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WHITE PAPER

Value of Hemodynamic Monitoring in Patients With Cardiogenic Shock Undergoing Mechanical Circulatory Support

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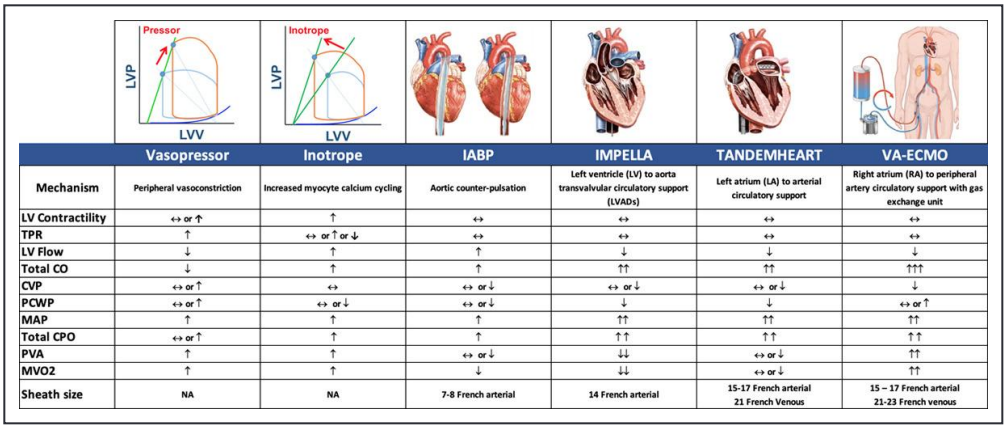
ABSTRACT: The recent widespread availability and use of mechanical circulatory support is transforming the management and outcomes of cardiogenic shock (CS). Clinical decision-making regarding the optimization of therapies for patients with CS can be guided effectively by hemodynamic monitoring with a pulmonary artery catheter (PAC). Because several studies regarding the benefit of PACs are ambiguous, the use of PACs is variable among clinicians treating patients with CS. More notable is that PAC use has not been studied as part of a randomized, controlled trial in patients with CS with or without mechanical circulatory support. Standardized approaches to hemodynamic monitoring in these patients can improve decision-making and outcomes. In this review, we summarize the hemodynamics of CS and mechanical circulatory support with PAC-derived measurements, and provide a compelling rationale for the use of PAC monitoring in patients with CS receiving mechanical circulatory support.

Key Words: assisted circulation ■ catheterization ■ hemodynamics ■ shock, cardiogenic

Cardiogenic shock (CS) is a condition of persistent hypotension and systemic hypoperfusion attributable to impaired left ventricular (LV), right ventricular (RV), or biventricular function. CS can result from myocardial, valvular, electrical, pulmonary arterial, or pericardial dysfunction, or combinations thereof. CS triggers a series of compensatory mechanisms that result in changes in heart rate, pulmonary and systemic vascular resistance (SVR), tissue microcirculation, renal function, volume status, and myocardial contractility in an attempt to restore tissue perfusion.[1]

Therapeutic options for patients in CS include use of pharmacotherapies such as inotropes and vasopressors (aimed at enhancing contractility and modulating vascular tone) and a host of mechanical circulatory support (MCS) devices that pump blood from 1 vascular compartment to

another to improve systemic hemodynamics (Figure 1). The choice and management of pharmacologic and mechanical therapies to optimize the hemodynamic profile poses challenges to clinicians, often requiring additional information derived from pulmonary artery catheters (PACs) for many critical clinical decisions. The therapeutic approach to patients with CS varies substantially among institutions and clinicians, especially as it relates to indications, timing, and choice of MCS devices.



	Vasopressor	Inotrope	IABP	IMPELLA	TANDEMHEART	VA-ECMO
Mechanism	Peripheral vasoconstriction	Increased myocyte calcium cycling	Aortic counter-pulsation	Left ventricle (LV) to aorta transvalvular circulatory support (LVADs)	Left atrium (LA) to arterial circulatory support	Right atrium (RA) to peripheral artery circulatory support with gas exchange unit
LV Contractility	↔ or ↑	↑	↔	↔	↔	↔
TPR	↑	↔ or ↑ or ↓	↔	↔	↔	↔
LV Flow	↓	↑	↑	↓	↓	↓
Total CO	↓	↑	↑	↑↑	↑↑	↑↑↑
CVP	↔ or ↑	↔	↔ or ↓	↔ or ↓	↔ or ↓	↓
PCWP	↔ or ↑	↔ or ↓	↔ or ↓	↓	↓	↔ or ↑
MAP	↑	↑	↑	↑↑	↑↑	↑↑
Total CPO	↔ or ↑	↑	↑	↑↑	↑↑	↑↑
PVA	↑	↑	↔ or ↓	↓↓	↔ or ↓	↑↑
MVO2	↑	↑	↓	↓↓	↔ or ↓	↑↑
Sheath size	NA	NA	7-8 French arterial	14 French arterial	15-17 French arterial 21 French Venous	15 – 17 French arterial 21-23 French venous

Figure 1. Mechanisms, technical requirements, and hemodynamic responses of various mechanical circulatory support devices. CO indicates cardiac output; CPO, cardiac power output; CVP, central venous pressure; IABP, intra-aortic balloon pump; LV, left ventricular; LVP, left ventricular pressure; LVV, left ventricular volume; MAP, mean arterial pressure; MVO_2, myocardial oxygen consumption; NA, not applicable; PCWP, pulmonary capillary wedge pressure; PVA, pressure-volume area; TPR, total peripheral resistance; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

Because many retrospective and prospective studies in specific patient populations showed no clinical benefit derived from the use of PACs,[2] society guidelines and hospital policies have been reluctant to recommend routine use of PACs in patients with CS with or without MCS. As a result, PAC use is highly variable among physicians and institutions despite 2 recent expert consensus articles advocating their use in CS and MCS.[1,3]

The purpose of this review is to delineate the role of PACs in the management of patients with CS for guiding timely initiation, optimization, and, when necessary, escalation of medical- and device-based therapies to avoid the onset of end-organ dysfunction and hopefully improve early and late outcomes.

EVIDENCE RELATED TO PAC USE IN CS AND MCS

Early retrospective registries failed to show benefit of PAC use. Subsequently, several randomized, controlled trials reached negative or neutral conclusions.[2] Use of the PAC for patients with acute decompensated congestive heart failure also demonstrated no benefit.[4] Acute decompensated congestive heart failure should be distinguished from CS in that patients with CS exhibit multiorgan hypoperfusion or elevated lactate levels.

Three important revelations were derived from these studies: (1) PAC use has never been studied explicitly in the setting of CS; (2) PAC use has never been evaluated in patients with CS receiving MCS; and (3) there has never been a prospective study using PAC-derived data to drive a treatment algorithm known to improve outcomes.[2]

Recent retrospective registry studies showed that outcomes in CS in patients with an Impella pump (Abiomed, Danvers, MA) were improved when PACs were used (49% vs 63%).[5] A second study, analyzing the National Inpatient Sample database, demonstrated that whereas PAC use was associated with worse outcome in an ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness)–acute decompensated congestive heart failure–like patient population, its use was associated with improved survival in patients with CS (30% vs 38% in the most recent year analyzed).[6] It is on the basis of such findings that PACs are being incorporated into CS treatment algorithms currently under evaluation at centers throughout the United States.[7,8]

With such a paucity of evidence, it is not surprising that current society guidelines and scientific statements[1,3,9–17] provide limited recommendations regarding PAC use in patients with cardiovascular disease in general and in patients with CS (with or without MCS) in particular (Table 1). At this time, the only Class IA indication listed in any society guidelines for PAC use is during the evaluation of cardiac transplantation candidacy by the International Society of Heart and Lung Transplant guidelines.[16]

Table 1. Current Guidelines and Scientific Statements on the Use of Pulmonary Artery Catheters (PACs) (Table view)

Guideline	Recommendation	COR	Level
2013 ACCF/AHA guideline for the management of HF[9]	Monitoring with a PAC should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate.	I	C
	Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms despite empiric adjustment of standard therapies and • whose fluid status, perfusion, or systemic or pulmonary vascular resistance is uncertain; • whose systolic pressure remains low, or is associated with symptoms, despite initial therapy; • whose renal function is worsening with therapy; • who require parenteral vasoactive agents; or • who may need consideration for MCS or transplantation.	IIa	C

Guideline	Recommendation	COR	Level
	Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute decompensated HF and congestion with symptomatic response to diuretics and vasodilators.	III: No benefit	B
2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction[10]	No specific recommendation.		
ACCF/SCAI/AATS/AHA/ASE/ASNC/HFSA/HRS/SCCM/SCCT/SCMR/STS 2012 appropriate use criteria for diagnostic catheterization[11]	Appropriate use for right heart catheterization: • Pulmonary hypertension • Known or suspected intracardiac shunt with indeterminate shunt anatomy or shunt fraction Appropriate use for right and left heart catheterization: • Preoperative assessment before valvular surgery • Pulmonary hypertension out of proportion to the severity of valvular disease • Left ventricular dysfunction out of proportion to the severity of valvular disease • Assessment of cardiomyopathies.		
2014 AHA/ACC guideline for the management of patients with valvular heart disease and 2017 AHA/ACC focused update[12,13]	No specific recommendation.		
Practice guidelines for central venous access: a report by the American Society of Anesthesiologists Task Force on Central Venous Access 2012[14]	Guidelines do not address placement and residence of PAC.		

