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Hemodynamic Rounds

The Science Behind Percutaneous Hemodynamic Support: A Review and Comparison of Support Strategies

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Patients in a variety of cardiovascular disease states may benefit from temporary percutaneous cardiac support, including those in acute decompensated heart failure, fulminant myocarditis, acute myocardial infarction with or without cardiogenic shock and those undergoing high-risk percutaneous coronary intervention. The ideal percutaneous cardiac support device is safe, easy to use and versatile enough to meet the needs of various clinical situations and patient cohorts. In addition, it should provide maximal hemodynamic support and protection against myocardial ischemia. With these goals in mind, the scientific principles that govern hemodynamic effectiveness and myocardial protection as they pertain to acute support devices are reviewed. © 2012 Wiley Periodicals, Inc.

Key words: hemodynamics; support; ventricular assist device; ischemia

CLINICAL INDICATIONS FOR PERCUTANEOUS CARDIAC SUPPORT

The practice of interventional cardiology is moving toward aggressive therapy for higher-risk and complex patient subsets to improve cardiac function, quality of life and overall survival. As a result, the field of percutaneous cardiac support devices has evolved rapidly. Three populations appear most likely to benefit from such devices: (1) those in need of high-risk percutaneous coronary intervention (PCI), (2) those with acute myocardial infarction with or without cardiogenic shock, to reduce infarct size and support end-organ perfusion, and (3) those with acute decompensated heart failure, be it due to acute coronary syndrome, myocarditis or exacerbation of a chronic heart failure state. Clinical indications for percutaneous cardiac assist device placement may therefore be grouped according to whether device placement occurs electively (high-risk PCI), urgently (acute myocardial infarction or mild to moderate decompensated heart failure), or emergently (cardiogenic shock due to acute myocardial infarction or severe decompensated heart failure).

Recently completed clinical trials such as the synergy between PCI with Taxus and cardiac surgery (SYNTAX) trial, as well as the upcoming evaluation of Xience prime versus coronary artery bypass surgery for effectiveness of left main revascularization (EXCEL), suggest that PCI may become more frequently utilized in the setting of high-risk multivessel and/or unprotected left main disease [1,2]. Updated guidelines by the American College of Cardiology and the American Heart Association support left main PCI in patients in whom the risks and benefits of a percutaneous approach appear as good, if not better, than coronary bypass surgery [3]. With the aging population, many patients with coronary artery disease will have hemodynamic instability, severe reductions in left ventricular function, or other comorbidities that elevate

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risk of both PCI and open-heart surgery. In such patients, PCI is often the most appropriate option, despite associated procedural and in-hospital risk. Cardiac assist devices have been increasingly called upon to minimize procedural risk, facilitate single- or multivessel PCI and improve short- and long-term outcome.

Patients with acute myocardial infarction with or without cardiogenic shock, a high-risk subset for in-hospital mortality, form another group in whom percutaneous cardiac assist devices may be increasingly utilized. Such patients are increasingly offered primary PCI, as supported by current guideline recommendations and clinical trials, regardless of age or comorbidity [3,4]. While associated in-hospital mortality has improved in these patients, few treatments other than early revascularization have shown potential to reduce infarct size. In addition, those with cardiogenic shock remain at elevated risk for both 30-day and 6-month mortality despite early revascularization and are oftentimes left with severe ventricular and end-organ dysfunction [5]. By facilitating emergent revascularization, maintaining end-organ perfusion and favorably impacting myocardial oxygen consumption, cardiac assist devices may both preserve cardiac function and improve survival.

Finally, patients with acute decompensated heart failure, either so-called "acute-on-chronic failure" in those with previous cardiac dysfunction, or acute fulminant decompensation, as in acute myocarditis, remain without good medical options to prevent worsening heart failure (WHF), progression to cardiogenic shock, or death [6]. Inotrope therapy, while beneficial in supporting the hemodynamic state acutely [7], is associated with worse morbidity and mortality, making invasive options such as cardiac assist devices potentially more palatable [8,9]. Indeed, the ability to rest the failing heart while maintaining peripheral perfusion without initiation or escalation of inotropic therapy has the potential to improve mortality in these patients while preserving cardiac function.

In each of these settings, the goals of cardiac support are distinctly different. For the elective setting, the goal is primarily to bridge a stable hemodynamic state through a complex interventional procedure; in essence to allow the cardiovascular system to weather transient derangements and resume normal function immediately postprocedure or shortly thereafter. In addition, the ideal device should alter myocardial ischemic threshold to allow time for complex PCI and any associated procedural complications to resolve, such as distal embolization or coronary dissection. In contrast, in the urgent and emergent settings, the goal is often to take over the work, partly or wholly, of a struggling heart, minimize ongoing ischemic damage (especially in acute myocardial infarction), and promote a stable hemodynamic state of systemic pressure and perfusion without the need for deleterious vasopressors and inotropes [8–12]. By resting the heart and simultaneously ensuring end-organ perfusion, the patient returns to an autonomous cardiovascular state with minimal decline in cardiac or end-organ function and, potentially, improved survival.

The goal of this review is to summarize the basic hemodynamic principles that form a basis for understanding and comparing the mechanisms by which currently available percutaneous support devices provide circulatory support and their impact on myocardial energetics. Issues related to ease-of-use and safety will also be discussed as substantiated by data in the literature. The primary devices to be reviewed include the intraaortic balloon pump (IABP), extracorporeal cardiopulmonary support (CPS or ECMO), left atrial-to-arterial pumping (e.g., TandemHeart, Cardiac Assist) and intracorporeal transvalvular ventricular-to-aortic pumping (e.g., Impella, Abiomed).

GOALS OF PERCUTANEOUS CARDIAC SUPPORT

From a clinical perspective, the ideal percutaneous cardiac support strikes an optimal balance between safety and efficacy, while maintaining adaptability to various clinical situations and patient cohorts. Indeed, the ideal device could be initiated rapidly using basic invasive cardiology techniques and would cause no vascular or other complications. In addition, it would provide normal or supra-normal levels of cardiac output and blood pressure (hemodynamic) support while reducing pulmonary capillary wedge pressure to normal, thus providing optimal conditions for maintaining perfusion of all vital organs (Fig. 1).

