A Critical Review of Hemodynamically Guided Therapy for Cardiogenic Shock: Old Habits Die Hard

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Abstract

Purpose of review Here, we review the importance of using hemodynamic data to guide therapy and risk stratification in cardiogenic shock as well as the various definitions of this syndrome that have been used in prior studies. Furthermore, we provide perspective regarding the controversy surrounding pulmonary artery (PA) catheter use as well as current society guidelines and scientific statements. Lastly, we review the technical aspects for accurate interpretation of data of cardiogenic shock.
Recent findings More recent studies specifically evaluating cardiogenic shock patients have shown higher mortality when PA catheters were not used. Furthermore, initiatives are underway to develop more standardized definitions of cardiogenic shock, including the SCAI Shock Classification Scheme. Only by having a standardized fashion of conveying severity of shock will we be able to more systematically study this patient population and improve outcomes moving forward.
Summary PA catheters are critical to the prognostication and management of a subset of patients with cardiopulmonary disease, particularly in those with pulmonary hypertension, cardiogenic shock, or requiring mechanical circulatory support or undergoing evaluation for advanced heart failure therapies.

Introduction

When the Swan-Ganz catheter was introduced in 1970, it was considered revolutionary in the then nascent era of cardiac catheterization [1]. Up until then, pulmonary artery catheterization was cumbersome and required significant technical skill to manipulate stiff catheters which often caused ectopy and required the use of fluoroscopy for correct positioning [2]. However, the inspiration for using a balloon-tipped catheter to "flow" into the pulmonary artery (PA) position using the natural fluid mechanics of cardiac circulation serendipitously came to Dr. H.J.C. Swan while watching sailboats progress on a calm sea in Santa Monica [3]. He then began work with his colleague, Dr. William Ganz, to develop a novel flexible catheter with an inflatable balloon tip. This invention suddenly facilitated the transfer of hemodynamic monitoring from the confines of the catheterization laboratory to the bedside without the use of fluoroscopy and with minimal ectopy.

Questions about the utility of PA-guided therapy have since emerged after several randomized controlled trials cast doubt regarding benefit in the routine management of critically ill patients [3]. Although swan guided therapy has stimulated controversy in some academic circles, there is no question that the PA catheter is an essential tool among most cardiac intensive care units in the management of cardiogenic shock. Here, we review the utility of invasive hemodynamic monitoring in cardiogenic shock. We also provide a review of contemporary literature in light of significant advances in therapy and an increasing repertoire of therapeutic tools for management of cardiogenic shock in the modern era, including temporary mechanical circulatory support devices (MCS).

Cardiogenic shock: classic definitions, novel parameters, and evolving paradigms

Essential to the evaluation and management of cardiogenic shock is the establishment of standard definitions for this high-acuity disease state. Shock is defined as a state of hypotension which results in tissue hypoperfusion. Cardiogenic shock is a state of diminished cardiac output leading to inadequate end-organ perfusion, with the primary insult coming from a reduction in myocardial contractility. This can occur from a variety of etiologies affecting the myocardium, endocardium, pericardium, or electrical conduction system. Subsequently, compensatory mechanisms of peripheral vasoconstriction and fluid retention lead to a rise in biventricular filling pressures. Coupled with ongoing hypotension which diminishes primary coronary perfusion pressure and mediates ongoing cardiac ischemia, a vicious downward spiral of cardiac dysfunction ensues [4].

Classic definitions

Historically, the standard definitions of cardiogenic shock have been described by landmark clinical trials such as SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) and IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) [5–7]. In the SHOCK trial, the definition of cardiogenic shock was any cardiac disorder that results in both clinical and biochemical evidence of tissue hypoperfusion. It was further clinically defined as a systolic blood pressure (SBP) < 90 mmHg for ≥30 min or support to maintain SBP ≥ 90 mmHg and markers of organ hypoperfusion such as urine output < 30 mL/h or cool extremities. Hemodynamic criteria were defined as a cardiac index of ≤ 2.2 L/min/m^2 and a pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg. The IABP-SHOCK II trial further refined these definitions by clarifying utilization of catecholamines to maintain SBP > 90 mmHg, while delineating further signs of impaired end-organ perfusion to include altered mental status, and lactate level > 2.0 mmol/L (Table 1).

Over the last several years, further nuance has been provided to these classic definitions. A recent American Heart Association Scientific Statement on Cardiogenic Shock outlined four classic phenotypes of shock based on volume status and peripheral circulation [8]. Classic "cold and wet" cardiogenic shock is defined as a state of diminished cardiac index with concomitant elevated systemic vascular resistance (SVR) and pulmonary congestion, while "cold and dry" euvolemic cardiogenic shock was defined as reduced cardiac index and elevated SVR, but with a normal PCWP.

These classic definitions of shock have traditionally been applicable for left-sided cardiogenic shock, in which the patient has clinical signs including rales, an S3, and a displaced apical impulse, and hemodynamics using a PA catheter reveal elevated SVR, PCWP, and reduced cardiac index. A novel hemodynamic parameter, the cardiac power output (CPO), was tested in a sub-study of patients from the SHOCK trial and found to correlate strongest with in-hospital mortality [9]. Defined as mean arterial pressure × cardiac output / 451, CPO in units of watts (W) was calculated in 181 out of 541 patients included with

Table 1. Cardiogenic shock definitions

	Year	Cohort	CS definition
SHOCK [5]	1999	AMICS	By both clinical and hemodynamic criteria: Clinical criteria: Hypotension (SBP <90 mmHg ≥30 min) or need for supportive measures to maintain SBP ≥90 mmHg Evidence of end-organ hypoperfusion Hemodynamic criteria: CI ≤2.2 L/min/m^2 PCWP ≥15 mmHg
IABP SHOCK II [7]	2013	AMICS	SBP <90 mmHg for >30 min or requiring catecholamines to maintain SBP > 90 mmHg Clinical signs of pulmonary congestion Impaired end-organ perfusion (i.e., altered mental status, cold, clammy skin and extremities; UOP<30 cc/h; lactate >2.0 mmol/L)
CULPRIT SHOCK [44]	2017	AMICS	SBP <90 mmHg for >30 min Catecholamines to maintain SBP >90 mmHg Signs of pulmonary congestion Signs of impaired perfusion with at least one of: Altered mental status Cold, clammy skin and extremities Oliguria with UOP <30 mL/h Lactate >2.0 mmol/L
INTERMACS [45]	2008	ALL CS	Heart failure patients profiled into the following groups: Profile 1: Critical cardiogenic shock ("Crash and burn"). Patients with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and/or lactate levels Profile 2: Progressive decline ("Sliding on inotropes"). Patient with declining function despite inotropic support, may be manifest by worsening renal function or inability to restore volume balance. Also describes declining status in patients unable to tolerate inotropic therapy Profile 3: Stable but inotrope dependent ("Dependent stability"). Patient stable on continuous intravenous inotropic support (or a temporary circulatory support device or both), but demonstrating repeated failure to wean from support. Profile 4: Resting symptoms. Patient can be stabilized close to normal volume status but experiences daily symptoms of congestion at rest or during ADL. Doses of diuretics generally fluctuate at very high levels. Can fluctuate between 4 and 5. Profile 5: Exertion intolerant. Comfortable at rest and with ADL but unable to engage in any other activity, living predominantly within the house. May have underlying refractory elevated volume status, often with renal dysfunction. If underlying organ function marginal, patient may be more at risk than INTERMACS 4. Profile 6: Exertion limited (walking wounded). Patient without evidence of fluid overload. Is comfortable at rest, and with activities of daily living and minor activities outside the home but fatigues after the first few minutes of any meaningful activity. Attribution to cardiac limitation requires careful measurement of peak oxygen consumption, in some cases with hemodynamic monitoring to confirm severity of cardiac impairment. Profile 7: Advanced NYHA III. A placeholder for more precise specification in future, this level includes patients who are without current or recent episodes of unstable