Guideline	Recommendation	COR	Level
Hemodynamic monitoring in shock and implications for management: International Consensus Conference, Paris, France, 27–28 April 2006[15]	Do not recommend the routine use of PAC for patients in shock.		
AHA scientific statement on contemporary management of cardiogenic shock 2017[1]	Consider selected use early in the treatment course in patients not responsive to initial therapy or in case of diagnostic or therapeutic uncertainty.		
The 2013 International Society for Heart and Lung Transplantation guidelines for MCS[16]	Right heart catheterization is useful in the assessment of persistent or recurrent HF symptoms after MCS device placement and to evaluate for evidence of RV failure or device malfunction.	I	B
	Right heart catheterization should be performed at regular intervals in patients being evaluated for or listed for heart transplant to document pulmonary artery pressures because irreversible pulmonary hypertension is associated with early allograft dysfunction/failure after heart transplantation.	I	A
	Right heart catheterization should be performed to help corroborate evidence of myocardial recovery. The PAC may be left in place with serial lowering of the pump speed to confirm acceptable hemodynamics with decreasing VAD support before pump explantation.	IIa	C

Guideline	Recommendation	COR	Level
International guidelines for management of severe sepsis and septic shock: 2012[17]	Against the routine use of PAC for patients with sepsis-induced ARDS.	I	A
SCAI/HFSA clinical expert consensus document on the use of invasive hemodynamics for the diagnosis and management of cardiovascular disease (2017)[3]	•Invasive hemodynamic assessment, with measurement of ventricular filling pressures, cardiac output, and systemic vascular resistance, is recommended for the diagnosis of cardiogenic shock. • Continuous hemodynamic monitoring with a PAC is recommended for acute management of patients receiving therapy with MCS. • Pulmonary artery catheterization is useful to guide withdrawal of mechanical circulatory and pharmacologic support in patients with myocardial recovery from cardiogenic shock. • In patients without recovery of myocardial and end-organ function, hemodynamic monitoring is useful to assess candidacy for and transition to advanced HF therapies, including durable MCS and heart transplantation.		

AATS indicates American Association for Thoracic Surgery; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; ARDS, acute respiratory distress syndrome; ASE, American Society of Echocardiography; ASNC, American Society of Nuclear Cardiology; COR, class of recommendation; HF, heart failure; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; MCS, mechanical circulatory support; RV, right ventricular; SCAI, Society for Cardiovascular Angiography and Interventions; SCCM, Society of Critical Care Medicine; SCCT, Society of Cardiovascular Computed Tomography; SCMR, Society for Cardiovascular Magnetic Resonance; STS, Society of Thoracic Surgeons; and VAD, ventricle assist device.

FACTORS INFLUENCING CLINICAL UTILITY OF PAC

The hemodynamic parameters obtained with a PAC can facilitate clinical decision-making, allow customization of a treatment plan, and guide optimization of therapy. As with any invasive diagnostic tool, the benefit must be balanced against risks. Complications of PACs include central venous access–related adverse events (<3.6%), arrhythmias and heart block (0.3% to 3.8%), and pulmonary

artery rupture (0.02% to 0.03%; Table I in the Data Supplement).[2] The best clinical results require accurate pressure signal acquisition and interpretation.[18]

To obtain the most accurate hemodynamic data, a systematic approach to PAC measurement technique is essential. Detailed attention to several factors (eg, proper zeroing and calibration of transducers and proper positioning of transducers relative to body landmarks; Table II in the Data Supplement) is required. Care providers of these patients must be trained to recognize the characteristics of waveforms (Figure I in the Data Supplement) and correct signal damping (identifying tubing kinks or other artifacts) and ensure proper positioning of the PAC.

It is also vital to consider the impact of respiration on pressure measurements. To reduce the effect of pleural and intrathoracic pressures, all measurements should be made at end-expiration, irrespective of the mode of ventilation. Therefore, during normal spontaneous (negative pressure) ventilation, all pressures should be measured at the peak of the waveform; measurements during positive pressure ventilation should be made at the troughs of the respiratory cycle. Examples of different types of respiratory variations of pulmonary capillary wedge pressure (PCWP) are provided in Figure 2A and 2B.[19] Use of the pressure values displayed on clinical monitors should be strongly discouraged because algorithms incorporated into such monitors ignore the impact of respiration and use only average pressure values. Accurate quantification of signals may be affected by arrhythmias such as atrial fibrillation and frequent premature atrial or ventricular contractions as well as the effects of labored respirations. Under these conditions, the best signal quality may be obtained by measurements during controlled respiration and selection of hemodynamic monitor signal averaging routines.

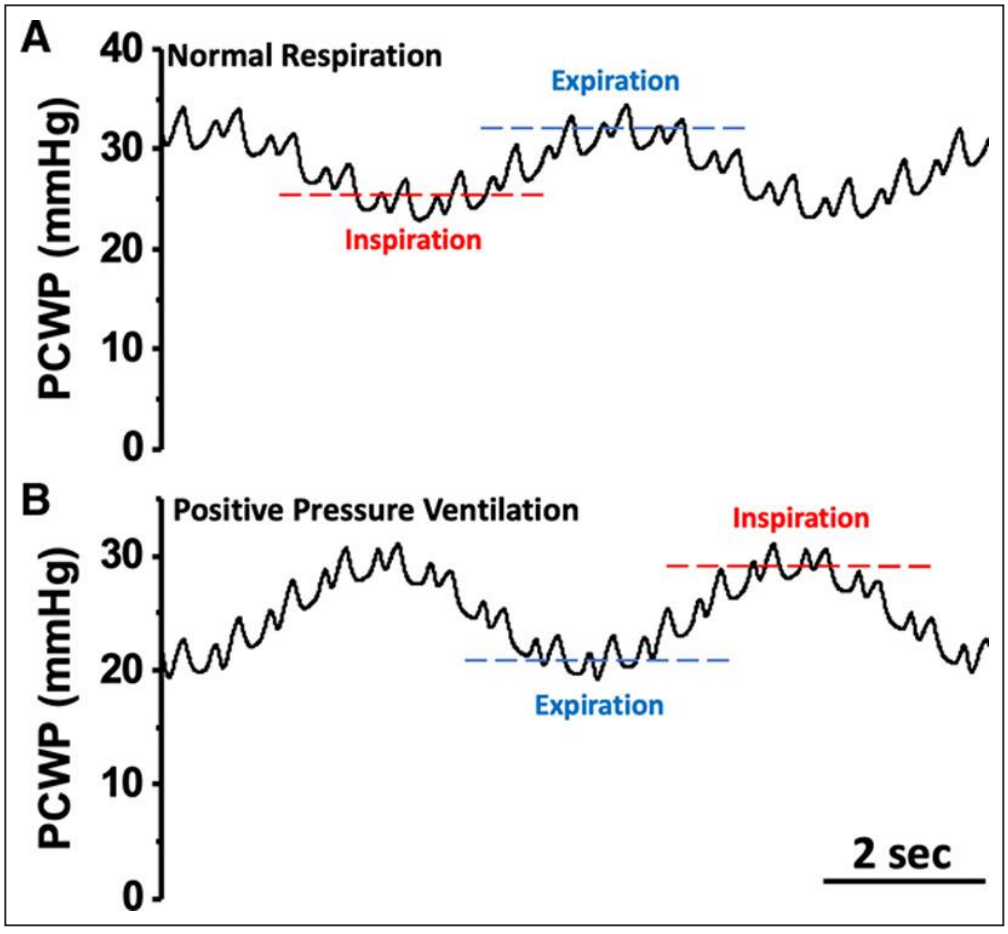


Figure 2. Effect of respiration on pulmonary capillary wedge pressure (PCWP) tracings. A, PCWP waveform during normal respiration, showing end-expiration during the peak of pressure variations. **B**, PCWP waveform during positive pressure ventilation, showing end-expiration during the nadir of pressure variations. Created with Harvi (http://harvi.online) with permission from PVLoops LLC.[19]

Given the technical aspects involved in acquiring and interpreting PAC pressure waveforms, appropriate training and experience is mandatory. Trottier and Taylor[20] found that one-third of critical care physicians participating in a study incorrectly identified pulmonary artery occlusion pressure tracings, even when the tracings were clear. Training for critical care providers other than physicians (eg, critical care registered nurses) is also important for best use of PAC data and should be emphasized if not mandated. Incorporation of standardized training programs for acquisition and interpretation of hemodynamics for all staff involved in the care of patients with CS is strongly recommended and can increase proficiency in hemodynamic monitoring.

HEMODYNAMIC CLASSIFICATIONS OF CS

Classically, CS is defined by systolic blood pressure <90 mm Hg or the need for inotropic or vasopressor or mechanical support to maintain systolic blood pressure >90 mm Hg in combination with evidence of end-organ hypoperfusion.[21,22] Requisite for the condition is an abnormally low cardiac index and normal or elevated intracardiac filling pressures (ie, central venous pressure [CVP] and PCWP). In this review, medically refractory CS is defined as CS that does not resolve within 30 to 60 minutes of standard resuscitation efforts that include volume optimization and upper limits of recommended doses of at least 1 inotrope or pressor, or both.

