

Cardiogenic Shock in Patients with Advanced Chronic Heart Failure

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ABSTRACT: Patients with end-stage heart failure (HF) who have failed optimal medical therapy provide a unique set of challenges compared to the more prevalent population of patients with cardiogenic shock (CS) due to ST-segment elevation myocardial infarction. Progression from “preshock” into a refractory state of CS is associated with a dismal outcome due to difficulties with the patient’s recognition, response to interventions, and candidacy for salvage options. Challenges include heterogeneity of CS (eg, different phenotypes, etiologies, duration, acuity of onset, hemodynamics, end-organ effects), lack of a universal definition of CS that is applicable to this patient population, and blunted hemodynamic response given the patient’s prolonged compensatory state. Individuals with advanced HF in CS require a multidisciplinary team-based assessment regarding when to escalate from medical therapy into temporary mechanical circulatory support, and they need an eligibility evaluation to determine their candidacy for advanced therapy. In this review, we discuss the definition and clinical phenotypes of CS, classification of CS in advanced HF patients, the utility of temporary mechanical circulatory support, and the role of the CS team.

INTRODUCTION

Individuals with advanced heart failure (HF) belong to a subset of patients who have chronic HF with New York Heart Association functional classification III or IV and a higher risk of mortality that will continue despite maximal guideline-directed medical therapy. Patients in this group must be considered for advanced treatment strategies, such as mechanical circulatory support (MCS), continuous inotropic infusions, cardiac transplantation, or end-of-life care. The 2013 American College of Cardiology/American Heart Association (ACCF/AHA) Guidelines Classification for management of heart failure classifies this group of patients as having stage D HF, which they also term “refractory HF,” “end-stage HF,” and “advanced HF.”¹

DEFINITION OF CARDIOGENIC SHOCK

A small subset of patients with advanced HF will enter into cardiogenic shock (CS), defined as systemic tissue hypoperfusion secondary to inadequate cardiac output despite adequate intravascular volume and filling pressures. In the CardShock study, 11% of 269 patients developed CS due to worsening chronic HF.²

Classic CS is characterized by the presence of both clinical and hemodynamic criteria. The 2015 Society for Cardiovascular Angiography and Interventions (SCAI)/American College of Cardiology/Heart Failure Society of America/Society of Thoracic Surgeons Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices

defined CS by the presence of persistent hypotension with hemodynamic evidence of hypoperfusion and adequate left ventricular filling pressures. Hypotension is defined as either systolic blood pressure (SBP) ≤ 90 mm Hg for at least 30 minutes or the need for supportive measures to maintain an SBP ≥ 90 mm Hg, or a drop in mean arterial blood pressure (MAP) > 30 mm Hg below the baseline. Hemodynamic criteria include severe reduced cardiac output (ie, cardiac index ≤ 1.8 L/min/m² without support or < 2.2 L/min/m² with support) and pulmonary capillary wedge pressure (PCWP) ≥ 15 mm Hg.³

Other definitions of CS in clinical practice guidelines include definitions used in the SHOCK and IABP-SHOCK II trials.⁴ However, these definitions are less useful in the patient with chronic HF who goes into CS due to their prolonged compensatory state. These patients are typically poorly represented in CS trials, with the focus shifting instead to the STEMI patient population. Importantly, CS in end-stage HF is not a binary diagnosis but rather a continuum that ranges from HF exacerbation with hemodynamic derangements (ie, a “preshock” state) to refractory CS associated with multiorgan failure and a high mortality rate.

CLINICAL PHENOTYPES OF CARDIOGENIC SHOCK AND UTILITY OF INVASIVE HEMODYNAMIC MONITORING

On the spectrum of illness, CS is the most severe expression of HF. It occurs in the setting of myocardial dysfunction

preceded by ischemic or nonischemic disturbance in myocardial contractility. This leads to poor tissue perfusion and ultimately to multiorgan failure. Ischemic etiologies are the leading cause of CS in advanced HF. Yet many patients with chronic HF can suddenly and inexplicably “fall off the cliff” into CS.

Individuals with classic “cold and wet” CS phenotype may have clinical evidence of both fluid overload and hypoperfusion and may look unwell, agitated, or panicked; they may also experience an acute change in sensorium. Cold, clammy, and mottled skin or urine output < 30 cc/hr may represent a lack of systemic circulation. Extensive rales, elevated jugular venous pressure, and/or hepatojugular reflux and peripheral edema, if present, may reflect the presence of elevated cardiac filling pressures and hypervolemia. However, the patient with chronic HF will typically have no rales due to compensatory pulmonary dilation and intraparenchymal adaptation to chronically elevated filling pressures. Instead, they often present with more vague complaints such as nausea and vomiting or rapid recent weight loss. Markers of reduced end-organ perfusion, such as elevated transaminases, bilirubin, blood urea, creatinine, and lactic acidosis, may be present and aid in the diagnosis of CS. Again, many of these lab values are already altered at baseline due to chronic renal insufficiency and persistent hyperbilirubinemia. Knowing these values is crucial to assessing acuity and severity in these patients.