Table 1. (Continued)

	Year	Cohort	CS definition
			fluid balance, living comfortably with meaningful activity limited to mild physical exertion.
NCSI [10]	2019	AMICS	Prolonged hypotension (SBP <90 mmHg, or inotropes/vasopressors to maintain SBP >90 mmHg) Signs of end-organ hypoperfusion (cool extremities, oliguria or anuria, or elevated lactate levels) Hemodynamic criteria represented by CI <2.2 L/min/m^2 or CPO <0.6 W
SCAI [29]	2017	ALL CS	CS patients staged based on severity of shock: A: "At risk" for CS. A patient who is not experiencing signs or symptoms of CS but is at risk for its development. B: "Beginning" CS (pre-shock/compensated shock). A patient who has clinical evidence of relative hypotension or tachycardia (SBP <90 mmHg, MAP <60 mmHg or >30 mmHg drop from baseline) without hypoperfusion (cold, clamped extremities, poor UOP, mental confusion, etc). Laboratories may be normal. C: "Classic" CS. A patient with hypoperfusion that requires an initial set of interventions (inotropes, pressor, MCS, or ECMO) beyond volume resuscitation to restore perfusion. These patients typically present with the classic shock phenotype of hypotension along with hypoperfusion. Laboratory findings may include impaired kidney function, elevated lactate, BNP, and/or liver enzymes. Invasive hemodynamics demonstrates depressed CI. D: "Deteriorating" CS. A patient who has failed to stabilize despite intense initial efforts and further escalation is required. Classification in this stage requires that the patient has had some degree of appropriate treatment and medical stabilization. In addition, at least 30 min has elapsed but the patient has not responded. Escalation is an increase in the number or intensity of intravenous therapies to address hypoperfusion, or addition of MCS. E: "Extremis" CS. A patient with circulatory collapse, frequently (but not always) in refractory cardiac arrest with ongoing CPR or ECMO-facilitated CPR.
CSWG [24]	Established 2017	ALL CS	Sustained episode of SBP <90 mm Hg for at least 30 min CI <2.2 L/(min m^2) determined to be secondary to cardiac dysfunction Requirement for either pharmacological support (vasopressors or inotropes) or short-term MCS (i.e., IABP, Impella, VAECMO)
EURO SHOCK [46]	Study start 2019	AMICS	SBP <90 mmHg >30 min, or a requirement for a continuous infusion of vasopressor or inotropic therapy to maintain SBP >90 mmHg Clinical signs of pulmonary congestion, plus signs of impaired organ perfusion with at least one of the following: Altered mental status Cold and clammy skin and limbs Oliguria with a UOP <30 mL/h Elevated lactate of >2.0 mmol/L
DANGER SHOCK [47]	Study start 2012	AMICS	Peripheral sign of tissue hypoperfusion with lactate ≥2.5 mmol/L Persistent (>30 min) SBP <100 mmHg and/or need for vasoactive therapy LVEF <45% on echocardiography

CS cardiogenic shock, *CI* cardiac index, *IABP* intra-aortic balloon pump, *LVEF* left ventricular ejection fraction, *MAP* mean arterial blood pressure, *MCS* mechanical circulatory support, *PCWP* pulmonary capillary wedge pressure, *SBP* systolic blood pressure, *UOP* urine output, *VAECMO* veno-arterial extracorporeal membrane oxygenation

predominant left-sided failure in the setting of acute myocardial infarction-cardiogenic shock. In multivariate analysis, CPO (OR 0.60 (0.44–0.83 CI), $p = 0.002$) was strongly associated with in-hospital mortality, independent of other significant variables such as age or history of hypertension. A CPO cutoff of 0.53 W was found to most accurately predict in-hospital mortality (c-statistic 0.69) [9]. In more recent analysis from the National Cardiogenic Shock Initiative, a CPO < 0.6 W and a serum lactate > 4 were independent predictors of mortality, further validating the utility of this novel hemodynamic calculation in monitoring patients with this highly complex disease state [10].

Other shock profiles exist outside of left-sided cardiogenic shock. Predominant right-sided cardiogenic shock can occur in right ventricular myocardial infarction, in acute pulmonary embolism, in acute-on-chronic right-sided valvulopathy including tricuspid regurgitation and pulmonary regurgitation, in acute-on-chronic pulmonary arterial hypertension, as sequelae after left ventricular assist device (LVAD) implantation, or as a result of complex congenital cardiac lesions. Specific evaluation of right heart failure requires hemodynamic parameters provided by real-time PA catheter monitoring, including right atrial pressure (RAP) to PCWP ratio, RV stroke work index, and pulmonary artery pulsatility index (PAPi). Calculated by subtracting the pulmonary artery diastolic pressure from the pulmonary artery systolic pressure and dividing by the RAP, the PAPi has been utilized primarily to predict RV failure after LVAD surgery [11]. However, it has also been utilized in patients presenting with RV myocardial infarction, proving to have the highest sensitivity and specificity to predict in-hospital mortality among this high-risk cohort [12].

Society for Cardiovascular Angiography & Interventions shock staging system

In 2019, the Society for Cardiovascular Angiography & Interventions (SCAI), in combination with other major societies encompassing both cardiovascular medicine and critical care medicine along with cardiothoracic surgery, published a clinical expert consensus statement on the classification of cardiogenic shock [13••], placing a clear emphasis on early recognition of these disease states, as well as demonstrating the spectrum of clinical presentation. In creating a five-step pyramid scheme for cardiogenic shock, the consensus document defines clinical description, clinical exam, biochemical markers, and hemodynamic evaluation along the continuum of cardiogenic shock, from Stage A (at risk) to Stage B (beginning) to Stage C (classic) to Stage D (deteriorating) to Stage E

(extremis). The new schema emphasizes that shock is a progressive state. There is inherent emphasis made on time to recognition, time to evaluation, and ultimately time to perfusion, whether that is with pharmacologic or MCS, to prevent the progression from Stage A to Stage E. This classification scheme has been applied in different studies, both retrospective and prospective, to accurately stratify the risk of in-hospital mortality [14, 15]. In the retrospective Mayo Clinic study, each progressive SCAI shock stage was associated with increased hospital mortality irrespective of cause of cardiogenic shock. In the prospective study by Baran et al., the initial SCAI stage predicted survival, further emphasizing the need for accurate and early hemodynamic monitoring. In a recent "State-of-the-Art Review: a Standardized and Comprehensive Approach to the Management of Cardiogenic Shock," a multidisciplinary approach utilizing standardized protocols was advocated that emphasizes early invasive hemodynamics with the aim of early diagnosis, early classification of shock severity using common nomenclature (SCAI CS staging system), and early phenotyping of CS type [16].