CS can be further characterized as LV-dominant, RV-dominant, or biventricular shock (Table 2[1,23–30]), each of which may be optimally treated by a different treatment strategy. LV-dominant CS is characterized by high PCWP and normal or reduced CVP in the setting of reduced LV function.

Table 2. Hemodynamic Profiles of Cardiogenic Shock Subtypes (Table view)

Hemodynamic Variables	Preshock Normotensive Hypoperfusion[2,5,26]	Preshock Hypotensive Normoperfusion[2,6]	LV Dominant Shock[1]	RV Dominant Shock[23,24]	BiV Shock[24]
Systolic arterial pressure, mm Hg	>90	<90	<90	<90	<90
CVP, mm Hg	Variable	Variable	<14	>14	>14
PCWP, mm Hg	Variable	Variable	>18	<18	Variable
CVP/PCWP	Depends on degree of LV and RV involvement	Depends on degree of LV and RV involvement	<0.86	>0.86	>0.86
PAPi (PAS − PAD)/RA[24,28–30]	Depends on degree of RV involvement	Depends on degree of RV involvement	>1.5	<1.5*	<1.5
Cardiac index, L/min/m^2	<2.2	≥2.2	<2.2	<2.2	<2.2
SVR, dynes-s/cm^{-5}	>1600	800–1600	800–1600	800–1600	800–1600

Hemodynamic Variables	Preshock Normotensive Hypoperfusion[2,5,26]	Preshock Hypotensive Normoperfusion[2,6]	LV Dominant Shock[1]	RV Dominant Shock[23,24]	BiV Shock[24]
CPO, W[27]	Variable	Variable	<0.6	<0.6	<0.6

BiV indicates biventricular; CPO, cardiac power output; CVP, central venous pressure; LV, left ventricular; PAD, pulmonary artery diastolic pressure; PAS, pulmonary artery systolic pressure; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RA, right atrial pressure; and SVR, systemic vascular resistance.
* Right ventricular (RV) dominant shock primarily attributable to RV dysfunction.

RV-dominant CS is characterized by elevated CVP, normal to low pulmonary artery pressure, normal or low PCWP, and relatively preserved LV function.[1] An important variant of RV-dominant CS includes patients with longstanding pulmonary artery hypertension, who typically have markedly elevated pulmonary arterial pressure and CVP and low or normal PCWPs but, as in other forms of RV-dominant failure, low cardiac index and blood pressure.[23] In RV-dominant CS with markedly elevated CVP and RV dilation, the limits of pericardial capacity may be reached and pericardial pressure (normally near 0 mm Hg) may rise, causing increases in cardiac chamber pressures, including PCWP, while impeding LV filling.[31] Although it is not possible to measure pericardial pressure in the clinical setting, leftward shifts of the interventricular septum provide a clue that such physiology may be in effect.

Biventricular shock is characterized by hypotension, elevated CVP, normal or elevated PCWP, and reduced LV function. Recent literature suggests that biventricular shock is present in as many as 40% of patients who, based on clinical assessments alone, were suspected of having LV-dominant CS.[24]

Before satisfying the classic criteria for shock, patients can present in a state of preshock (Table 2). In the appropriate clinical setting, preshock is characterized by either relatively normal blood pressure with early signs of end-organ hypoperfusion (eg, lactate accumulation) in which systolic blood pressure is maintained at >90 mm Hg by abnormally elevated SVR (normotensive hypoperfusion)[25] or relative hypotension without evidence of hypoperfusion (hypotensive normoperfusion).[26] As discussed further below, additional research concerning ability to identify patients with hypotension with normoperfusion may be required because clinical and biochemical criteria and tools for establishing normoperfusion are limited.

Inappropriate vasodilation mediated by systemic inflammatory response syndrome has also been reported in CS, resulting in a mixed picture with hemodynamic parameters suggestive of low cardiac index and low SVR.[32]

The Society of Cardiovascular Angiography and Interventions (SCAI) recently introduced stages of shock[26] and recent data suggest that in-hospital mortality increases with increasing SCAI stages.[33] SCAI staging should not be considered to replace the classic definitions of CS based on hemodynamic and metabolic measurements. Hemodynamic-based classification of preshock, left-sided shock, right-sided shock, or mixed shock (as detailed in Table 2) serves a different purpose than the SCAI stages of CS. The former provides specific information on hemodynamic deficits and helps clarify adequacy of specific treatment plans. The SCAI stages do not provide such information but are intended to capture the severity and acuity of a patient's condition largely for prognostication and for grouping of patients of different risk profiles.[33,34] Both forms of preshock (hypotensive normoperfusion and normotensive hypoperfusion) would be considered within SCAI stage B

(beginning shock), whereas all others would be classified in stages C, D, or E depending on the types of therapies and their ability to stabilize and reverse the state of CS.

PAC-DERIVED HEMODYNAMIC PARAMETERS

Many reports have detailed the parameters that are either directly measured or derived from PAC measurements. A brief review is provided here and in Table III in the Data Supplement.

Measured Parameters

Parameters measured by PAC include CVP; pulmonary artery systolic (PAS) pressure and pulmonary artery diastolic (PAD) pressure; PCWP, which is also commonly referred to as pulmonary arterial occlusion pressure; and cardiac output by thermodilution. PACs can simultaneously measure blood oxygen saturation at the proximal and distal ports, values that are of fundamental concern in the care of patients in CS (with or without MCS).

PAC-derived measurements of PAS pressure and PAD pressure can discriminate precapillary and postcapillary pulmonary hypertension and are key for quantifying pulmonary vascular resistance and indexes of RV function.[35]

The assessment of cardiac output by thermodilution or Fick methods (direct or indirect), cardiac index (cardiac output indexed to body surface area; cardiac index = cardiac output/body surface area), and mixed venous oxygen saturation (SvO_2) provide measurements of systemic blood flow. These parameters may not directly indicate end-organ or tissue-level perfusion because of concomitant microvascular dysfunction that ensues in later stages of CS.[36,37]

Derived Parameters

In addition to directly measured parameters, derived parameters can be used to tailor therapy for patients with CS (Table III in the Data Supplement).[38,39] Pulmonary vascular resistance and SVR (absolute and indexed to body size) characterize pulmonary and systemic vascular properties, respectively. LV stroke work and LV stroke work index quantify the external mechanical work of the heart. LV stroke work and LV stroke work index multiplied by heart rate yield cardiac power output (CPO) and cardiac power index, respectively (CPO is typically expressed in Watts by dividing the product of mean arterial pressure in mm Hg and cardiac output in L/min by 451). CPO and cardiac power index have been more specifically linked with the risk of in-hospital mortality in CS,[27] and are now commonly used to track efficacy of treatments. Values of CPO <0.6 Watts at the time of presentation have been linked with significantly worse outcomes in acute myocardial infarction complicated by CS, despite appropriate treatment.[27]

Indexes of RV function include RV stroke work, RV stroke work index, and the CVP/PCWP ratio. Under normal conditions, CVP is significantly less than PCWP; a CVP/PCWP >0.86 is suggestive of impaired RV function, though this index is more specific if CVP itself is elevated above normal. Most recently, the pulmonary artery pulsatility index (PAPi = [PAS − PAD]/CVP) has proved useful in more specifically evaluating the degree of RV dysfunction.[28,29] PAPi <0.9 indicates significantly impaired RV function and, along with other findings, may suggest the need for RV support.[23]

All measurements available from the PAC viewed together are important for differentiating the various subtypes of CS (Table 2) and can help tailor therapies based on the shock subtype with the goals of resolving the hemodynamic profile of shock and preventing sequelae.

MCS CLASSIFICATION AND HEMODYNAMIC PROFILES

An increasing number and variety of MCS devices have been developed for use in CS[40] (Figure 1) to augment efficacy or to replace pharmacotherapy to avoid potentially detrimental effects. Specifically, data show that the greater the number of inotropes and vasopressors used, the worse the outcome in CS.[41,42] Patients requiring 0, 1, 2, 3, or ≥4 drugs have expected survival rates of 68%, 46%, 35%, 35%, and 26%, respectively.[42] These results speak to the futility of drug treatment alone in severe CS, especially if more than 1 drug is required.

MCS devices can be classified based on their mechanism of action, the sites from which they withdraw blood from the body, the site of blood return,[40] and whether they provide oxygen and carbon dioxide gas exchange. Devices include aortic counterpulsation pumps, transvalvular percutaneous LV assist devices (pLVADs), percutaneous left atrial decompression devices, and extracorporeal membrane oxygenation (ECMO) devices. Of note is that despite comparable effects on blood pressure and cardiac output, different forms of MCS may have significantly different effects on the heart and lungs, specifically as determined by PCWP (which is linked with LV end-diastolic pressure [LVEDP]) and myocardial oxygen demand (MVO_2), as reviewed in detail previously[40] (Figure 1).