Although the phenotypical “cold and wet” CS is associated with a low cardiac index and high systemic vascular resistance and PCWP, there are actually four different hemodynamic phenotypes of CS; however, they are difficult to determine without invasive hemodynamic monitoring, and the patient may move from one category to another (Table 1).⁵ Two other types of CS with a low prevalence are normotensive shock and right ventricular shock. Patients with normotensive shock represent approximately 5% of cases in the SHOCK trial registry and have an SBP > 90 mm Hg due to supranormal systemic vascular

resistance and a low cardiac index. Right ventricular (RV) shock is present in approximately 5% of patients with post-MI CS, but in patients with advanced chronic HF, baseline RV dysfunction can cloud the picture. The creation and utilization of newer hemodynamic criteria—such as right atrial pressure/PCWP ≥ 0.8, pulmonary artery pulsatility index < 1.85, and RV stroke work index < 600 mm Hg x mL/m²—are useful to confirm RV dysfunction in patients with advanced HF. Determination of the cardiac power output is a more sophisticated parameter for assessing LV function, especially in those with acute on chronic HF. These data are crucial for patients with acute and chronic HF and confirms the need for hemodynamic monitoring.

CLASSIFICATION OF CARIOGENIC SHOCK

To better understand the hemodynamic stability of patients with chronic stage D HF who are failing medical therapy, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) developed a classification system that stratifies patients according to severity of illness and, based on elevated morbidity and mortality risk, predicts who will benefit from expedited temporary MCS (tMCS).⁶ Patients are grouped into one of seven “severity” profiles ranging from advanced NYHA III (category 7) to critical CS (category 1), the “crash and burn” stage characterized by life-threatening hypotension refractory to vasoactive medications (Table 2).⁶ There are also three modifiers to enhance the profile descriptions, including the need for temporary MCS and/or frequent hospitalizations as well as recurrent arrhythmias.

Although the INTERMACS profiles categorize patients based on the severity of stage D HF, it does not distinguish an INTERMACS 1 patient supported on the intra-aortic balloon pump (IABP) or venoarterial extracorporeal membrane oxygenation (VA-ECMO), nor does it add a factor such as cardiac arrest status post-resuscitation or fatal arrhythmias

		VOLUME STATUS	
		WET	DRY
PERIPHERAL PERFUSION STATUS	Cold	Classic CS (“Cold & Wet”) High SVR, low CI, high PCWP	Euvolemic CS (“Cold & Dry”) High SVR, low CI, low/normal PCWP
	Warm	Mixed CS (“Warm & Wet”) Normal SVR, low CI, high PCWP	Vasodilatory Shock (no CS) Low SVR, high CI, low PCWP

Table 1.

Clinical phenotypes in cardiogenic shock. Adapted from van Diepen et al.⁵ CS: cardiogenic shock; SVR: systemic vascular resistance; CI: cardiac index; PCWP: pulmonary capillary wedge pressure

PROFILE	TITLE	TAG NAME	DESCRIPTION
1 ^{#*}	Critical cardiogenic shock	“Crash and burn”	Life-threatening hypotension refractory to IV inotropes
2 ^{#*}	Progressive decline	“Sliding on inotropes”	IV inotropes required with worsening end-organ function
3 ^{#*}	Inotrope dependent	“Dependent stability”	Stable blood pressure and end-organ function but failure to wean from IV inotropes
4 ^{#§}	Resting symptoms - home on oral therapy		Daily symptoms of congestion at rest or with ADLs and high doses of diuretics
5 ^{#§}	Exertion intolerant		Unable to engage in any activity above ADLs
6 ^{#§}	Exertion limited	“Walking wounded”	Can participate in minor activities but quickly fatigued
7 [*]	Advanced NYHA III		Comfortable with meaningful activity but limited to mild exertion

Modifiers:

temporary circulatory support

* arrhythmia

§ frequent flyer

Table 2.

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile. Adapted from Stevenson et al.⁶ IV: intravenous; ADLs: activities of daily living

requiring defibrillation. The SCAI has published a clinical expert consensus statement on the classification of cardiogenic shock that stratifies patients in five stages (stages A thru E) plus a cardiac arrest modifier (Table 3).⁷ This could provide the first step in establishing a common language to study this patient population and determine best care practices going forward. The stages in the stratification scheme provide a better description of hemodynamic status with or without a particular corresponding therapy or mechanical circulatory support. This will allow the clinician to further distinguish among patients who would otherwise be grouped into similar INTERMACS profiles.