Principles of Hemodynamic Support

The basic goal of hemodynamic support is to produce a stable and physiologically acceptable blood pressure, cardiac output, and pulmonary venous pressure. When these goals are attained, end-organ perfusion is maintained, blood can be adequately oxygenated by the lungs and diuresis is promoted in states of volume overload. While also relevant to high-risk PCI, the ability to achieve and maintain adequate hemodynamic support has traditionally been most appreciated for patients presenting with low cardiac output acute heart failure, acute myocardial infarction, and cardiogenic shock.

Vasopressor and inotropic therapies have traditionally been utilized as first line treatment for hemodynamic support [13,14]. However, while shown to

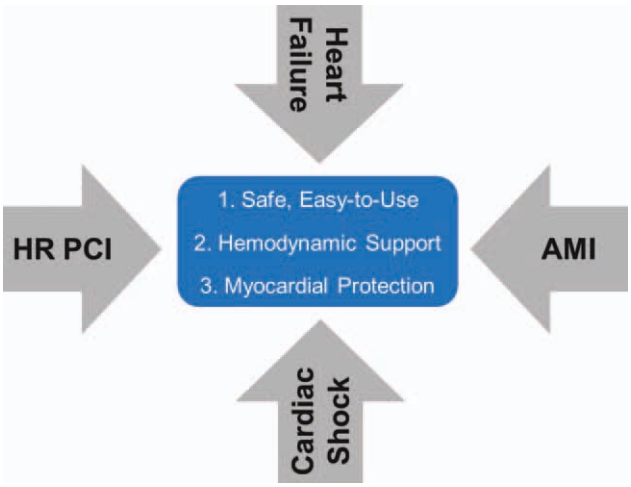

Fig. 1. Indications and goals of the ideal cardiac assist device. The ideal cardiac assist device should be safe, easy-to-use and provide adequate hemodynamic support and protect against myocardial ischemia to enhance outcomes in high-risk cohorts, including those with heart failure, acute myocardial infarction, cardiogenic shock, and those in need of high-risk percutaneous coronary intervention. AMI = acute myocardial infarction, HR PCI = high-risk percutaneous coronary intervention.

increase blood pressure and cardiac output, the impact on end organ perfusion can be variable (depending on the degree of peripheral vasoconstriction) and there are well-established adverse effects on the heart itself [8–12,15,16]. Indeed, the combination of multiple agents appears to be associated with worse outcome [16]. Part of the problem may be a lack of understanding when the goals of hemodynamic support have been reached, as under-reaching or overstepping such goals may be partly responsible for the higher morbidity and mortality associated with these agents. To this end, heavy reliance has typically been placed on the pulmonary artery catheter (PAC) to titrate medication dosage to various hemodynamic parameters, including cardiac output (CO), pulmonary capillary wedge pressure and systemic vascular resistance. Yet, despite this, multiple studies have shown little to no benefit in PAC-guided therapy in such patients [17–19].

Most recently, prognostic information of cardiac power output (CPO) has been explored. Defined as the cardiac output multiplied by the mean arterial pressure (divided by 451 to convert to units of Watts), the parameter takes into account the ability of the heart to generate systemic flow and blood pressure, thus providing a target for optimizing hemodynamic support [20]. Such a parameter is congruent with collective experience, which had suggested that cardiac output is necessary but not sufficient for end-organ perfusion; adequate mean arterial pressure is also required.

Multiple studies have now corroborated the independent association and predictive power of CPO on mortality in various severe cardiac dysfunctional states, including myocardial infarction-related cardiogenic shock, ischemic and nonischemic cardiomyopathy and acute myocarditis [20–22]. Further, CPO was able to predict worsening heart failure (WHF) in patients presenting with milder degrees of acute heart failure as well as those nearing cardiogenic shock [6]. In contrast, CO and the other more traditional hemodynamic parameters did not show independent associations with mortality [22]. Studies have also now established a cut-point CPO associated with a reduced incidence of worsening heart failure and mortality in high-risk patients. In those admitted with acute heart failure, for example, a CPO < 0.6W maximized sensitivity and specificity in predicting worsening heart failure at 30 days, while a CPO cut-point of 0.53W proved predictive of mortality in cardiogenic shock [21,22].

Taken together, although there currently exists no prospective data on the clinical utility of CPO targets, the ideal cardiac assist device would provide augmentation of both cardiac output and mean arterial pressure (and thereby augment CPO) to ensure systemic perfusion and end-organ function while also ensuring that pulmonary venous pressure is below a level that causes pulmonary edema. For patients undergoing high-risk PCI, stabilization of mean arterial pressure during PCI is the primary goal, with maintenance of CPO important only if significant drops in native cardiac output occur, as with PCI-related complication or global ischemia. In contrast, those with heart failure and cardiogenic shock, including those presenting with acute myocardial infarction, are more dependent on device-mediated increases in CPO, ideally to maintain CPO $>$x0.6W without use of deleterious vasopressors and inotropes. Cardiac assist devices may be judged on their ability to achieve and significantly surpass these thresholds of CO, mean arterial pressure and CPO, to achieve hemodynamics that are more favorably associated with improved survival in high-risk patients.