Randomized, controlled trials of patients with CS demonstrated no mortality benefit with the use of an intra-aortic balloon pump.[43] Ineffectiveness of the intra-aortic balloon pump along with implantation challenges with percutaneous left atrial decompression devices has resulted in pLVADs and ECMO being the most widely used MCS devices in CS. As illustrated in Figure 3 and detailed previously,[40] ECMO use in the presence of profound LV dysfunction can increase LVEDP and PCWP in response to the increase in afterload pressure (Figure 3A). In some cases, this can induce or worsen pulmonary edema.[44–46] Increased LV afterload can also result in aortic valve closure and predispose to thrombus formation in the aortic root or the ventricle.[47] In contrast, pLVADs directly unload the left ventricle, simultaneously reducing PCWP and LVEDP (Figure 3B). ECMO bypasses the LV (and RV) and increases total pressure-volume area, which correlates with increased MVO_2. Accordingly, a pLVAD is often added to ECMO to counteract its LV and pulmonary loading effects (Figure 3C).[46]

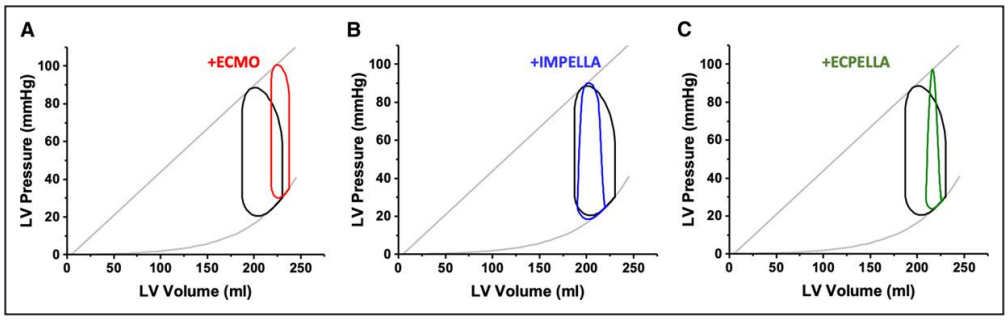


Figure 3. Effects of extracorporeal membrane oxygenation (ECMO), Impella, and ECMO plus an Impella device (ECPELLA) on pressure-volume loops. A, Impact of ECMO on pressure-volume loops, showing increase in end-diastolic pressures (EDPs), increase in effective arterial elastance, and decrease in left ventricular (LV) stroke volume. **B**, Pressure-volume loops with only Impella, showing reduction in EDP, triangulation of the loop as a result of continuous flow across the aortic valve, and no increase in effective arterial elastance. **C**, With the addition of Impella to ECMO (ECPELLA), reduction of the EDP is noted along with triangulation of the waveform. Created with Harvi (http://harvi.online) with permission of PVLoops LLC.[19]

The hemodynamics of MCS are most explicitly depicted in terms of pressure-volume analysis. Although this format has limited direct application in clinical practice, significant insights can be

gleaned from the fact that basic PAC-derived parameters have direct links with features of the pressure-volume loop (Figure 4). Using these parameters along with rudimentary measures of LV and RV size, the key features of LV and RV pressure-volume loops can be traced. Linking these measurements with so-called “single beat” estimates of ventricular end-systolic[48] and end-diastolic[49] pressure-volume relationships provides practical insights into ventricular mechanics and hemodynamics of CS and MCS.

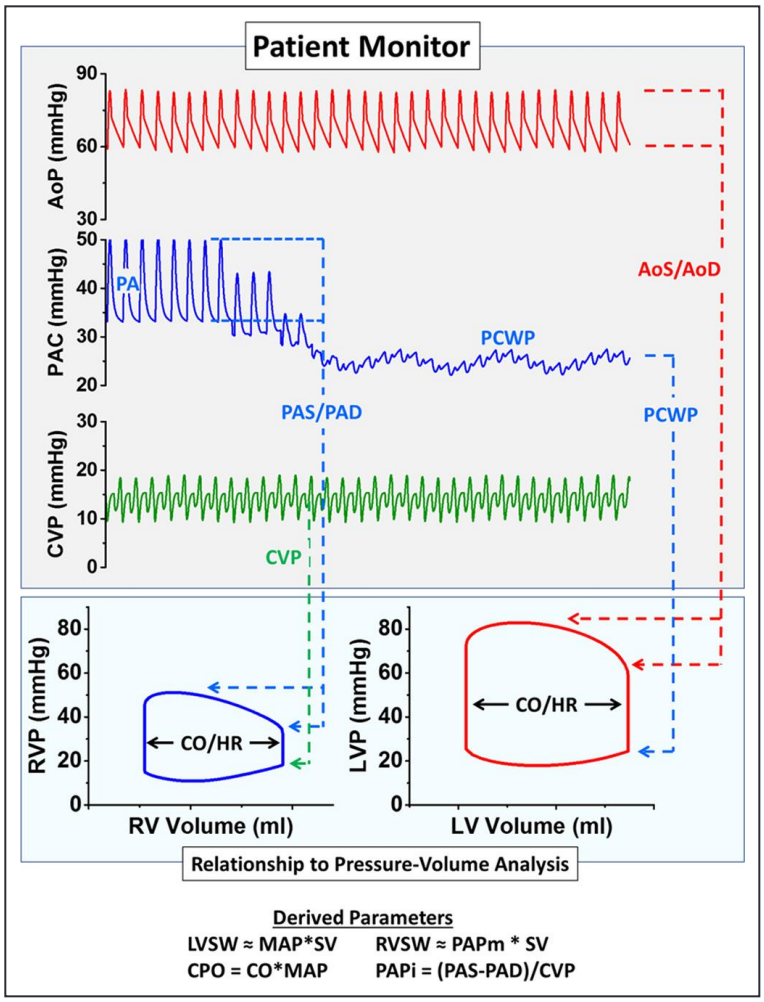


Figure 4. Bedside hemodynamic parameters and their relationship to pressure-volume analysis. In addition to standard arterial blood pressure (AoP) and heart rate (HR) monitoring, basic parameters obtained from the pulmonary artery catheter (PAC) include pulmonary artery systolic pressure (PAS), pulmonary artery diastolic pressure (PAD), pulmonary capillary wedge pressure (PCWP), and central venous pressure (CVP). Cardiac output (CO) is obtained by thermodilution or Fick principle; CO/HR yields stroke volume. The parameters link directly to key features of right and left ventricular pressure-volume loops. This can be combined with basic information of right- and left-ventricular size, providing even more specificity to the loop. Other parameters can be obtained as detailed in supplemental Table III in the Data Supplement. AoD indicates aortic diastolic pressure; AoS, aortic systolic pressure; CPO, cardiac power output; EDV, end-diastolic volume; LVP, left ventricular pressure; LVSW, left ventricle stroke work; MAP, mean arterial pressure; PAPi, pulmonary artery pulsatility index; PAPm, mean pulmonary artery pressure; RVP, right ventricular pressure; RVSW, right ventricle stroke work; and SV, stroke volume.

Because the hemodynamic effects of each form of MCS can vary significantly among patients, as do the individual patient responses,[40] PAC use becomes critical in the management of patients on MCS.

ROLE OF CLINICAL, NONINVASIVE, AND LABORATORY ASSESSMENTS IN CS AND MCS

CVP and PCWP can change frequently and rapidly in patients with CS because of changes in underlying condition and variations in medication doses, variations in volume status, and in response to MCS. Clinical assessment of PCWP, CVP, and cardiac index are unreliable, with a prediction accuracy <50%.[50–52] PACs, when used properly, provide accurate and continuous measurement of these parameters.

Although laboratory and bedside assessments such as urine output, serum creatinine level, and lactic acid level play a crucial role in staging and prognostication of cardiogenic shock,[26] they tend to lag behind hemodynamic changes at variable rates depending on the extent of hemodynamic compromise, organ vascular autoregulation, and underlying chronic organ disease.[53,54] As with all laboratory tests, none is used in isolation. Progressive elevations of lactate combined with other clinical signs of end-organ hypoperfusion can provide a useful index of the need to transfer a patient to a center for escalation of support for patients with CS.

Efforts have been directed at noninvasive estimations of hemodynamic parameters. Whereas correlations can be demonstrated between Doppler-based estimations of pressures and flow and invasive measurements, significant differences exist in individual patients.[55] These measurements are episodic, not continuous, which limits their practicality for monitoring effects over time. Other indirect assessments of cardiac output, pressures, and volume status are equally problematic in their variability.[55,56] Although such methods have been widely adopted in intensive care units, their accuracy has not been adequately validated in patients with CS and MCS. Accordingly, their use cannot be endorsed when clinical decision-making depends on accurate assessment of a patient's complete hemodynamic profile. It is also important to reemphasize that clinical decision-making based on inaccurate information from PACs (either attributable to improper insertion technique or inappropriate interpretations) can be equally detrimental to outcomes.

HEMODYNAMIC-BASED MCS SELECTION

The need for left-sided mechanical cardiac support is usually signified by low blood pressure, low cardiac output, reduced SvO_2, and normal or increased PCWP despite inotropic/pressor support. Whereas other parameters including physical examination are important for decision-making, it is the PAC data that accurately define the nature and severity of hemodynamic compromise in real time.

