tests from 4 clinically stable, seemingly well-compensated patients, 47 to 74 years of age who were supported with a durable LVAD are shown in **Figure 8C** (with cardiac index coded by symbol). These patients had reasonably controlled blood pressures (70 to 95 mm Hg, as assessed by Doppler opening pressure) and devices showed no evidence device thrombosis or malfunction (e.g., lactate dehydrogenase values 190 to 385 U/l). One patient (red) starts in the "left heart failure" zone at low speed and moves to the normal zone with increased speed. Another patient (blue) remains with low CVP and PCWP ranges independent of speed, suggesting a hypovolemic state that might benefit from volume administration and/or reduction of diuretic therapy. A third patient (cyan) remains with elevated CVP and PCWP despite increases in speed, always with adequate cardiac index, suggesting a fluid overload state that would, perhaps, benefit from more diuresis. A fourth patient (green) remains with elevated CVP with minor effects on PCWP, suggestive of right-sided dysfunction.

Although applied here to patients with durable devices, the same principles should apply to patients receiving short-term percutaneous MCS.

The approach outlined in the preceding text illustrates that development of innovative approaches that capitalize on standard hemodynamic measures founded on advanced hemodynamic theories have the potential to help in the management of MCS patients. Whether this approach results in improved outcomes, compared with current guidelines for patient management by the International Society for Heart and Lung Transplant (21), is the topic of ongoing research. A preliminary retrospective study suggests that use of invasive hemodynamic-guided optimization of RPMs and medical therapy has the potential to improve clinical outcomes (22). As previously demonstrated, more direct application of hemodynamics can assist directly in device selection and patient management.

SUMMARY

There is an increasing number of MCS options for treating patients with acute and chronic hemodynamic compromise. The characteristics of these devices vary significantly, and underlie significant differences in their primary hemodynamic effects and secondary responses. Clinical data to guide optimal device selection and use are currently lacking. Novel approaches utilizing standard hemodynamic measures have the potential to be impactful. However, the more fundamental principles of cardiac mechanics, ventricular-vascular coupling, and ventricular-vascular-device coupling reviewed herein provide an even broader foundation for clarifying the issues and generating testable hypotheses to improve clinical outcomes. Application of these principles is in its infancy, but already yielding encouraging results (7). Basic principles that we identified for each mode of MCS have been illustrated using a cardiovascular simulation with a set of parameters that is representative of patients undergoing MCS. However, patients present with a vast range of combinations of cardiac, vascular, and metabolic characteristics; each patient may be considered unique. Understanding the fundamentals of ventricular-vascular-device interactions as summarized herein and elsewhere (8,15) provides a foundation for understanding individual patient responses. In this regard, it is noteworthy that there is even less understanding of the physiology of MCS solutions for profound biventricular failure, including total artificial hearts, biventricular percutaneous devices, or biventricular durable devices. The concepts reviewed also provide the foundation for addressing those complex settings.

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KEY WORDS cardiac index, cardiac output, central venous pressure, extracorporeal circulatory membrane oxygenation, pulmonary capillary wedge pressure, ventricular assist devices

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