Principles of Myocardial Protection

While most obvious in the setting of acute myocardial infarction, ischemia also occurs in other severe cardiac disease states, including acute heart failure, high-risk PCI, and cardiogenic shock and contributes to clinical deterioration. Therefore, targeting a hemodynamic state that maximizes energy supply to the heart while minimizing energy demand of the myocardium as a goal for the ideal cardiac-assist device is likely to benefit multiple patient populations. Such a goal achieves maximization of myocardial performance at

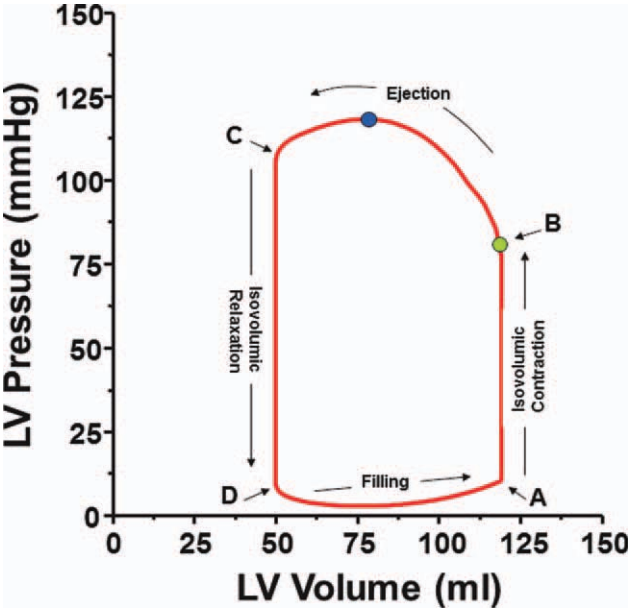

Fig. 2. Pressure-volume (PV) loop. In the absence of mitral or aortic valve pathologies, point A denotes time of mitral valve closing, point B denotes time of aortic valve opening, point C denotes time of aortic valve closure and point D denotes time of mitral valve opening. The four phases of the cardiac cycle (isovolumic contraction, ejection, isovolumic relaxation, and diastolic filling) are identified on the diagram. Green dot shows the point of aortic valve opening, which signifies aortic diastolic pressure. Blue dot shows the point of peak ventricular pressure which coincides with arterial systolic pressure.

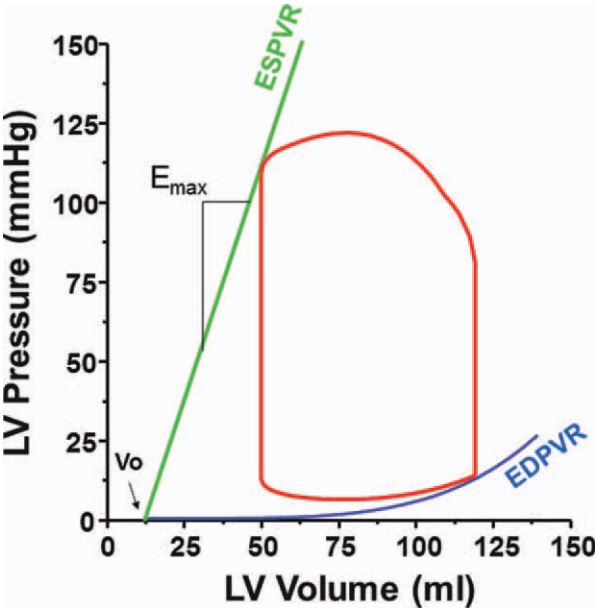

Fig. 3. Parameters associated with the pressure–volume loop. ESPVR = end-systolic pressure–volume relationship, EDPVR = end-diastolic pressure–volume relationship, E_{max} = slope of ESPVR, V_0 = volume at which end-systolic pressure is zero.

the moment and, in the long term, optimal preservation of myocardial tissue. Along with arguments related to favorable energy supply and demand balance, other factors impacted by percutaneous circulatory assist devices will undoubtedly have an impact on myocardial preservation. For example, LV unloading has also been shown to produce important reductions in endothelin release, calcium overload and the rate of apoptosis which may well contribute to reductions and infarct size in the setting of myocardial ischemia [23]. It is likely that many other mechanisms are also involved.

Myocardial oxygen demand (left ventricular unloading). Factors that contribute to myocardial oxygen consumption have been carefully elucidated over the past 50 years and include primarily heart rate, contractility, preload, afterload, and muscle mass [24,25]. There are different means of indexing contractility (ejection fraction, dP/dt_{max}, E_{max}), preload (end-diastolic pressure or end-diastolic volume) and afterload (arterial impedance, effective arterial elastance, arterial pressure, wall stress) for purposes of understanding the determinants of oxygen consumption. From a physiological perspective, however, these relatively complex interrelations are most conveniently unified through pressure-volume analysis [26].

By way of review (Fig. 2, in the absence of aortic or mitral regurgitation), point A on the pressure-volume diagram represents end-diastole, the time when the heart begins contraction. As the myocardium contracts, the mitral valve closes and pressure builds rapidly without any change in volume (isovolumic contraction). At point B, the aortic valve opens as ventricular pressure surpasses aortic diastolic pressure and a volume of blood begins to be ejected. The ventricular pressure continues to rise to a maximum after which it reaches point C (end systole), when the aortic valve closes. Pressure then falls rapidly with a constant volume within the ventricle (isovolumic relaxation). At Point D, the mitral valve opens and the ventricle begins filling with a new volume of blood entering from the atrium for the next cycle. The PV loop is bounded inferiorly by the end-diastolic pressure-volume relationship (EDPVR) and superiorly by the end-systolic pressure-volume relationship (ESPVR) (Fig. 3). The EDPVR uniquely defines the passive properties of the LV and the slope of the ESPVR (E_{max}, also frequently referred to as *end-systolic elastance*, or E_{es}), along with the volume axis intercept (Vo), provides a load-independent index of ventricular contractility.

Research performed over the past three decades has shown that left ventricular pressure–volume area (PVA) provides the strongest index of oxygen consumption per beat (Fig. 4) [27–29]. PVA is the area on the pressure–volume diagram bounded by the end-

systolic and end-diastolic pressure–volume relationships and the systolic portion of the pressure–volume curve. In brief, PVA is equal to the sum of the external stroke work performed by the heart during a given cardiac cycle (SW, which is the area inside the pressure–volume loop) plus the residual energy stored within the myocardium at the end of the beat, also referred to as the potential energy (PE): PVA = SW + PE. PVA thus equals the total mechanical energy performed by the heart on each beat. Because PVA relates to oxygen consumption per beat, one of the most effective means of reducing oxygen consumption is by reducing heart rate to as low a value as tolerated clinically to maintain blood pressure and cardiac output. The other important concept is that PVA is a load independent index of myocardial oxygen consumption such that it does not matter what portion of PVA is due to SW or what portion is due to PE (Fig. 5). Thus, there are infinite combinations of PE and SW that can be arrived at by varying preload and afterload that yield the same PVA; for all of those different combinations, however, myocardial oxygen consumption will be the same. Finally, the relationship between PVA and myocardial oxygen consumption varies with contractility (E_{max}), so that with increased E_{max}, the curve is shifted upwards in a parallel manner, reflecting greater oxygen consumption at any given level of PVA (Fig. 6).