Identification of the shock subtype coupled with an appreciation for the expected impact of a device on parameters such as cardiac output, PCWP, CVP, and mean arterial pressure can help the practitioner choose the device or device combination (as illustrated in Figure 3) that best matches the needs of a particular patient. As such, use of real-time hemodynamic data available from the PAC, their trends over time, and prognostic implications of metabolic signals provide a powerful combination for appropriate MCS selection and timely management of CS.

In addition to anticipated hemodynamic effects, it must also be acknowledged that the choice of MCS is more often based on clinical factors related to body size, vascular access considerations, physician preference, institutional resources, the anticipated goals of support, metabolic and respiratory status, concurrent infection, and overall adverse event profile of a device.

HEMODYNAMIC-BASED PATIENT MANAGEMENT DURING MCS

Once MCS has been initiated, PAC-derived hemodynamics guide its management. Cardiac output and cardiac index provide a starting point for assessing whether the composite of device and native heart flow is reasonable for the patient's body size. SvO_2 provides an additional index of the adequacy of total flow for the physiological state of the patient. Serum lactate provides supplemental information, but delays in lactate clearance and laboratory delays in obtaining results render SvO_2 more immediately valuable for guiding therapy.

CPO appears important in that it not only provides an index of the risk of in-hospital mortality upon presentation with CS in the setting of acute myocardial infarction but also provides an index of the adequacy of support. Current, although limited, evidence suggests that achieving a CPO >0.8 Watts may be associated with improved outcomes.[27]

PCWP is important for indexing both the degree of pulmonary venous congestion and LV end-diastolic pressure. Tracking PCWP during MCS informs the user if the chosen form of MCS provides sufficient decongestion and unloading of the LV (discussed further below). PCWP and LV end-diastolic pressure can become dissociated in the presence of pulmonary venous disease, abnormalities of atrial size and function, and mitral valve stenosis. Accordingly, discrepancies between PCWP and LV end-diastolic pressure have been reported especially in conditions such as atrial fibrillation and rheumatic valve disease, and in the presence of large, stiff left atria.[57,58]

PAD pressure is frequently used as a surrogate for PCWP. PAD pressure and PCWP may differ, especially in patients with pulmonary hypertension or mitral insufficiency, or when PAC measurements are not from pulmonary functional zone III.[59] At a minimum, PCWP should be measured at the time of PAC insertion so that the difference between PAD pressure and PCWP can be quantified; that difference can then be referenced during subsequent measurements of PAD pressure.

Measurement of CVP and PCWP, individually or in combination with other parameters (eg, CVP/PCWP ratio, PAPi, RV stroke work, RV stroke work index) provides essential information on volume status and the degree of RV dysfunction, which can guide the need for fluid administration, diuretic therapy, or renal replacement therapy, or indicate the need for initiating RV mechanical support.

All MCS approaches aim to increase cardiac output, but the impact on other components of the hemodynamic profile can differ significantly among devices, and among patients subjected to the same device. This is further illustrated in Figure 5, showing 3 different case scenarios of patients presenting with hypotension and decreased cardiac index despite inotropic support. Patient 1 (red) is a classic example of a patient with primary left heart failure. At baseline, PCWP is markedly elevated, CVP is elevated, and cardiac output is reduced. With introduction of and progressively increased pLVAD support, PCWP declines and cardiac output increases. With decreased PCWP, RV afterload is decreased, which results in a secondary decrease in CVP.

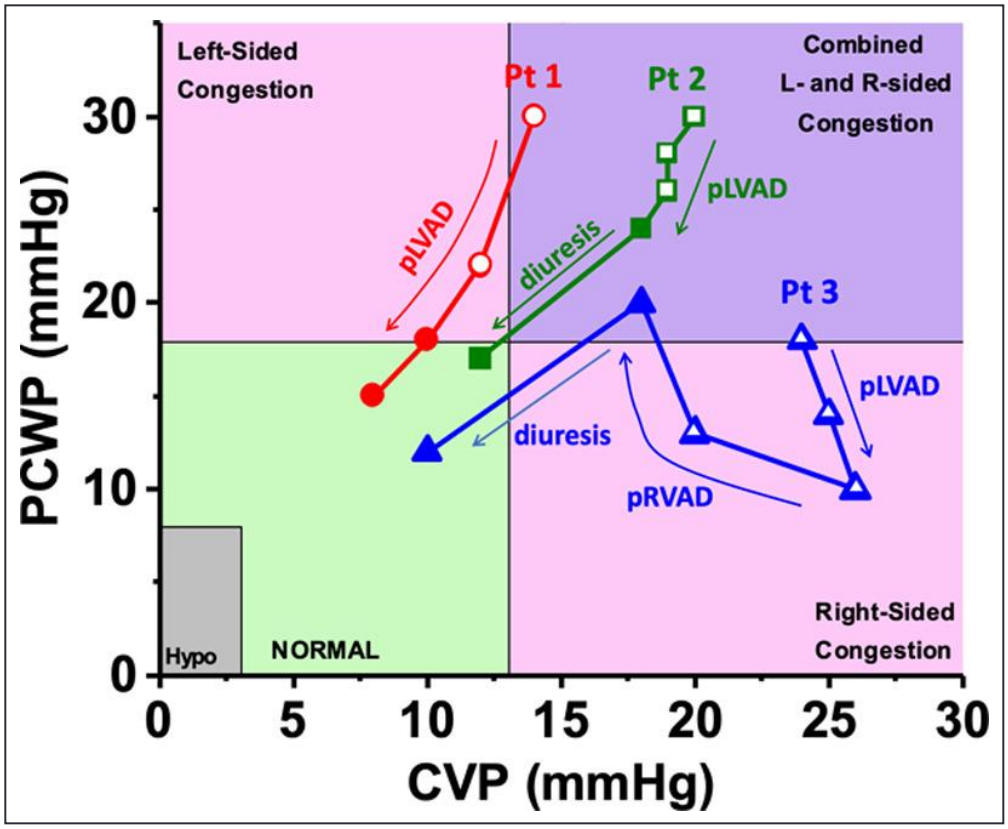


Figure 5. Three case examples of patients presenting with hypotension and decreased cardiac index despite inotropic support. Use of PACs allows for customization of therapy. Details are provided in the text. Created with Harvi (http://harvi.online) with permission of PVLoops LLC.[19] CVP indicates central venous pressure; PCWP, pulmonary capillary wedge pressure; pLVAD, percutaneous left ventricular assist device; and pRVAD, percutaneous right ventricular assist device.

Patient 2 (green) shows marked elevations of both CVP and PCWP. With increasing pLVAD support, there is a mild decrease in PCWP and minimal changes of CVP. This hemodynamic pattern indicates a volume overload state and requires intensification of diuretic therapy and, if unsuccessful, some form of renal replacement therapy.

Patient 3 presents with predominant right-sided congestion but also mild elevated PCWP. Pulmonary artery pressure is 30/20 with a PAPi of ~0.5, indicating significant RV dysfunction. Nevertheless, because the patient has reduced cardiac index and elevated PCWP (upper limit of normal), implantation of pLVAD is a reasonable first step. However, with introduction of and progressive increase in the pLVAD power, PCWP dropped precipitously, and CVP increased further, an indication that the RV is not capable of keeping up with flow from the pLVAD. With initiation of pRVAD, PCWP increases and the LV is filled, increasing cardiac index. Although reduced, CVP remains significantly elevated. With increased diuresis, both PCWP and CVP decrease to normal levels. Whereas there are several different therapeutic approaches to each of these 3 patients, the PAC data measured the hemodynamic effectiveness of decided-upon therapies and revealed the need to address volume status.

ESCALATION OF MCS

Escalation refers to switching from 1 form of MCS to another that provides higher flow and greater pulmonary or systemic venous unloading, or both, or the need to add a second device because of inadequate support provided by the first device alone. When considering escalation of therapy, it is

crucial to recognize that as time proceeds in CS, there is a higher likelihood of progressing into multiorgan failure. The PAC provides continuous data in real-time to determine the efficacy of pharmacologic and mechanical support strategies, and also provides clinically important trends that, if properly interpreted, may call for an escalation of care. If, as assessed by PAC data, the degree of support provided by the initially chosen form of MCS is not adequate, rapid escalation of therapy may be warranted. Typical sequences of MCS escalation include transitioning from an intra-aortic balloon pump to an Impella device, or from an Impella CP to an Impella 5.0, from an Impella CP to ECMO, or adding a percutaneous RV assist device (RVAD) in a patient already treated with an Impella device (the latter is discussed further below). Similarly, patients with isolated RVAD support who continue to deteriorate clinically should also be evaluated for escalation to biventricular support, especially if PAC shows increased PCWP.