Evolving paradigms

The increasing heterogeneity and phenotyping of different cardiogenic shock states, along with the clear recognition that time to perfusion is paramount to prevent the further downward spiral of organ hypoperfusion, highlights the need for accurate hemodynamic monitoring early in patients who are at risk for the development of shock or in beginning stages according to the SCAI Shock Classification. These recent advances in our knowledge of cardiogenic shock, along with scientific societal impetus to improve systems of care to reduce the associated high mortality, have the potential to improve the care delivery of this critically ill population. However, previous studies regarding the utility of invasive hemodynamic monitoring continue to pose challenges to contemporary care of cardiogenic shock.

The controversy over PA catheters

In 1996, the SUPPORT trial investigators analyzed a critically ill adult population from ICUs across multiple academic medical centers in an observational study, finding via case-matching analysis that use of right heart catheterization (RHC) in the first 24 h of care was associated with higher 30-day mortality (OR 1.24; 95% CI 1.03–1.49), in addition to an increase in mean length of stay and cost per hospital stay [17]. However, the percentage of patients with "congestive heart failure" as disease category was only 7% in the group without

RHC and 10% in the group with RHC, suggesting that widespread use of RHC in patients with respiratory failure or undifferentiated multisystem organ dysfunction may not be appropriate. This led to further analysis with the landmark Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) Trial in 2005, which was a randomized controlled trial of 433 patients at 26 institutions assigned to receive PA catheter–guided therapy vs. therapy by clinical assessment alone [3]. In a population of patients with acute-on-chronic decompensated heart failure without cardiogenic shock, the routine use of PA catheter–guided therapy in addition to clinical assessment had no difference on the primary end point of days alive and out of the hospital during the first 6 months (133 days vs. 135 days, HR 1.00 95% CI 0.82–1.21, $p = 0.99$) or mortality (43 patients vs. 38 patients, OR 1.26 95% CI 0.78–2.03, $p = 0.35$). Subsequently, nationwide trends in overall use of PA catheter declined significantly overall between 1999 and 2013 (6.28 per 1000 admissions to 2.02 per 1000 admissions, $p < 0.001$), in addition to decreasing specifically for heart failure admissions, when examining Centers for Medicare and Medicaid Services inpatient claims data (National Trends in Use and Outcomes of Pulmonary Artery Catheters Among Medicare Beneficiaries) [18].

It bears importance to note that ESCAPE and SUPPORT, among other trials ("Pulmonary Artery Catheters for Adult Patients in Intensive Care," Cochrane Database Syst Rev; "Assessment of the Clinical Effectiveness of Pulmonary Artery Catheters in Management of Patients in Intensive Care (PAC-Man): a Randomized Controlled Trial") [19, 20] and societal guidelines [21], both tested the use of PA catheter in patients with acute decompensated heart failure and recommend against routine use in heart failure hospitalizations. However, patients with cardiogenic shock have been excluded from the above trials investigating all-comer critically ill states or in routine admissions for decompensated heart failure. A recent retrospective study utilizing the National Impatient Sample investigating the use of PA catheter in patients who developed CS during index hospitalization showed that PA catheter use was associated with lower mortality (35.1% vs. 39.2%, p < 0.001) which remained lower in the PA catheter group after propensity matching. By the end of the study period (final year), mortality for CS patients with PA catheter was 29.7% compared with 38.1% in those without it [22]. In a subspecified group of patients with acute myocardial infarction–related cardiogenic shock being supported with temporary percutaneous ventricular assist device therapy, another study utilizing the National Inpatient Sample found that the use of PA catheter was associated with improved outcomes [23]. More recently, the Cardiogenic Shock Working Group, a large multicenter registry representing real-world patients with CS in the contemporary MCS era, found that complete PA catheter–derived hemodynamic data prior to MCS initiation is associated with survival from CS across all SCAI CS stages and having no PA catheter assessment was associated with higher in-hospital mortality than complete PA catheter assessment [24••]. The PA catheter in shock states can help identify clinical trajectory, need for escalation of care, and how to address contributing factors if present such as distributive or obstructive contributors. With advancements and increases in temporary MCS use in patients with cardiogenic shock [25], in addition to traditional pharmacologic treatments with vasodilators and inodilators, as well as the need for aggressive early recognition, evaluation, and management of the shock state, the utilization of the PA catheter in cardiogenic shock remains paramount to proper treatment.

Current society guidelines and scientific statements

Recent society guidelines have had limited recommendations regarding PA catheter utilization in different forms of shock. The 2006 International Consensus Conference on Hemodynamic Monitoring in Shock and Implications for Management did not recommend the routine use of PA catheter for patients in shock [26]. The 2012 Surviving Sepsis Campaign: international guidelines for management of septic shock recommends against the routine use of PA catheters in patients with sepsis-induced acute respiratory distress syndrome (I, A) [27]. For routine management of heart failure without evidence of tissue hypoperfusion, the ACC/AHA 2013 guidelines for management of heart failure recommend against the routine use of PA catheters in acute decompensated heart failure patients who are normotensive and responding to medical therapy. However, they recommend monitoring with a PA catheter only in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate (I, C) or in patients who have unclear fluid status, low systemic systolic pressure, worsening of renal function with therapy, and requirement of parenteral vasoactive agents, or who are being considered for advanced heart therapies (durable left ventricular assist device or transplantation) (IIa, C) [21]. Similarly, the 2013 ISHLT guidelines for MCS recommend PA catheter utilization in the following clinical situations: after MCS if persistent or recurrent HF symptoms to evaluate for evidence of RV failure or device malfunction (I, B); after

MCS placement when evaluating for myocardial recovery before pump explantation (IIa, C); and at regular intervals in patients being evaluated for or listed for heart transplant for evaluation of irreversible pulmonary hypertension (I, A), which is the only Class IA indication listed in any society guidelines [28]. However, in light of recent evidence showing potential benefit of invasive hemodynamic monitoring in CS with tissue hypoperfusion, there has been recent updates to scientific statements regarding the use of the PA catheter in CS and MCS. The 2017 AHA scientific statement on contemporary management of cardiogenic shock states to consider PA catheter utilization early in the treatment course in patients not responsive to initial therapy or in case of diagnostic or therapeutic uncertainty [8]. Similarly, the 2017 SCAI/HFSA clinical expert consensus document on the use of invasive hemodynamics for the diagnosis and management of cardiovascular disease recommended invasive hemodynamic assessment for diagnosis of cardiogenic shock; continuous hemodynamic monitoring with a PA catheter in patients with MCS; to guide weaning of MCS; and to assess candidacy for and transition to advanced heart failure therapies (durable left ventricular assist device or transplantation) [29].