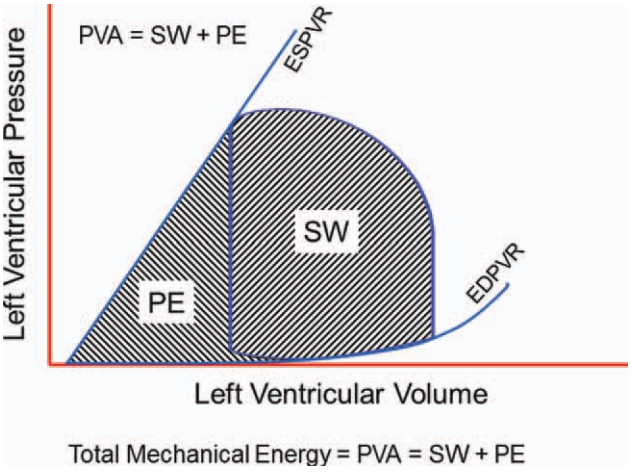

Fig. 4. Pressure–volume area (PVA). The PVA, composed of the external stroke work (SW) and the mechanical potential energy (PE) stored in the myocardium at end diastole, represents the total mechanical work performed by the heart and correlates closely with total myocardial oxygen consumption per beat. ESPVR = end-systolic pressure–volume relationship, EDPVR = end-diastolic pressure–volume relationship.

The pressure–volume framework reviewed above is particularly useful for demonstrating the hemodynamic and metabolic impact of different percutaneous cardiac support devices. The hemodynamic and metabolic impact of a support device depends on the flow rate of the pump and whether blood is pumped from the LV, LA or from the RA (as is the case with CPS or ECMO). The effects of pumping can also depend on the hemodynamic state from which support is initiated, which can vary from near normal to a state of deep cardiogenic shock. These factors, along with the reason for implementing

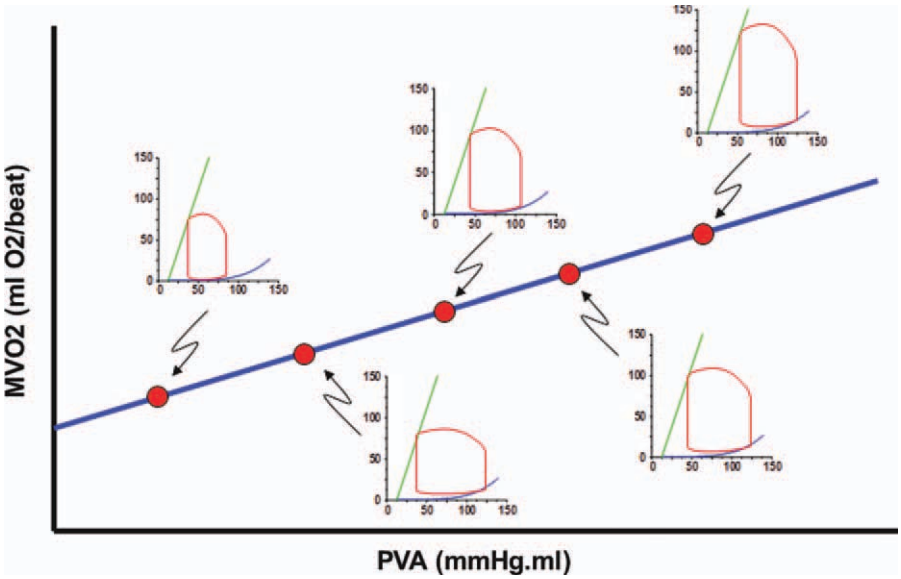

Fig. 5. Relationship between pressure–volume area and oxygen consumption. Note that different components of stroke work and potential energy can contribute to the same PVA (pressure volume area), and therefore elicit identical oxygen consumption. MVO2 = oxygen consumption.

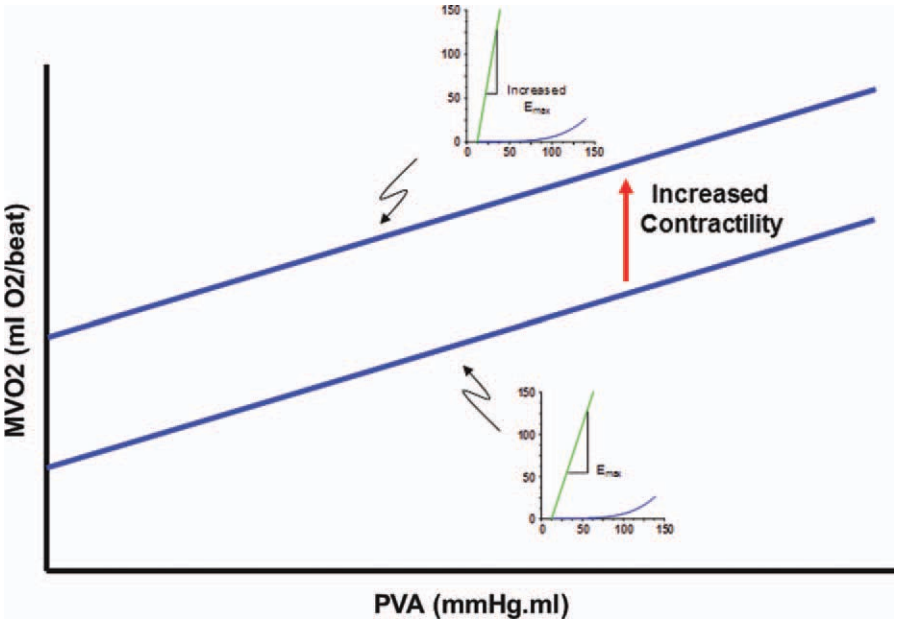

Fig. 6. Effect of contractility on oxygen consumption. Increasing contractility results in increased oxygen consumption (MVO2) at any given PVA (pressure volume area). E_{max} = slope of end-systolic pressure volume relationship.

hemodynamic support, contribute to the clinician's choice of which device to use in any given patient.