Escalation of support should also be considered when the use of a primary hemodynamic support device results in unintended hemodynamic effects. For example, it is now well-recognized that LV distention and pulmonary edema can be deleterious consequences of ECMO support and that the combination of ECMO plus an Impella device relieves such LV and pulmonary congestion[45,46,60–62] (Figure 3C). This is illustrated in the PCWP tracings of Figure 6, which shows an example of a patient who presented in CS with elevated PCWP and was put on ECMO.[46] PCWP increased further, which indicated the need for LV decompression. pVAD support was initiated, rapidly reducing the PCWP and decompressing the LV and the lungs. More generally, this case illustrates that use of the PAC allowed for (1) rapid identification of elevated PCWP on presentation, (2) rapid identification of deteriorating hemodynamic status upon activating the initial form of MCS (ECMO), (3) the determination of corrective action (in this case, the escalation and addition of Impella), and (4) confirmation of rapid resolution of the problem. It can be questioned whether such rapid and decisive clinical decision-making can be made without a PAC in place.

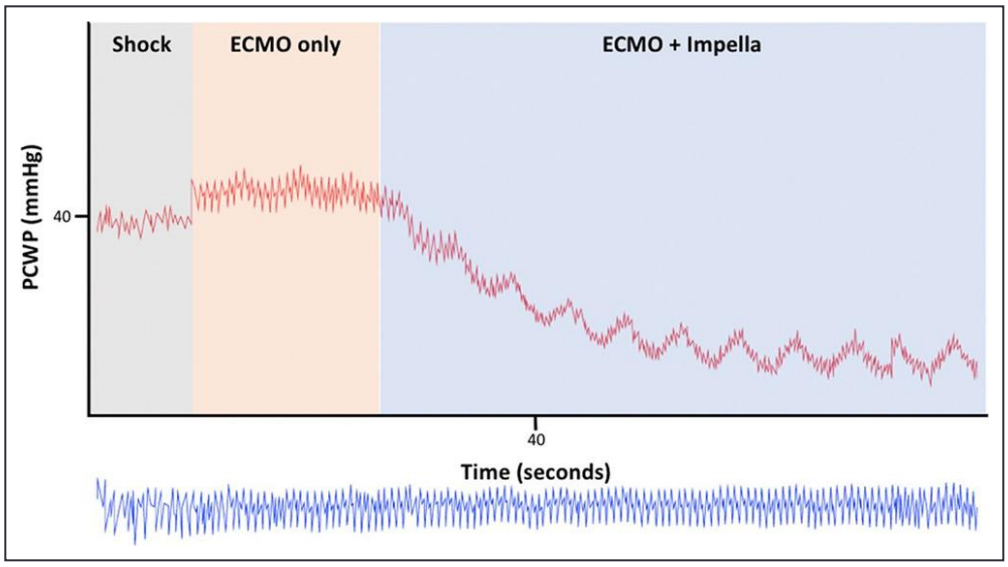


Figure 6. Changes in pulmonary capillary wedge pressure (PCWP) with extracorporeal membrane oxygenation (ECMO) and Impella. PCWP at the time of presentation in cardiogenic shock, which increases after initiation of ECMO and rapidly decreases with the initiation of Impella support.[47] Reprinted with permission from Elsevier from Schrage B, Burkhoff D, Rübsamen N, Becher PM, Schwarzl M, Bernhardt A, Grahn H, Lubos E, Söffker G, Clemmensen P, et al. Unloading of the left ventricle during venoarterial extracorporeal membrane oxygenation therapy in cardiogenic shock. *JACC Heart Fail*. 2018;6:1035–1043.[47]

INDICATIONS FOR RV MECHANICAL SUPPORT

For a patient already on LV assist device (LVAD) support (either percutaneous or durable), elevated CVP, low PCWP, and low device flow are collectively indicative of the need to add RV support, whether it be pharmacologic or MCS (eg, as illustrated in patient scenario 3 in Figure 5). Deranged right heart hemodynamic findings can emerge quickly if LVAD support is initiated before acquisition of PAC data in patients with RV-dominant shock. On the other hand, in patients at risk for right heart failure, availability of PAC data before device selection showing elevated CVP, reduced PAPi, and low PCWP would alert the clinician to the potential need of early initiation of RVAD support and, in some cases, that RVAD support alone, without LVAD support, is indicated. PAC placement can be challenging after RVAD placement, and physicians should consider careful insertion and positioning of a PAC before or at the time of RVAD placement.

Once an RVAD is in place, PAC monitoring can help guide the optimization of RVAD output, particularly when used in combination with LVAD support. In the case of biventricular support, at a given LVAD speed, increases in RVAD output can decrease CVP and increase PCWP. Similarly, at a constant RVAD pump speed, increases in LVAD pump speed can decrease PCWP while increasing CVP. Thus, optimal adjustment of device speeds relative to one another requires real-time, reliable evaluation of both absolute and relative changes in right heart hemodynamic parameters. In addition, persistently elevated CVPs and PCWPs after optimization of blood pressure and cardiac output should trigger the need for volume management strategies. The recent recognition of the higher-than-expected frequency of biventricular involvement in patients with CS[24] underscores the potential role of RV support devices and the need for PAC to manage this complex population.

Similar considerations apply to the case of isolated RVAD support. For example, high RVAD speeds may result in desired reductions in CVP and increases in cardiac output, but excessive increases in PCWP with the potential to induce pulmonary edema. This information can be readily obtained with PACs.

ROLE OF PAC DURING MCS WEANING

Generally accepted protocols for weaning from drugs and MCS do not exist. Weaning protocols are therefore based on local experience and expertise. The first important step is to identify when a patient is eligible for a weaning trial based on stable vital signs and acceptable blood gases, blood chemistries (eg, creatinine, lactate), and hemodynamics despite receiving low dose (or no) inotropic or pressor support. Next, a gradual, step-by-step reduction of the level of circulatory support with assessment of vital signs and hemodynamics (particularly PCWP, CVP, and cardiac output) is performed at each step.[63] So long as hemodynamic stability (based on PAC-derived parameters) and clinical assessment of peripheral perfusion remain adequate, reduction of support progresses until device-specific minimal recommended flow levels are reached and the device is explanted. For the more complex situation of weaning when a patient is supported by 2 devices (eg, ECMO and Impella), the use of invasive hemodynamic parameters can be even more critical.

Data from PAC are important for assessing volume status, SVR, pulmonary vascular resistance and reactivity if elevated, and right heart function. In many cases, despite reescalation of pharmacology therapy, LV and RV function may fail to improve and patients fail to wean from temporary support. If end-organ function is preserved (including neurologic status), such patients may qualify to transition to either heart transplant or durable ventricular assist device implant. Each of the aforementioned hemodynamic factors is critical for determining candidacy for such therapies.

SUMMARY

PACs provide precise and continuous data linked directly with RV and LV performance (Figure 4), and comprehensively explain the hemodynamics of CS and the impact of MCS.[40] Optimization of MCS and device escalation is facilitated through the use of PAC-derived hemodynamic parameters that identify volume status, leading to appropriate use of diuretics or dialysis. PAC use, therefore, allows the potential to diagnose, guide, optimize, and wean therapies in CS most efficiently, with or without MCS. Finally, studies showing that PAC use does not improve outcomes do not apply to the management of patients with cardiogenic shock or those treated with MCS. Emerging data suggest that PAC use is associated with improved survival in patients with CS supported by MCS devices.[5,6]

Based on our current practice experience among CS researchers, we make the following recommendations:

1. PACs should be used in patients presenting with CS that is not resolved within 30 to 60 minutes with the use of a recommended dose of 1 inotrope or pressor.
2. PACs should be used in patients who present with CS that appeared to resolve based on blood pressure in whom clinical parameters (eg, urine output, mental status, lactate levels) fail to improve.
3. PACs should be used in all patients undergoing MCS to monitor effectiveness, optimize device settings, assess the need for escalation (including the need for device combinations) and guide timing and rate of weaning.

The role of PAC use in patients with persistent normotensive-hypoperfusion preshock (ie, systolic blood pressure >90 mm Hg without inotropes or pressors but with clear evidence of worsened end-organ function) deserves consideration and further investigation. As demonstrated by Jentzer et al,[33] these patients are at significant risk of mortality. Clarification of hemodynamic profile (cardiac index, SVR, volume status) in such patients can guide medical management to hasten improvement of end-organ perfusion and potentially prevent progression into overt CS.

In view of the paucity of data, there is a pressing need for additional evidence on PAC use in CS and during MCS. Society guidelines have insufficient high-quality data to recommend PAC use in these patients. Although randomized, controlled trials would provide the best evidence in this regard, randomized prospective trials are an unrealistic expectation in this population. The use of prospective registry-based data may serve to support the recommendations provided in this review.