Practical consideration and indications

While there are no recommendations to apply PA catheters routinely to heterogeneous populations of critically ill patients or all patients with acute decompensated heart failure, growing evidence is supporting the benefit of early invasive hemodynamic monitoring in patients with CS who have signs of tissue hypoperfusion such as elevated lactate levels or markers of end-organ dysfunction. Potential benefit of early use of MCS is prevention of multi-organ failure and improved outcomes [30]. Early implementation of PA catheters in CS leads to rapid diagnosis and identification of shock phenotype which can allow for early escalation of therapy. Once MCS is initiated, PA catheter hemodynamics determine the efficacy of the initially chosen form of MCS and the need for MCS escalation. Table 2 summarizes most common forms of percutaneous mechanical circulatory support.

Acute myocardial infarction

There is also data supporting invasive hemodynamic monitoring in acute myocardial infarction complicated by CS. The National Cardiogenic Shock Initiative demonstrated that adherence to a protocol-based approach emphasizing "best practices" including utilization of a PA catheter (92%

of patients had PA catheter monitoring) was associated with improved outcomes [10]. Similarly, in a retrospective registry of acute myocardial infarction complicated by CS treated with Impella, survival improved when a PA catheter was used (49% vs 63%, $p < 0.0001$) [31].

Right ventricular failure

Hemodynamic data provided by a PA catheter can help with early identification of univentricular vs biventricular failure in CS, thus guiding appropriate therapies. Masked right ventricular failure frequently complicates left ventricular failure, and availability of PA catheter data before device selection would alert the clinician to the potential need for early initiation of right ventricular MCS [11, 12, 32, 33].

Left ventricular unloading

Escalation of support can also be considered when the use of an initial support device results in unintended hemodynamic effects. It is now well recognized that LV distention and pulmonary edema can be deleterious consequences of venous-arterial extracorporeal membrane oxygenation. Routine use of LV unloading devices in venous-arterial extracorporeal membrane oxygenation is controversial, but recent evidence has emerged recommending its use [34]. Invasive hemodynamic monitoring can identify scenarios where LV unloading is needed (e.g., lack of arterial line pulsatility, elevated PCWP) by a continuous axial flow device.

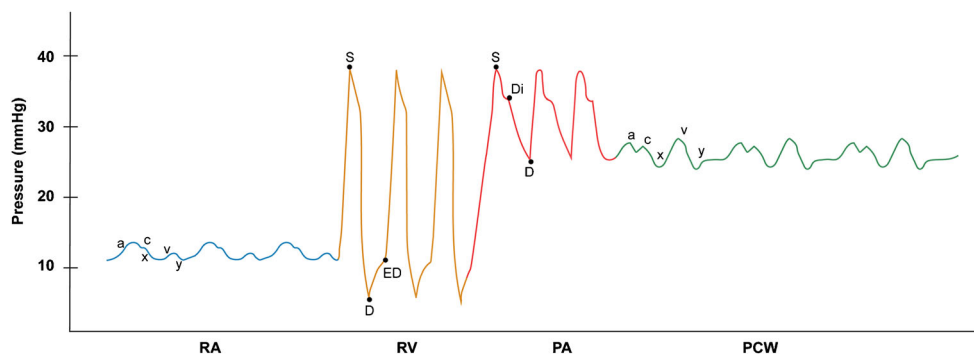## Systemic inflammatory response syndrome

The impact of systemic inflammatory response syndrome (SIRS) in CS is significant. In later stages of CS, a paradoxical vasodilatory phase of CS can occur due to SIRS secondary to endogenous cytokine release [35, 36]. Clinical SIRS as evidenced by fever, elevated white blood cell count, and low SVR was observed in many patients with confirmed CS complicating acute myocardial infarction in the randomized SHOCK trial and often led to a secondary clinical diagnosis of suspected sepsis. However, out of the 54 patients in the SIRS group, 14 were "culture-negative" and had no source of infection identified [37]. PA catheter utilization in this subset of CS patients is important to identify this "mixed picture," guide therapy, and avoid mismanagement in acute care of the critically ill patient.

Technical considerations and accurate interpretation

Adequately acquiring hemodynamic data from a PA catheter along with accurate interpretation is important for appropriate decision-making in CS, and clinical decision-making based on inaccurate information from PA catheters can have unfavorable outcomes (Fig. 1). Trottier and

Table 2. Comparison of common forms of percutaneous mechanical circulatory support

	IABP	Impella	Rt Protek Duo TandemHeart	Left sided TandemHeart	VA-ECMO
Pump mechanism	Aortic counter pulsation	Trans-aortic valve axial continuous flow	Centrifugal	Centrifugal	Centrifugal
Flow (up to)	0.5–1.0 L/min	CP: 3.5 L/min 5.0: 5.0 L/min 5.5: 6.0 L/min	>4 L/min	>4 L/min	>4 L/min
Catheter/Cannula size	8–9 Fr	CP: 13–14 Fr 5.0: 21–23 Fr 5.5: 21–23 Fr	29–31 Fr	21 Fr inflow; 15–19 Fr outflow	21–25 Fr inflow; 15–19 Fr outflow
Sheath/cannula location	Femoral artery Axillary artery	CP: femoral artery 5.0 and 5.5: femoral artery cutdown, axillary artery, transcaval	Single cannula dual lumen right internal jugular vein	Inflow cannula into LA via femoral vein and transseptal puncture Outflow cannula into femoral artery	Inflow cannula into the RA via femoral vein Outflow cannula into femoral artery
Oxygenator	No	No	w/wo	w/wo	Yes
Hemodynamics					
Ventricular support	LV	LV	RV	LV	BiV
Afterload	↓	↓	–	↑	↑↑↑
LVEDP	↓	↓	–	↓	↑
PCWP	↓	↓	–	↓	↑