Myocardial oxygen supply. Under normal conditions, the heart extracts more oxygen from blood than any other organ in the body, attaining arterial-venous oxygen content differences of more than 10–12 ml O_2/100 ml blood, with typical arterial oxygen content of 20 ml O_2/100 ml blood. In addition, unlike other organs, the heart relies nearly completely on aerobic metabolism, necessitating oxygen to sustain myocardial contraction [30]. Therefore, under conditions of increased myocardial oxygen demand, there exist only two methods of meeting such demand: (1) increasing coronary blood flow (CBF) or (2) increasing the concentration of oxygen in blood via supplemental oxygen or increasing carrying capacity [31]. Because there are no currently approved methods for increasing oxygen carrying capacity of blood, augmentation of CBF is the preferred strategy for increasing myocardial oxygen supply, especially in the setting of obstructive coronary lesions.

The rate of coronary blood flow is governed by the principles of fluid dynamics, such that flow is directly related to the pressure difference across the vascular bed and inversely related to coronary vascular resistance. Myocardial resistance increases during myocardial contraction such that myocardial blood flow occurs mostly during diastole [32]. The pressure gradient that drives CBF is the difference between mean arterial pressure during diastole and the downstream pressure which relates to both mean right atrial pressure and left ventricular end-diastolic pressure. If heart rate and epicardial resistance are fixed, as occurs in stable coronary disease, CBF can generally be increased by augmenting mean arterial pressure, by decreasing right atrial and LV end-diastolic pressure or by reducing microvascular resistance (Fig. 7). Microvascular resistance is regulated tightly by metabolic, neural, humoral, autoregulatory, extravascular compressive and diastolic phase-related factors [31]. From a practical standpoint, however, microvascular resistance is related closely to the stiffness or tension in the myocardial wall [32].

The ideal cardiac assist device, therefore, would be able to augment coronary blood flow through favorably increasing mean arterial pressure especially during diastole (the main effect of intraaortic balloon pumping), decreasing EDP, and/or significantly reducing wall tension and associated microvascular resistance. Thus, cardiac assist devices that reduce EDP and increase mean arterial pressure may prove best at augmenting CBF by impacting both perfusion pressure and microvascular resistance.

Optimizing oxygen supply and demand. From the above discussion, it follows that devices that have a beneficial impact on both oxygen supply and demand might ultimately prove most beneficial from a myocardial protection standpoint. Importantly, as reductions in EDP and EDV favorably impact both sides to this equation (increased oxygen supply and decreased oxygen demand), cardiac assist devices that target these

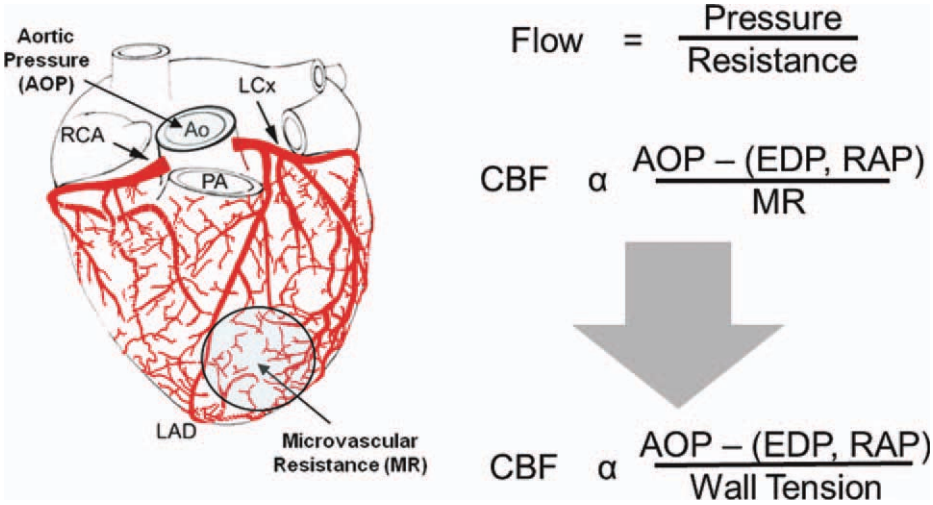

Fig. 7. Factors that contribute to coronary blood flow (CBF). Flow is equal to pressure divided by resistance. For CBF, perfusion pressure is proportional to the difference between mean aortic pressure (AOP) and both end-diastolic pressure (EDP) and right atrial pressure (RAP) divided by microvascular resistance (MR). Minimum microvascular resistance correlated with wall tension.

two parameters may prove most beneficial. Therefore, the ideal cardiac assist device would reduce myocardial oxygen demand and wall tension by shifting the PV loop leftward (via reductions in EDP, EDV, peak pressure, and ESV), reducing both SW and PE, while simultaneously increasing oxygen supply by augmenting mean arterial pressure and CBF.

Principles of Safety and Ease-of-Use

Physicians and patients are willing to accept risk and procedural time when implanting cardiac support devices because they are generally used in critically ill patients and there is an expectation of substantial clinical benefit. However, the hemodynamic effectiveness, risks and procedure times vary among devices, making such considerations important when deciding which device to use in which setting. Safety and ease-of-use considerations are best divided into those associated with procedural insertion and those associated with maintenance of cardiac support after implantation. Safety considerations may further be divided into vascular, cardiac, and other system derangements, while ease-of-use considerations may be divided into ease of implantation and requirements for maintenance and discontinuation of support.