ARTICLE INFORMATION

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Supplemental Materials

Data Supplement Figure I

Data Supplement Tables I–III

REFERENCES

1. van Diepen, S, Katz, JN, Albert, NM, Henry, TD, Jacobs, AK, Kapur, NK, Kilic, A, Menon, V, Ohman, EM, Sweitzer, NK, et al; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232–e268. doi: 10.1161/CIR.0000000000000525
2. 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
3. Sorajja, P, Borlaug, BA, Dimas, VV, Fang, JC, Forfia, PR, Givertz, MM, Kapur, NK, Kern, MJ, Naidu, SS. SCAI/HFSA clinical expert consensus document on the use of invasive hemodynamics for the diagnosis and management of cardiovascular disease. *Catheter Cardiovasc Interv*. 2017;89:E233–E247. doi: 10.1002/ccd.26888
4. 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
5. O'Neill, WW, Grines, C, Schreiber, T, Moses, J, Maini, B, Dixon, SR, Ohman, EM. Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device. *Am Heart J*. 2018;202:33–38. doi: 10.1016/j.ahj.2018.03.024
6. Hernandez, GA, Lemor, A, Blumer, V, Rueda, CA, Zalawadiya, S, Stevenson, LW, Lindenfeld, J. Trends in utilization and outcomes of pulmonary artery catheterization in heart failure with and without cardiogenic shock. *J Card Fail*. 2019;25:364–371. doi: 10.1016/j.cardfail.2019.03.004
7. Basir, MB, Kapur, NK, Patel, K, Salam, MA, Schreiber, T, Kaki, A, Hanson, I, Almany, S, Timmis, S, Dixon, S, et al; National Cardiogenic Shock Initiative Investigators. Improved outcomes associated with the use of shock protocols: updates from the National Cardiogenic Shock Initiative. *Catheter Cardiovasc Interv*. 2019;93:1173–1183. doi: 10.1002/ccd.28307
8. Rab, T, Ratanapo, S, Kern, KB, Basir, MB, McDaniel, M, Meraj, P, King, SB, 3rd, O'Neill, W. Cardiac shock care centers: JACC review topic of the week. *J Am Coll Cardiol*. 2018;72:1972–1980. doi: 10.1016/j.jacc.2018.07.074

9. Yancy, CW, Jessup, M, Bozkurt, B, Butler, J, Casey, DE, Jr, Drazner, MH, Fonarow, GC, Geraci, SA, Horwich, T, Januzzi, JL, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:1810–1852. doi: 10.1161/CIR.0b013e31829e8807
10. O'Gara, PT, Kushner, FG, Ascheim, DD, Casey, DE, Jr, Chung, MK, de Lemos, JA, Ettinger, SM, Fang, JC, Fesmire, FM, Franklin, BA, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425. doi: 10.1161/CIR.0b013e3182742cf6
11. Patel, MR, Bailey, SR, Bonow, RO, Chambers, CE, Chan, PS, Dehmer, GJ, Kirtane, AJ, Wann, LS, Ward, RP. ACCF/SCAI/AATS/AHA/ASE/ASNC/HFSA/HRS/SCCM/SCCT/SCMR/STS 2012 appropriate use criteria for diagnostic catheterization: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2012;59:1995–2027. doi: 10.1016/j.jacc.2012.03.003
12. Nishimura, RA, Otto, CM, Bonow, RO, Carabello, BA, Erwin, JP, 3rd, Guyton, RA, O'Gara, PT, Ruiz, CE, Skubas, NJ, Sorajja, P, et al; ACC/AHA Task Force Members. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:e521–e643. doi: 10.1161/CIR.0000000000000031
13. Nishimura, RA, Otto, CM, Bonow, RO, Carabello, BA, Erwin, JP, 3rd, Fleisher, LA, Jneid, H, Mack, MJ, McLeod, CJ, O'Gara, PT, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135:e1159–e1195. doi: 10.1161/CIR.0000000000000503
14. Rupp, SM, Apfelbaum, JL, Blitt, C, Caplan, RA, Connis, RT, Domino, KB, Fleisher, LA, Grant, S, Mark, JB, Morray, JP, et al. Practice guidelines for central venous access: a report by the American Society of Anesthesiologists Task Force on Central Venous Access. *Anesthesiology*. 2012;116:539–573. doi: 10.1097/ALN.0b013e31823c9569
15. Antonelli, M, Levy, M, Andrews, PJ, Chastre, J, Hudson, LD, Manthous, C, Meduri, GU, Moreno, RP, Putensen, C, Stewart, T, et al. Hemodynamic monitoring in shock and implications for management: International Consensus Conference, Paris, France, 27–28 April 2006. *Intensive Care Med*. 2007;33:575–590. doi: 10.1007/s00134-007-0531-4
16. Feldman, D, Pamboukian, SV, Teuteberg, JJ, Birks, E, Lietz, K, Moore, SA, Morgan, JA, Arabia, F, Bauman, ME, Buchholz, HW, et al; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*. 2013;32:157–187. doi: 10.1016/j.healun.2012.09.013
17. Dellinger, RP, Levy, MM, Rhodes, A, Annane, D, Gerlach, H, Opal, SM, Sevransky, JE, Sprung, CL, Douglas, IS, Jaeschke, R, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39:165–228. doi: 10.1007/s00134-012-2769-8
18. American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines

for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology*. 2003;99:988–1014. doi: 10.1097/00000542-200310000-00036

19. Burkhoff, D, Dickstein, ML, Schleicher, T. Welcome to Harvi. https://harvi.online. Published 2015. Accessed December 1, 2019.
20. Trottier, SJ, Taylor, RW. Physicians' attitudes toward and knowledge of the pulmonary artery catheter: Society of Critical Care Medicine membership survey. *New Horiz*. 1997;5:201–206.
21. Hochman, JS, Sleeper, LA, Webb, JG, Sanborn, TA, White, HD, Talley, JD, Buller, CE, Jacobs, AK, Slater, JN, Col, J, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock: SHOCK Investigators: should we emergently revascularize occluded coronaries for cardiogenic shock? *N Engl J Med*. 1999;341:625–634. doi: 10.1056/NEJM199908263410901
22. Thiele, H, Schuler, G, Neumann, FJ, Hausleiter, J, Olbrich, HG, Schwarz, B, Hennersdorf, M, Empen, K, Fuernau, G, Desch, S, et al. Intraaortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock: design and rationale of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial. *Am Heart J*. 2012;163:938–945. doi: 10.1016/j.ahj.2012.03.012
23. Kapur, NK, Esposito, ML, Bader, Y, Morine, KJ, Kiernan, MS, Pham, DT, Burkhoff, D. Mechanical circulatory support devices for acute right ventricular failure. *Circulation*. 2017;136:314–326. doi: 10.1161/CIRCULATIONAHA.116.025290
24. Lala, A, Guo, Y, Xu, J, Esposito, M, Morine, K, Karas, R, Katz, SD, Hochman, JS, Burkhoff, D, Kapur, NK. Right ventricular dysfunction in acute myocardial infarction complicated by cardiogenic shock: a hemodynamic analysis of the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial and registry. *J Card Fail*. 2018;24:148–156. doi: 10.1016/j.cardfail.2017.10.009
25. Menon, V, Slater, JN, White, HD, Sleeper, LA, Cocke, T, Hochman, JS. Acute myocardial infarction complicated by systemic hypoperfusion without hypotension: report of the SHOCK trial registry. *Am J Med*. 2000;108:374–380. doi: 10.1016/s0002-9343(00)00310-7
26. Baran, DA, Grines, CL, Bailey, S, Burkhoff, D, Hall, SA, Henry, TD, Hollenberg, SM, Kapur, NK, O'Neill, W, Ornato, JP, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: this document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv*. 2019;94:29–37. doi: 10.1002/ccd.28329
27. 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
28. Korabathina, R, Heffernan, KS, Paruchuri, V, Patel, AR, Mudd, JO, Prutkin, JM, Orr, NM, Weintraub, A, Kimmelstiel, CD, Kapur, NK. The pulmonary artery pulsatility index identifies severe right ventricular dysfunction in acute inferior myocardial infarction. *Catheter Cardiovasc Interv*. 2012;80:593–600. doi: 10.1002/ccd.23309
29. Morine, KJ, Kiernan, MS, Pham, DT, Paruchuri, V, Denofrio, D, Kapur, NK. Pulmonary artery pulsatility index is associated with right ventricular failure after left ventricular assist device surgery. *J Card Fail*. 2016;22:110–116. doi: 10.1016/j.cardfail.2015.10.019
30. Kang, G, Ha, R, Banerjee, D. Pulmonary artery pulsatility index predicts right ventricular failure after left ventricular assist device implantation. *J Heart Lung Transplant*. 2016;35:67–73. doi: 10.1016/j.healun.2015.06.009
31. Harjola, VP, Mebazaa, A, Čelutkienė, J, Bettex, D, Bueno, H, Chioncel, O, Crespo-Leiro, MG, Falk, V, Filippatos, G, Gibbs, S, et al. Contemporary management of acute right ventricular failure: a statement from

the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology. *Eur J Heart Fail*. 2016;18:226–241. doi: 10.1002/ejhf.478