Fig. 1. Normal pulmonary artery catheter pressure waveform tracing. RA (blue waveform): "a" atrial systole/contraction, "c" closure of tricuspid valve, "x" atrial relaxation, "v" ventricular systole/contraction (and atrial diastole), "y" passive filling of RV. RV (yellow waveform): "S" systole, "D" diastole, "ED" end diastole. PA (red waveform): "S" systole, "D" diastole, "Di" dicrotic notch, mean PA pressure is PAS + (PAD × 2) / 3. PCW (green waveform): "a" atrial contraction, "v" ventricular contraction, mean PCW pressure is mean of "a" descent. RA, right atrium; RV, right ventricle; PA, pulmonary artery; PCW, pulmonary capillary artery wedge.
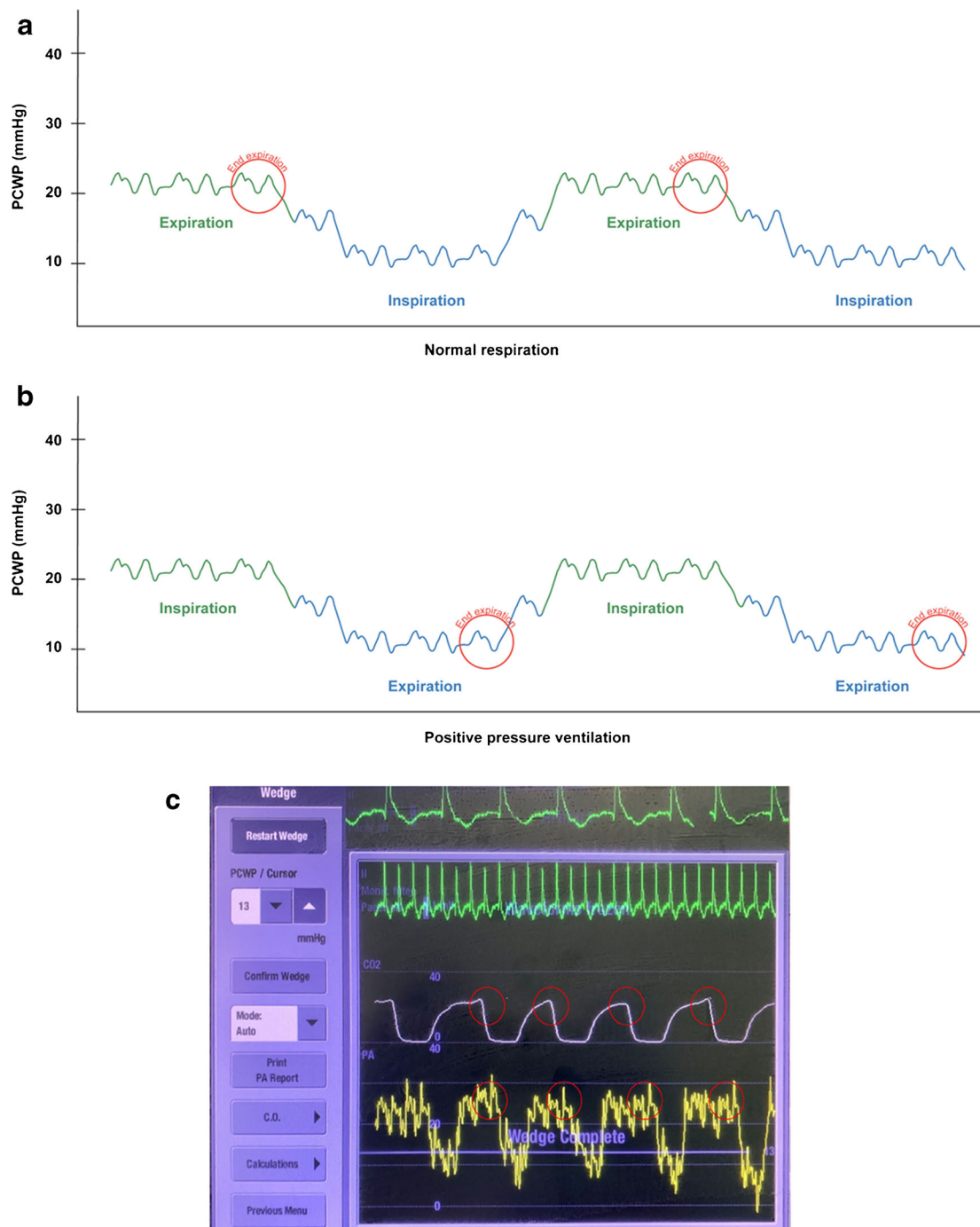
Fig. 2. Pulmonary capillary wedge pressure tracings during different modes of respiration during **a** normal respiration: PCWP measured at end expiration; **b** PVV: in a typical patient under mechanical ventilation, positive-pressure ventilation increases intrathoracic pressures. Usual hemodynamic tracings during positive-pressure ventilation rise during inhalation and fall during exhalation, and typical PCWP measurements are made in the troughs of the respiratory cycle. **c** PVV: note here that there is more significant negative intrathoracic pressure generated by the patient's respiratory muscles (Pmus) compared to the contribution from the ventilator positive pressure (Pvent). As a result, the PCWP tracing at end-tidal CO_2, which signifies end expiration (top right of the shark fin), is measured similarly in this ventilated patient as it would be in a spontaneously breathing patient just prior to the onset of the negative waveform deflection. Red circles indicate end expiration. Therefore, the accurate measurement of pulmonary wedge pressure is ~30. PCWP, pulmonary capillary wedge pressure; PVV, positive-pressure ventilation.

Table 3. Pulmonary artery catheter-derived hemodynamic parameters

Hemodynamic parameter	Formula (if present)	Normal range (unit)	Commonly used prognostic cut-offs in the current era
MAP Mean arterial pressure	SBP + (DBP × 2) / 3	65–105 mmHg	SBP <100 mmHg [48] SBP <90 mmHg [5], [7, p.], [44]
RAP (mean) Right atrial pressure	Direct measurement	2–6 mmHg	–
PAP (mean) Pulmonary artery pressure	PAS + (PAD × 2) / 3	9–18 mmHg	–
PCWP (mean) Pulmonary capillary artery pressure	Direct measurement	6–12 mmHg	–
SVO_2 Mixed venous O_2 saturation	Direct measurement	60–80%	–
CO Cardiac output	Thermo or FICK	4–8 L/min	–
CI Cardiac index	CO / BSA	2.5–4.0 L/min/m^2	–
SVR* Systemic vascular resistance	(MAP – mRAP) / CO	9–20 Wood (800–1200 dyne.s.cm^{-5})	–
PVR* Pulmonary vascular resistance	(mPAP – PCWP) / CO	0.25–1.5 Wood (<250 dyne.s.cm^{-5})	>2.5 increased mortality post-heart transplant [49]
TPG Transpulmonary gradient	mPAP – PCWP	<12 mmHg	>12 increased mortality post-heart transplant [50]
DPG Diastolic pulmonary gradient	PAD – PCWP	<7 mmHg	≥7 mmHg worse survival in pulmonary hypertension [51]
LVSWI Left ventricular stroke work index	(MAP – PCWP) × (CI / HR) Or (MAP – PCWP) × SVI × 0.0136	2.4–4.2 mmHg.L/M^2 Or 50–62 g/m^2/beat	–
RVSWI Right ventricular stroke work index	(mPAP – RAP) × (CI / HR) Or (mPAP – RAP) × SVI × 0.0136	0.10–0.25 mmHg.L/M^2 Or 5–10 g/m^2/beat	–
CPO Cardiac power output	MAP – CO / 451	>1 W	<0.6 [9, 10]
PAPi Pulmonary artery pulsatility index	(PAS – PAD) / CVP	>2.0	<1.85 in LVAD had 94% sensitivity and 81% specificity for identifying RVF [11] <1.0 in AMI had 100% sensitivity and 98% specificity for predicting in-hospital mortality and/or requirement of a percutaneous RV support device [12]
RAP/PCWP ratio	RAP/PCWP	<0.6	>0.86 RVF in AMI [52] >0.63 RVF after LVAD [53]