The principal safety concern in cardiac support device utilization has been vascular access site complication. After introduction to clinical practice in 1968, the intraaortic balloon pump was applied to patients undergoing elective high-risk PCI [33,34]. Using an 8 French (F) or 9F arterial sheath, vascular complications were seen in roughly 10% of patients, including limb ischemia, hematoma, overt bleeding, and blood transfusion [34,35]. At the other extreme, large bore venous and arterial catheters utilized in percutaneous cardiopulmonary support (typically 18F) have been associated with far greater vascular complications, being experienced by as many as 40% of patients [36]. Intermediate-sized cannulae have resulted in complication rates midway between these extremes [37,38]. From the PCI literature, it is clear that smaller diameter sheaths result in a marked reduction in vascular complications and combined venous and arterial access results in higher access site complications than sole arterial access [39,40]. From a safety standpoint, therefore, a goal of cardiac assist devices remains minimizing access sites in both quantity and caliber.

Cardiac complications during device implantation vary by individual device. Transseptal puncture, for example, has been associated with complications ranging from pericardial tamponade to aortic puncture. In contrast, the IABP and ECMO technologies do not result in direct cardiac trauma since no catheters enter the heart. Other complications of device placement include stroke (due to air embolism or atheroembolic disease) and hemolysis. Hemolysis has been noted with improper placement of pumps, such as TandemHeart and Impella, while renal failure and stroke are more common with prolonged ECMO, and stroke not uncommon with IABP [41,42]. Air embolism is a risk in systems that require deairing, such as TandemHeart and ECMO, while atheroembolism and arterial dissection are concerns with large and inflexible cannulae insertion (TandemHeart, ECMO and Impella 5.0).

TABLE I. Strategy of Circulatory Support

Strategy	Therapy/device	Mechanism	Comments
Medical management	Inotropes	Increase contractility, HR	
Counterpulsation	IABP	Pressure augmentation	Increased diastolic, reduced systolic aortic pressure; decreased PCWP; no active flow
Extracorporeal bypass heart pump	Tandem Heart	LA -> AO flow	Indirectly unloads LV by decompressing LA; up to 4 Umin flow (retrograde)
	ECMO	RA -> AO flow	Provides oxygenation; no LV unloading; up to 5 Umin flow (retrograde)
Intracorporeal transvalvular heart pump	Impella 2.5	LV -> AO flow	Directly unloads LV; up to 2.5 Umin flow (antegrade)
Impella 5.0	LV -> AO flow	Directly unloads LV; up to 5.0 Umin flow (antegrade)	

Available therapy for percutaneous support ranges from medical management and counterpulsation support to extracorporeal bypass pumps and implantable transvalvular pumps. The strategy and specific devices and mechanism of action are listed in tabular form.

Ease-of-insertion varies depending on whether one or two access sites are required, whether the Seldinger percutaneous technique can be utilized as opposed to direct surgical cut-down and whether advanced interventional techniques and/or support staff are required (e.g., transseptal puncture, preclose technique, perfusionist). For example, the IABP and Impella 2.5 devices utilize solitary arterial access, with relatively small diameter access sites (8–13F), whereas the 15F TandemHeart and ECMO require venous and arterial access and/or direct cut-down (17F TandemHeart and 18F ECMO), and the TandemHeart requires transseptal puncture. The larger Impella 5.0, while remaining a sole arterial access device, also typically requires surgical cut-down for insertion. In addition, the time from insertion to activation of the device varies among devices, as some require significant de-airing and priming (TandemHeart and ECMO).

Ease-of-use during maintenance of support also varies, with some devices requiring minimal ancillary support (IABP, Impella), while others may require a perfusionist and critical care personnel (ECMO) in some institutions. In contrast to continuous flow devices (ECMO, TandemHeart and Impella), the IABP requires a stable nontachycardic electrical rhythm or pressure tracing for optimal function. All require some level of anticoagulation, although this is kept to a minimum with the IABP versus other devices.

Termination of support ideally should be performed without surgical closure; direct manual compression or preclose techniques have been utilized for the IABP, 15F TandemHeart, Impella 2.5 and 17F TandemHeart cannulae, whereas the larger bore Impella 5.0 and ECMO usually require direct surgical closure. The preclose technique has also been successfully used in arterial devices as large as 24 French on a routine basis in experienced centers. Venous access for cannulas as large as 26 French can be closed with a large O-silk figure of eight stitch. Finally, ECMO cannot be maintained as long as other devices, due to significant pulmonary, cardiac, and hematologic complications that arise as bypass time approaches 6 hr [43].

In summary, although the first consideration in choosing which support device to use for a given clinical scenario is often the amount of hemodynamic support and myocardial protection required, which varies significantly between the different devices that are available, factors contributing to the choice should also include ease-of-use and safety. Such considerations include size and quantity of required vascular access, whether access can be attained via the Seldinger technique or requires surgical cut-down, whether the device needs to cross the aortic valve or requires a transeptal puncture, the degree of anticoagulation required, the need for specialized technicians to initiate or maintain support over long periods of time, whether inside-the-body priming or a stable electrical rhythm and pressure tracing are required, and whether vascular access closure upon device removal requires surgical support or whether manual compression or preclosure techniques are sufficient.

Therapy Comparisons

The most commonly used therapeutic strategies for hemodynamic support are shown in Table I. First line therapy is usually medical management and consists of the use of inotropic medications or pressors to return systemic hemodynamics quickly to more reasonable levels. Counterpulsation therapy is often the next line of therapy and is often added to inotropic medications when the effect of that therapy has not achieved satisfactory improvements in hemodynamic parameters or when high doses resulting in clinically unacceptable side effects are present. Two forms of extracorporeal bypass pumps are used regularly today and differ in the mechanism used to support the circulation. This group includes the TandemHeart system (which is a left atrial-to-aortic system) and the ECMO or CPS

TABLE II. Device Comparison Using Circulatory Simulation

		HR	PCWP	AOP	CO	CPO	PVA	MVO2
	Baseline:	100	27	82/51 (62)	3.91	0.54	4907	5.55
Inotropes		118	27	89/57 (69)	4.71	0.72	5433	6.94
IABP + inotropes		118	26	85/53 (73)	5.03	0.82	5242	6.83
TandemHeart		100	21	93/74 (80)	5.15	0.91	4980	5.58
ECMO		100	30	96/74 (81)	5.39	0.96	5473	5.81
Impella2.5		100	24	85/64 (70)	4.53	0.71	4694	5.44
Impella5.0		100	20	86/79 (81)	5.23	0.94	4175	5.20