32. Kohsaka, S, Menon, V, Lowe, AM, Lange, M, Dzavik, V, Sleeper, LA, Hochman, JS; SHOCK Investigators. Systemic inflammatory response syndrome after acute myocardial infarction complicated by cardiogenic shock. *Arch Intern Med*. 2005;165:1643–1650. doi: 10.1001/archinte.165.14.1643
33. Jentzer, JC, van Diepen, S, Barsness, GW, Henry, TD, Menon, V, Rihal, CS, Naidu, SS, Baran, DA. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. *J Am Coll Cardiol*. 2019;74:2117–2128. doi: 10.1016/j.jacc.2019.07.077
34. Burkhoff, D, Garan, AR, Kapur, NK. The SCAI cardiogenic shock staging system gets taken for a test drive. *J Am Coll Cardiol*. 2019;74:2129–2131. doi: 10.1016/j.jacc.2019.08.1020
35. Galiè, N, Humbert, M, Vachiery, JL, Gibbs, S, Lang, I, Torbicki, A, Simonneau, G, Peacock, A, Vonk Noordegraaf, A, Beghetti, M, et al; ESC Scientific Document Group. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2016;37:67–119. doi: 10.1093/eurheartj/ehv317
36. Bonanno, FG. Clinical pathology of the shock syndromes. *J Emerg Trauma Shock*. 2011;4:233–243. doi: 10.4103/0974-2700.82211
37. Khirfan, G, Ahmed, MK, Almaaitah, S, Almoushref, A, Agmy, GM, Dweik, RA, Tonelli, AR. Comparison of different methods to estimate cardiac index in pulmonary arterial hypertension. *Circulation*. 2019;140:705–707. doi: 10.1161/CIRCULATIONAHA.119.041614
38. Kochav, SM, Flores, RJ, Truby, LK, Topkara, VK. Prognostic impact of pulmonary artery pulsatility index (PAPi) in patients with advanced heart failure: insights from the ESCAPE trial. *J Card Fail*. 2018;24:453–459. doi: 10.1016/j.cardfail.2018.03.008
39. Torgersen, C, Schmittinger, CA, Wagner, S, Ulmer, H, Takala, J, Jakob, SM, Dünser, MW. Hemodynamic variables and mortality in cardiogenic shock: a retrospective cohort study. *Crit Care*. 2009;13:R157. doi: 10.1186/cc8114
40. 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
41. Samuels, LE, Kaufman, MS, Thomas, MP, Holmes, EC, Brockman, SK, Wechsler, AS. Pharmacological criteria for ventricular assist device insertion following postcardiotomy shock: experience with the Abiomed BVS system. *J Card Surg*. 1999;14:288–293. doi: 10.1111/j.1540-8191.1999.tb00996.x
42. Basir, MB, Schreiber, TL, Grines, CL, Dixon, SR, Moses, JW, Maini, BS, Khandelwal, AK, Ohman, EM, O'Neill, WW. Effect of early initiation of mechanical circulatory support on survival in cardiogenic shock. *Am J Cardiol*. 2017;119:845–851. doi: 10.1016/j.amjcard.2016.11.037
43. Thiele, H, Zeymer, U, Neumann, FJ, Ferenc, M, Olbrich, HG, Hausleiter, J, Richardt, G, Hennersdorf, M, Empen, K, Fuernau, G, et al; 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
44. Keebler, ME, Haddad, EV, Choi, CW, McGrane, S, Zalawadiya, S, Schlendorf, KH, Brinkley, DM, Danter, MR, Wigger, M, Menachem, JN, et al. Venoarterial extracorporeal membrane oxygenation in cardiogenic shock. *JACC Heart Fail*. 2018;6:503–516. doi: 10.1016/j.jchf.2017.11.017
45. Rao, P, Khalpey, Z, Smith, R, Burkhoff, D, Kociol, RD. Venoarterial extracorporeal membrane oxygenation for cardiogenic shock and cardiac arrest. *Circ Heart Fail*. 2018;11:e004905. doi: 10.1161/CIRCHEARTFAILURE.118.004905

46. Schrage, B, Burkhoff, D, Rübsamen, N, Becher, PM, Schwarzl, M, Bernhardt, A, Grahn, H, Lubos, E, Söffker, G, Clemmensen, P, et al. Unloading of the left ventricle during venoarterial extracorporeal membrane oxygenation therapy in cardiogenic shock. *JACC Heart Fail*. 2018;6:1035–1043. doi: 10.1016/j.jchf.2018.09.009
47. Weber, C, Deppe, AC, Sabashnikov, A, Slottosch, 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. Chen, CH, Fetics, B, Nevo, E, Rochitte, CE, Chiou, KR, Ding, PA, Kawaguchi, M, Kass, DA. Noninvasive single-beat determination of left ventricular end-systolic elastance in humans. *J Am Coll Cardiol*. 2001;38:2028–2034. doi: 10.1016/s0735-1097(01)01651-5
49. Klotz, S, Dickstein, ML, Burkhoff, D. A computational method of prediction of the end-diastolic pressure-volume relationship by single beat. *Nat Protoc*. 2007;2:2152–2158. doi: 10.1038/nprot.2007.270
50. Brinkley, DM, Jr, Ho, KKL, Drazner, MH, Kociol, RD. The prognostic value of the relationship between right atrial and pulmonary capillary wedge pressure in diverse cardiovascular conditions. *Am Heart J*. 2018;199:31–36. doi: 10.1016/j.ahj.2018.01.006
51. Uriel, N, Sayer, G, Addetia, K, Fedson, S, Kim, GH, Rodgers, D, Kruse, E, Collins, K, Adatya, S, Sarswat, N, et al. Hemodynamic ramp tests in patients with left ventricular assist devices. *JACC Heart Fail*. 2016;4:208–217. doi: 10.1016/j.jchf.2015.10.001
52. Narang, N, Chung, B, Nguyen, A, Kalathiya, RJ, Laffin, LJ, Holzhauser, L, Ebong, IA, Besser, SA, Imamura, T, Smith, BA, et al. Discordance between clinical assessment and invasive hemodynamics in patients with advanced heart failure. *J Card Fail*. 2020;26:128–135. doi: 10.1016/j.cardfail.2019.08.004
53. Tarvasmäki, T, Haapio, M, Mebazaa, A, Sionis, A, Silva-Cardoso, J, Tolppanen, H, Lindholm, MG, Pulkki, K, Parissis, J, Harjola, VP, et al; CardShock Study Investigators. Acute kidney injury in cardiogenic shock: definitions, incidence, haemodynamic alterations, and mortality. *Eur J Heart Fail*. 2018;20:572–581. doi: 10.1002/ejhf.958
54. Lehman, LW, Saeed, M, Moody, G, Mark, R. Hypotension as a risk factor for acute kidney injury in ICU patients. *Comput Cardiol (2010)*. 2010;37:1095–1098.
55. de Scordilli, M, Pinamonti, B, Albani, S, Gregorio, C, Barbati, G, Daneluzzi, C, Korcova, R, Perkan, A, Fabris, E, Geri, P, et al. Reliability of noninvasive hemodynamic assessment with Doppler echocardiography: comparison with the invasive evaluation. *J Cardiovasc Med (Hagerstown)*. 2019;20:682–690. doi: 10.2459/JCM.0000000000000841
56. Cecconi, M, De Backer, D, Antonelli, M, Beale, R, Bakker, J, Hofer, C, Jaeschke, R, Mebazaa, A, Pinsky, MR, Teboul, JL, et al. Consensus on circulatory shock and hemodynamic monitoring: task force of the European Society of Intensive Care Medicine. *Intensive Care Med*. 2014;40:1795–1815. doi: 10.1007/s00134-014-3525-z
57. Naeije, R, Chin, K. Differentiating precapillary from postcapillary pulmonary hypertension. *Circulation*. 2019;140:712–714. doi: 10.1161/CIRCULATIONAHA.119.040295
58. Reddy, YNV, El-Sabbagh, A, Nishimura, RA. Comparing pulmonary arterial wedge pressure and left ventricular end diastolic pressure for assessment of left-sided filling pressures. *JAMA Cardiol*. 2018;3:453–454. doi: 10.1001/jamacardio.2018.0318
59. Wilson, RF, Beckman, SB, Tyburski, JG, Scholten, DJ. Pulmonary artery diastolic and wedge pressure relationships in critically ill and injured patients. *Arch Surg*. 1988;123:933–936. doi: 10.1001/archsurg.1988.01400320019002
60. Patel, SM, Lipinski, J, Al-Kindi, SG, Patel, T, Saric, P, Li, J, Nadeem, F, Ladas, T, Alaiti, A, Phillips, A, et al.

Simultaneous venoarterial extracorporeal membrane oxygenation and percutaneous left ventricular decompression therapy with Impella is associated with improved outcomes in refractory cardiogenic shock. *ASAIO J*. 2019;65:21–28. doi: 10.1097/MAT.0000000000000767

61. Pappalardo, F, Schulte, C, Pieri, M, Schrage, B, Contri, R, Soeffker, G, Greco, T, Lembo, R, Müllerleile, K, Colombo, A, et al. 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/ejhf.668
62. Akanni, OJ, Takeda, K, Truby, LK, Kurlansky, PA, Chiuzan, C, Han, J, Topkara, VK, Yuzefpolskaya, M, Colombo, PC, Karmpaliotis, D, et al. EC-VAD: combined use of extracorporeal membrane oxygenation and percutaneous microaxial pump left ventricular assist device. *ASAIO J*. 2019;65:219–226. doi: 10.1097/MAT.0000000000000804
63. Atkinson, TM, Ohman, EM, O'Neill, WW, Rab, T, Cigarroa, JE; Interventional Scientific Council of the American College of Cardiology. A practical approach to mechanical circulatory support in patients undergoing percutaneous coronary intervention: an interventional perspective. *JACC Cardiovasc Interv*. 2016;9:871–883. doi: 10.1016/j.jcin.2016.02.046