AMI acute myocardial infarction, *BSA* body surface area, *DBP* systemic diastolic blood pressure, *LVAD* durable left ventricular assist device, *PAD* diastolic pulmonary artery pressure, *PAS* systolic pulmonary artery pressure, *RVF* right ventricular failure, *SBP* systemic systolic blood pressure, *SVI* stroke volume index
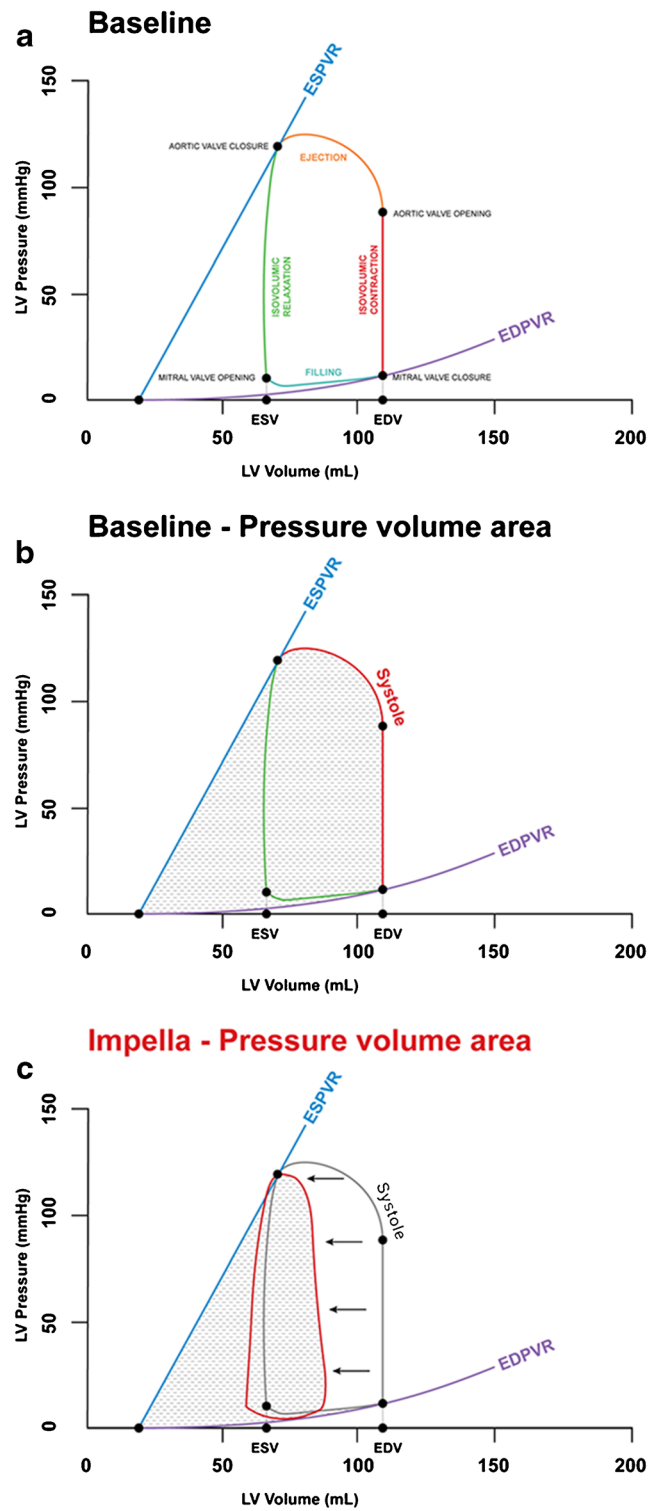
Fig. 3. Pressure volume loop of left ventricle: **a** normal PVL, **b** normal PVL with PVA highlighted in gray, **c** impact of Impella on PVA. PVA, pressure volume area; PVL, pressure volume loop.

Taylor found that one-third of critical care physicians participating in a study incorrectly identified PCWP tracings [38]. Detailed attention to several factors when performing a right heart catheterization is required. In a prospective study, a standard-of-care clinical protocol was instituted where if PCWP saturation suggested incomplete occlusion (i.e., < 90% or not within 5% of systemic arterial saturation), up to 2 additional attempts are made to obtain an occlusive PCWP saturation. Utilization of this protocol resulted in significantly lower PCWP, higher PVR, and clinically relevant pulmonary hypertension reclassification of 11.8% of patients [39••]. A systematic approach to PA catheter insertion and waveform measurement is essential [40]. The pressure transducer should be zeroed to atmospheric pressure at the level of the left atrium (usually located in the midthorax level). The pressure tracing quality should be examined. Any signs of signal dampening should be investigated and corrected. All measurements should be made at end expiration, irrespective of the mode of ventilation (Fig. 2a). During normal spontaneous ventilation (negative pressure), all pressures should be measured at the peak of the waveform. However, measurements during positive-pressure ventilation should be made at the troughs of the respiratory cycle ("end of the valley") (Fig. 2b). However, there are certain scenarios where mechanically ventilated patients can still generate negative-pressure ventilation which could be misleading when measuring PCWP. Waveform capnography and end-tidal CO_2 monitoring can be useful adjuncts to accurate hemodynamic monitoring in mechanically ventilated patients (Fig. 2c). Additionally, under the conditions of labored respiration or wide respiration variation, the best signal quality may be obtained by measurements during controlled respiration and selection of hemodynamic monitor signal averaging routines [41••]. Different hemodynamic parameters obtained from the PA catheter are summarized in Table 3.

Future considerations

The modern era has seen substantial progress in defining different hemodynamic parameters and modules to aid in the diagnosis, prognosis, and treatment of cardiopulmonary disease. While the PA catheter remains the cornerstone of invasive hemodynamic monitoring in current clinical practice, the introduction of the left ventricular conductance catheter and subsequently derived left ventricular pressure-volume loop (PVL) by Baan et al. in 1984 is increasingly being studied to evaluate hemodynamics of MCS [42]. Left ventricular conductance catheters measure instantaneous conductance in the left ventricle, which is then converted to ventricular blood volume using complex formulas. More recently, non-invasive PVL methods have been evaluated in vivo and have shown to be feasible in patients with a durable left ventricular assist device [43]. Under normal conditions, the PVL is roughly trapezoidal. The 4 sides of the loop represent phases of the cardiac cycle: (1) isovolumic contraction; (2) ejection; (3) isovolumic relaxation; and (4) filling (Fig. 3a). The shape of the loop depends on ventricular preload and afterload. Although PVL utilization in current clinical practice is limited, PVL-derived data can be additive to PA catheter hemodynamics in an increasingly complex subset of CS patients requiring temporary MCS.

PVLs can be useful for demonstrating the hemodynamics of different MCS devices and confirming favorable hemodynamic impact. Left ventricular unloading reduces myocardial oxygen demand, optimizes myocardial energetics, and may facilitate myocardial recovery. Left ventricular pressure–volume area provides the strongest index of myocardial oxygen consumption (Fig. 3b). It is equivalent to the total mechanical energy performed by the heart on each beat and is represented on the PVL by the area bounded by the end-systolic and end-diastolic pressure–volume relationship curves and the systolic portion of the pressure–volume curve. Direct LV unloading with a continuous axial flow pump leads to reduction of the pressure–volume area due to a reduction in end-diastolic volume and end-diastolic pressure (preload) (Fig. 3c). It also contributed to the overall reduction of the pressure–volume area since the isovolumic periods of ejection and relaxation no longer exist due to continuous pumping of volume from the left ventricle to the aorta [43].