The hemodynamics including HR, PCWP, AOP, CO, and CPO, as well as the derived PVA and MVO2 are shown first for the baseline failure condition (top) and then modeled for each subsequent therapeutic maneuver. The PV Loop for each condition is shown in red while the baseline loop is shown in black. The IABP condition is shown with inotropes still on board, but they have been weaned off in all of the remaining technology demonstrations.

system which, for the purposes of cardiac support, is essentially a right atrial-to-aortic system. In this comparison, we will use the term ECMO (extracorporeal membrane oxygenation) rather than CPS (cardiopulmonary support) since percutaneous ECMO systems are used for support today both in the cath lab and for more prolonged support in the ICU. These ECMO systems are generally veno-arterial systems meaning that the blood is generally drained from a groin vein (femoral vein) and returned to a systemic artery (femoral artery). This discussion will not address the veno–veno systems used primarily for patients who need only oxygenation support. Finally, the Impella system is currently the only example of the intracorporeal transvalvular technology in use today and includes both the Impella 2.5 and the Impella 5.0 platform (Impella 5.0 and Impella LD). The Impella systems use a transvalvular LV-to-aorta methodology.

The impact of these various interventions in cardiogenic shock can be compared using PV loop analysis to illustrate the hemodynamics effects and implications for myocardial oxygen consumption. Reducing myocardial oxygen demand is achieved primarily by reducing or "unloading" peak left ventricular pressure and volume and is best characterized by the ventricular pressure–volume (PV) loop as discussed earlier (Fig. 2).

Pressure–volume loops for the various device comparisons were generated using previously detailed simulations of different types of ventricular support devices (Appendix) [44–48]. Using the principles outlined in this article and using the metrics of systemic hemodynamic support (e.g., CPO) and the metrics of oxygen demand (PVA) and O_2 consumption (MVO2), we can compare the different support strategies. We will start with a simulation of acute cardiac decompensation typical of that seen in an acute myocardial infarction. Our baseline condition from which we will compare the various therapies is illustrated at the top of Table II. The PV loops for the various therapies (shown in red) are compared to the baseline PV loop (shown in black; left side of Table II).

Inotropic medications. Inotropes increase the contractility of the myocardium primarily through increased calcium cycling and are used to rapidly increase the blood pressure to vulnerable and critical central systems. The simulation results in Table II demonstrate that increased contractility results in increased arterial pressure. While EDP may be slightly

TABLE III. Summary of Support Strategy and Comparison of Therapies

	Medical management	Counterpulsation	Heart pumps			
			Bypass		Trans-valvular	
	Inotropes	IAB	ECMO	TandemHeart	Impella 2.5	Impella 5.0
Systemic support (CPO)	++	+	+++	+++	++	+++
Myocardial protection (O_2 supply increase)	0	++	0	++	++	+++
Myocardial protection (O_2 demand decrease)	−−−	+	−−	−/+	++	+++
Ease-of-use	+++	++	−	−−	++	+

Devices/therapies are compared based on systemic support, myocardial protection (both supply and demand) and ease of use.
Key: + positive impact; 0 neutral; − negative impact

reduced, this change is typically clinically insignificant. The overall effect is an increase in systemic blood pressure, a chronotropic response of increased heart rate, an elevation of the CO and CPO and an elevation of the PVA and MVO2. The change in the PV loop compared to the baseline failure state is seen in Table II with the new loop representation shown in red. Note that the new ESPVR line illustrated by the simulation corresponds to the increased contractility with inotrope administration.

Counterpulsation. Counterpulsation is often added to patients who remain compromised after initial attempts at correction with inotropes and optimization of intravascular volume status. Counterpulsation therapy is typically used in addition to inotropic drug therapy as a direct clinical manifestation of the fact that IABP counterpulsation alone does not directly pump blood but relies on the native heart to provide forward flow. Balloon deflation during ejection serves to reduce the effective afterload against which the heart beats, but does not result in substantial improvements in cardiac output. Diastolic aortic pressure augmentation provided by the IABP itself achieves an increased level of pressure and flow support to increase coronary blood flow. This strategy of combined IABP and inotropic support, however, is often counter-productive since the systemic flow augmentation is still accomplished at the expense of increasing the native cardiac work and oxygen consumption despite the afterload-reducing effects of the IABP. Particularly in the setting of cardiogenic shock, this can exacerbate myocardial ischemia promoting the downward spiral of shock. A number of investigators have reported minimal, if any, direct hemodynamic impact of IABP counterpulsation [49–52].

Progressing from baseline acute decompensation through inotropes and then through to the addition of IABP, (IABP+Inotropes; Table II) we see a slight reduction of PCWP, a slight increase in mean aortic pressure, an increase in CO and CPO with a slight reduction of the PVA and MVO2. Note however, that the PVA and MVO2 can remain above the baseline condition of the acute decompensation. Therefore, the systemic hemodynamic condition is improved at the expense of a higher heart rate and more oxygen demand. The increased oxygen demand and increased work are at odds with the ideal goal of decreased work and diminished demand when dealing with an injured and ischemic myocardium. Although not addressed by this simulation, coronary blood flow (CBF) is augmented during counterpulsation therapy primarily by increasing the driving (diastolic) pressure.

Extracorporeal bypass heart pumps. Two technologies used today employ extracorporeal pumps. TandemHeart (Cardiac Assist, Pittsburg, PA) employs a left atrial-to-aorta (LV-to-Ao) support strategy while the CPS or ECMO systems (using a variety of extracorporeal pumps and circuits) use a systemic venous pickup (RA-to-Ao) with the addition of an interposed oxygenator.