Conclusion

There is no demonstrated mortality benefit in applying PA catheters routinely to heterogeneous populations of critically ill patients or all

patients with acute decompensated heart failure. However, in current clinical practice and moving forward, PA catheters should be utilized in the evaluation and management of cardiogenic shock and temporary MCS. Invasive hemodynamics are critical for diagnosis and treatment of this subset of patients with cardiopulmonary disease.

Declarations

Conflict of interest
Iyad N. Isseh, Ran Lee, Rola Khedraki, and Karlee Hoffman declare that they have no conflict of interest.

Relationships with industry and other entities
All authors report no disclosures.

Human and animal rights
All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

1. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970;283(9):447–51. https://doi.org/10.1056/NEJM197008272830902.

2. Swan HJ, Raja SN. The pulmonary artery catheter in anesthesia practice. Anesthesiology. 2005;103(4):890–3. https://doi.org/10.1097/00000542-200510000-00029.

3. Binanay C, Califf RM, Hasselblad V, O'Connor CM, Shah MR, Sopko G, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. JAMA. 2005;294(13):1625–33. https://doi.org/10.1001/jama.294.13.1625.

4. Hollenberg SM, Kavinsky CJ, Parrillo JE. Cardiogenic shock. Ann Intern Med. 1999;131(1):47–59. https://doi.org/10.7326/0003-4819-131-1-199907060-00010.

5. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, 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(9):625–34. https://doi.org/10.1056/NEJM199908263410901.

6. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med. 2012;367(14):1287–96. https://doi.org/10.1056/NEJMoa1208410.

7. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet. 2013;382(9905):1638–45. https://doi.org/10.1016/S0140-6736(13)61783-3.

8. van Diepen S, et al. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. Circulation. 2017;136(16):e232–68. https://doi.org/10.1161/CIR.0000000000000525.

9. Fincke R, Hochman JS, Lowe AM, Menon V, Slater JN, Webb JG, et al. 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(2):340–8. https://doi.org/10.1016/j.jacc.2004.03.060.

10. Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A, et al. Improved outcomes associated with the use of shock protocols: updates from the National

Cardiogenic Shock Initiative. Catheter Cardiovasc Interv. 2019;93(7):1173–83. https://doi.org/10.1002/ccd.28307.

11. 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(2):110–6. https://doi.org/10.1016/j.cardfail.2015.10.019.

12. Korabathina R, Heffernan KS, Paruchuri V, Patel AR, Mudd JO, Prutkin JM, et al. The pulmonary artery pulsatility index identifies severe right ventricular dysfunction in acute inferior myocardial infarction. Catheter Cardiovasc Interv. 2012;80(4):593–600. https://doi.org/10.1002/ccd.23309.

13.•• Baran DA, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock. Catheter Cardiovasc Interv. 2019;94(1):29–37. https://doi.org/10.1002/ccd.28329.

Most recent SCAI classification of cardiogenic shock

14. Jentzer JC, et al. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. *J Am Coll Cardiol*. 2019;74(17):2117–28. https://doi.org/10.1016/j.jacc.2019.07.077.

15. Baran DA, Long A, Badiye AP, Stelling K. Prospective validation of the SCAI shock classification: single center analysis. Catheter Cardiovasc Interv. 2020;96(7):1339–47. https://doi.org/10.1002/ccd.29319.

16. Tehrani BN, Truesdell AG, Psotka MA, Rosner C, Singh R, Sinha SS, et al. A standardized and comprehensive approach to the management of cardiogenic shock. JACC: Heart Failure. 2020;8(11):879–91. https://doi.org/10.1016/j.jchf.2020.09.005.

17. Connors AF, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT investigators. JAMA. 1996;276(11):889–97. https://doi.org/10.1001/jama.276.11.889.

18. Ikuta K, Wang Y, Robinson A, Ahmad T, Krumholz HM, Desai NR. National trends in use and outcomes of pulmonary artery catheters among Medicare beneficiaries, 1999–2013. *JAMA Cardiol*. 2017;2(8):908–13. https://doi.org/10.1001/jamacardio.2017.1670.

19. Rajaram SS, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev*. 2013;2:CD003408. https://doi.org/10.1002/14651858.CD003408.pub3.

20. Harvey S, Harrison DA, Singer M, Ashcroft J, Jones CM, Elbourne D, et al. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. Lancet. 2005;366(9484):472–7. https://doi.org/10.1016/S0140-6736(05)67061-4.

21. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey de Jr, Drazner MH, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;62(16):e147–239. https://doi.org/10.1016/j.jacc.2013.05.019.

22. Hernandez GA, Lemor A, Blumer V, Rueda CA, Zalawadiya S, Stevenson LW, et al. Trends in utilization and outcomes of pulmonary artery catheterization in heart failure with and without cardiogenic shock. J Card Fail. 2019;25(5):364–71. https://doi.org/10.1016/j.cardfail.2019.03.004.

23. Nalluri N, Patel NJ, Atti V, Kumar V, Basir MB, O'Neill WW. Temporal trends in utilization of right-sided heart catheterization among percutaneous ventricular assist device recipients in acute myocardial infarction complicated by cardiogenic shock. *Am J Cardiol*. 2018;122(12):2014–7. https://doi.org/10.1016/j.amjcard.2018.08.065.

24.•• Reshad GA, et al. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. JACC: Heart Failure. 2020;8(11):903–13. https://doi.org/10.1016/j.jchf.2020.08.012.

Most recent publication showing benefit for PA catheters in cardiogenic shock

25. Berg DD, Barnett CF, Kenigsberg BB, Papolos A, Alviar CL, Baird-Zars VM, et al. Clinical practice patterns in temporary mechanical circulatory support for shock in the critical care cardiology trials network (CCCTN) registry. Circ Heart Fail. 2019;12(11):e006635. https://doi.org/10.1161/CIRCHEARTFAILURE.119.006635.

26. Antonelli M, Levy M, Andrews PJD, Chastre J, Hudson LD, Manthous C, et al. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France, 27-28 April 2006. Intensive Care Med. 2007;33(4):575–90. https://doi.org/10.1007/s00134-007-0531-4.

27. Dellinger RP, et al. Surviving Sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165–228. https://doi.org/10.1007/s00134-012-2769-8.

28. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, et al. The 2013 International Society for Heart and Lung Transplantation guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant. 2013;32(2):157–87. https://doi.org/10.1016/j.healun.2012.09.013.

29. Sorajja P, Borlaug BA, Dimas VV, Fang JC, Forfia PR, Givertz MM, et al. 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(7):E233–47. https://doi.org/10.1002/ccd.26888.

30. Basir MB, Schreiber TL, Grines CL, Dixon SR, Moses JW, Maini BS, et al. Effect of early initiation of mechanical circulatory support on survival in cardiogenic shock. Am J Cardiol. 2017;119(6):845–51. https://doi.org/10.1016/j.amjcard.2016.11.037.

31.   O'Neill WW, et al. Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device. Am Heart J. 2018;202:33–8. https://doi.org/10.1016/j.ahj. 2018.03.024.

32.   Lala A, Guo Y, Xu J, Esposito M, Morine K, Karas R, et al. Right ventricular dysfunction in acute myocardial infarction complicated by cardiogenic shock: a hemo-dynamic analysis of the should we emergently revascularize occluded coronaries for cardiogenic SHOCK (SHOCK) trial and registry. J Card Fail. 2018;24(3):148–56. https://doi.org/10.1016/j. cardfail.2017.10.009.

33.   Jacobs AK, Leopold JA, Bates E, Mendes LA, Sleeper LA, White H, et al. Cardiogenic shock caused by right ven-tricular infarction: a report from the SHOCK registry. J Am Coll Cardiol. 2003;41(8):1273–9. https://doi.org/ 10.1016/s0735-1097(03)00120-7.

34.   Benedikt S, et al. Left ventricular unloading is associ-ated with lower mortality in patients with cardiogenic shock treated with venoarterial extracorporeal mem-brane oxygenation. Circulation. 2020;142(22):2095–106. https://doi.org/10.1161/CIRCULATIONAHA. 120.048792.

35.   Millar JE, Fanning JP, McDonald CI, McAuley DF, Fra-ser JF. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. *Crit Care*. 2016;20(1):387. https:// doi.org/10.1186/s13054-016-1570-4.

36.   Cuinet J, Garbagnati A, Rusca M, Yerly P, Schneider AG, Kirsch M, et al. Cardiogenic shock elicits acute inflam-mation, delayed eosinophilia, and depletion of im-mune cells in most severe cases. *Scientific Reports*. 2020;10(1):7639. https://doi.org/10.1038/s41598-020-64702-0.

37.   S. Kohsaka, Systemic inflammatory response syn-drome after acute myocardial infarction complicated by cardiogenic shock, *Arch Intern Med*, vol. 165, no. 14, p. 1643, 2005, doi: https://doi.org/10.1001/archinte. 165.14.1643.

38.   Trottier SJ, Taylor RW. Physicians' attitudes toward and knowledge of the pulmonary artery catheter: Society of Critical Care Medicine membership survey. New Horiz. Aug. 1997;5(3):201–6.

39.•• Viray Michael C. *et al.*, Role of pulmonary artery wedge pressure saturation during right heart catheterization, *Circulation: Heart Failure*, vol. 13, no. 11, p. e007981, Nov. 2020, doi: https://doi.org/10.1161/ CIRCHEARTFAILURE.120.007981.

Accuracy of right heart catheterization using pulmonary wedge saturation

40.   E. L. Bonno, M. C. Viray, G. R. Jackson, B. A. Houston, and R. J. Tedford, Modern right heart catheterization: beyond simple hemodynamics, *Advances in Pulmonary Hypertension*, vol. 19, no. 1, pp. 6–15, Jun. 2020, doi: https://doi.org/10.21693/1933-088X-19.1.6.

41.•• Abhinav S, et al. Value of hemodynamic monitoring in patients with cardiogenic shock undergoing mechani-cal circulatory support. Circulation. 2020;141(14):1184–97. https://doi.org/10.1161/ CIRCULATIONAHA.119.043080.

Support of PA catheter use in cardiogenic shock and mechanical support.

42.   Baan J, van der Velde ET, de Bruin HG, Smeenk GJ, Koops J, van Dijk AD, et al. Continuous measurement of left ventricular volume in animals and humans by conductance catheter. Circulation. Nov. 1984;70(5):812–23. https://doi.org/10.1161/01. CIR.70.5.812.

43.   Jain Pankaj *et al.*, Insights into myocardial oxygen consumption, energetics, and efficiency under left ventricular assist device support using noninvasive pressure-volume loops, *Circulation: Heart Failure*, vol. 12, no. 10, p. e006191, 2019, doi: https://doi.org/10. 1161/CIRCHEARTFAILURE.119.006191.

44.   H. Thiele *et al.*, PCI strategies in patients with acute myocardial infarction and cardiogenic shock, *N Engl J Med*, vol. 377, no. 25, pp. 2419–2432, 21 2017, doi: https://doi.org/10.1056/NEJMoa1710261.

45.   Kirklin JK, Naftel DC, Stevenson LW, Kormos RL, Pagani FD, Miller MA, et al. INTERMACS database for durable devices for circulatory support: first annual report. J Heart Lung Transplant. 2008;27(10):1065–72. https://doi.org/10.1016/j.healun.2008.07.021.

46.   A. Banning *et al.*, The EURO SHOCK Trial: design, aims and objectives randomised comparison of extra cor-poreal membrane oxygenation (ECMO) delivered after acute-PCI plus standard of care versus standard of care alone after acute PCI, in patients presenting with Acute Coronary syndrome and Cardiogenic Shock. *EuroIntervention*. https://eurointervention.pcronline. com/article/the-euro-shock-trial-design-aims-and-objectivesrandomised-comparison-of-extra-corporeal-membrane-oxygenation-ecmo-delivered-after-acute-pci-plus-standard-of-care-versus-standard-of-care-alone-after-acute-pci-in-patients-presenting-with-acute-coronary-syndrome-and-cardiogenic-shock. Accessed 10 Jan 2021.

47.   Udesen NJ, Møller JE, Lindholm MG, Eiskjær H, Schäfer A, Werner N, et al. Rationale and design of DanGer shock: Danish-German cardiogenic shock tri-al. Am Heart J. 2019;214:60–8. https://doi.org/10. 1016/j.ahj.2019.04.019.

48.   Katz JN, Stebbins AL, Alexander JH, Reynolds HR, Pieper KS, Ruzyllo W, et al. Predictors of 30-day mor-tality in patients with refractory cardiogenic shock fol-lowing acute myocardial infarction despite a patent infarct artery. Am Heart J. Oct. 2009;158(4):680–7. https://doi.org/10.1016/j.ahj.2009.08.005.

49.   Costard-Jäckle A, Fowler MB. Influence of preoperative pulmonary artery pressure on mortality after heart transplantation: testing of potential reversibility of pulmonary hypertension with nitroprusside is useful

in defining a high risk group. J Am Coll Cardiol. 1992;19(1):48–54. https://doi.org/10.1016/0735-1097(92)90050-w.

50.   Erickson KW, Costanzo-Nordin MR, O'Sullivan EJ, Johnson MR, Zucker MJ, Pifarré R, et al. Influence of preoperative transpulmonary gradient on late mortality after orthotopic heart transplantation. J Heart Transplant. Oct. 1990;9(5):526–37.

51.   Gerges C, Gerges M, Lang MB, Zhang Y, Jakowitsch J, Probst P, et al. Diastolic pulmonary vascular pressure gradient: a predictor of prognosis in 'out-of-proportion' pulmonary hypertension. Chest. 2013;143(3):758–66. https://doi.org/10.1378/chest.12-1653.

52.   Lopez-Sendon J, Coma-Canella I, Gamallo C. Sensitivity and specificity of hemodynamic criteria in the diagnosis of acute right ventricular infarction.

Circulation. 1981;64(3):515–25. https://doi.org/10.1161/01.cir.64.3.515.

53.   Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. J Thorac Cardiovasc Surg. 2010;139(5):1316–24. https://doi.org/10.1016/j.jtcvs.2009.11.020.

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