As seen in Table II, the LA-to-Ao strategy (TandemHeart) reduces EDP while providing significant increases in both CO and MAP. Because of this level of systemic support, inotropes can be removed in the simulation, while still maintaining adequate hemodynamic levels. Despite the reduction in heart rate associated with the discontinuation of inotropes, the PVA remains at or slightly increased over the baseline condition due to the increase in arterial pressure that is commensurate with the LA-to-Ao support strategy. The net effect is an increase in oxygen delivery due to increased aortic pressure but there may be little impact on oxygen consumption.

ECMO as a strategy for circulatory support results in even better systemic hemodynamic support but is disadvantaged by moving further away from the ventricle we are seeking to unload. Despite higher arterial pressure, more CO and higher CPO, we see a significantly larger PVA and MVO2 primarily due to an increase in both left ventricular preload and afterload pressure (ECMO; Table II). The increased preload arises from left atrial filling through residual pulmonary venous return thereby increasing EDV and EDP and thus increasing the PVA and myocardial oxygen consumption. Confirmation of this effect was recently reported by Kawashima who noted consistent elevation

of PVA across a spectrum of failure severity models supported by ECMO [52].

Intracorporeal transvalvular heart pumps. The Impella platform consists of three commercially available pumps. The Impella 2.5 is placed thru a 13F sheath and is a purely percutaneous application of the intracorporeal transvalvular heart pump. The larger Impella 5.0 requires a surgical cutdown, while the Impella LD technology is designed to be placed directly in the ascending aorta if the chest is already opened. From the perspective of systemic hemodynamic support and myocardial protection, since all three of these technologies employ an LV-to-Ao support strategy, the 5.0 and LD abide by the same principles as the Impella 2.5 and will not be considered separately.

Like the extracorporeal heart pumps, the Impella 2.5 maintains systemic hemodynamics above critical levels without inotropes, although with less absolute elevation in CPO compared to TandemHeart and ECMO (Table II). A transvalvular support strategy like Impella takes advantage of the fact that the ability of any pump to produce forward flow is dependent on the pressure difference between the inlet and the outlet of the device. A larger positive pressure difference from inlet to outlet yields a lower flow rate. For the extracorporeal bypass strategies, this pressure difference (between LA and Ao, or RA and Ao) is always net positive. For a transvalvular strategy the pressure difference is markedly reduced during systole and can even drop to zero if the ventricle is able to generate enough pressure to open the aortic valve. Thus, the ability of the device to augment forward flow is maximized during systole. This principle allows an LV-to-Ao pump to augment systemic hemodynamics more profoundly than a pump with an equivalent power applied in an LA- or RA-to-Ao strategy. Conversely, the relatively less powerful Impella 2.5 pump, applying its support from LV-to-Ao is able to maintain critical hemodynamic levels comparable to the more powerful extracorporeal bypass pumps by taking advantage of this systolic boost.

From the perspective of myocardial protection, the increase in MAP (in particular due to increased diastolic aortic pressure) combined with the reduction in EDP with Impella will promote increased coronary flow as has been demonstrated in patients [53]. The LV-to-Ao support strategy is also the first demonstrated in this simulation to reduce the PVA and MVO2 below the baseline condition, indicating a reduction in myocardial oxygen consumption. This effect is more pronounced in the Impella 5.0 simulation. The reduction of PVA stems from a reduction in EDV and EDP (preload) similar to the TandemHeart, but without the significant increase in systolic aortic pressures that was seen with both of the extracorporeal strategies. Additionally, with the LV-to-Ao approach, the isovolumic periods of ejection and relaxation no longer exist since the pump is constantly delivering volume from the LV to the ascending aorta independent of the phase of the cardiac cycle. This too contributes to the overall reduction of PVA.

CONCLUSIONS

Despite best efforts, patients admitted with acute myocardial infarction, decompensated heart failure or cardiogenic shock, as well as those undergoing high-risk PCI continue to have significant morbidity and mortality rates with standard guideline-based therapy, including revascularization, vasopressor, inotrope, and diuretic therapy, and other forms of support (e.g., mechanical ventilation). For the sickest patients, progressive cardiac and other end-organ dysfunction is the inevitable short- or long-term consequence of failing to meet metabolic demands (heart failure, cardiogenic shock) or achieve successful revascularization (acute myocardial infarction, high-risk PCI). Clearly, therefore, there is a distinct need to push our understanding of the principles guiding safety, ease-of-use, hemodynamic support and myocardial protection of cardiac support devices that add value to current treatment strategies.

Although the current manuscript discusses the principles that identify the ideal cardiac support device, in truth the ideal device for one indication may differ from that for another indication, based the immediate needs of the patient and the level of risk that will be tolerated. For example, a safe and rapidly instituted device to provide myocardial protection in the setting of acute myocardial infarction may not necessarily need to provide maximal hemodynamic support. Conversely, a device that provides particularly potent hemodynamic support may be required for those in cardiogenic shock, whether or not the device can be instituted rapidly and easily. Table III summarizes the differences in the various support technologies and contrasts these devices according to systemic hemodynamic support, myocardial protection (O_2 supply increase and O_2 demand decrease) and ease of use.

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APPENDIX

The simulation used in this article is based on a model has been described in detail previously [44–48,54–57] and integrates time-varying elastance models of the cardiac chambers with Windkessel representations of the systemic and pulmonary vascular systems. There are several lines of evidence that support the utility and accuracy of the integrated model. First, the individual components of the model used to simulate the heart chambers (time varying elastances) and the vasculatures (resistance-capacitance networks) have been studied and validated for over 40 years. In addition, there have been at least nine publications in which the integrated model has been used successfully to illustrate important hemodynamic principles and to predict hemodynamic effects of several clinical therapies, including the Batista procedure, the Dor procedure and the impact of inhaled pulmonary vasodilators [44–48,54–57]. Most relevant, however, the integrated

model was validated quantitatively against measurements in an animal model of acute heart failure in which an LA-to-Aorta device was used [48]. Having said this, the main goal of using the simulation is to illustrate the important principles of how the different devices impact on ventricular hemodynamics. Although the simulation provides quantitative numerical results and we present quantitative results (Table II), it is the qualitative effects (i.e., the way the loops are impacted) and the trends in the numeric values that are of primary interest. It cannot be claimed that the results are quantitatively accurate.