TEMPORARY MECHANICAL SUPPORT IN ADVANCED HEART FAILURE

Escalation of CS while on maximal inotropic therapy and delaying tMCS implantation has been associated with a rapid increase in mortality in patients with profound CS. Samuels et al. showed that inpatient mortality rose from 21% to 42% to 80% when patients received single high-dose, two high-dose, and three high-dose inotropes after cardiotomy.⁸ Patients with acute or chronic HF are also less likely to improve with conventional medical interventions alone and no tMCS support since their limited cardiac reserve makes them less responsive to inotropes compared to the STEMI patient population.

Over the past 15 years, however, the use of tMCS has increased rapidly in the treatment of patients with refractory CS.⁹ There are currently four types of tMCS devices available for hemodynamic support: the IABP, the TandemHeart percutaneous ventricular assist device (LivaNova), the Impella pumps (Abiomed, Inc), and the centrifugally driven VA-ECMO.¹⁰ Although the recent increased use of tMCS has been associated with a reduction in inpatient mortality rates, this treatment may pose challenges for the patient with acute or chronic HF. Unlike STEMI, these patients usually have many more comorbidities and varying stages of renal dysfunction. They are often not a candidate for advanced therapies and, unlike someone with acute STEMI, have no quick intervention that could promote recovery. Thus, the use of tMCS in these patients requires more thoughtful consideration of the end goal after stabilization.

As a general rule, it is preferable to use axillary tMCS devices because they enable patient mobility and a more stable and durable device position for prolonged hemodynamic support. Axillary arterial IABP and Impella 5.0 (and the new 5.5 pumps) have been used as mechanical hemodynamic support for bridging patients to either an LV assist device (LVAD) or heart transplant with excellent outcomes. Estep et al. demonstrated

STAGE/NAME	DESCRIPTION
A "At Risk"	Patient is not currently experiencing signs or symptoms of CS but is at risk (ie, MI, CHF)
B "Beginning CS"	Patient has clinical evidence of relative hypotension without hypoperfusion
C "Classic CS"	Patient manifests with hypoperfusion that requires intervention (inotrope/pressor or MCS) beyond volume resuscitation to restore perfusion
D "Deteriorating/Doom"	Patient is similar to category C but is getting worse and failing to respond to initial interventions
E "Extremis"	Patient has circulatory collapse, frequent refractory cardiac arrest with ongoing CPR, or is being supported by multiple simultaneous acute interventions including ECPR

Modifier A: cardiac arrest—the presence of cardiac arrest, at any stage, would be considered a subtype (ie, B_A, C_A, D_A, E_A)

Table 3.

The Society for Cardiovascular Angiography and Interventions classification of cardiogenic shock. Adapted from Baran et al.⁷ CS: cardiogenic shock; MI: myocardial infarction; CHF: congestive heart failure; MCS: mechanical circulatory support; CPR: cardiopulmonary resuscitation; ECPR: extracorporeal membrane oxygenation-facilitated CPR

this with left axillary IABP in patients with end-stage HF; these patients had a cumulative survival of 92% and a post-transplant 90-day survival of 90% with high tolerability and a low rate of complications.¹¹ In patients with refractory CS and hemodynamic instability who could benefit from LV unloading, the axillary Impella 5.0 pumps could both fully unload the left heart and increase cardiac output, thereby providing better hemodynamic support. A multicenter study by Hall et al. demonstrated that 67% of patients with end-stage HF who received the Impella 5.0 pump support were successfully bridged to either an LVAD or heart transplant; the 1-year survival was 65% for those receiving durable MCS, 75% for those post-LVAD, and 87% for those who received transplantation.¹² The new-generation Impella 5.5 pump, FDA-approved in September 2019 for management of CS for up to 14 days, provides approximately 6 L/min cardiac output support. The improved cannula design appears to provide better flexibility and position stability when implanted via axillary artery and has a lower hemolysis rate.

If a patient is not a candidate for advanced therapies, careful consideration of "limited" interventions is needed to avoid futility and further escalation of health care costs.

ROLE OF THE CARDIOGENIC SHOCK TEAM

Patients with CS require a standardized comprehensive assessment from a multidisciplinary team that can evaluate hemodynamic and functional status and make timely,

streamlined decisions that optimize treatment and, potentially, outcomes. Ideally, the CS shock team includes an interventional cardiologist, advanced HF and transplant cardiologist with experience in MCS management, cardiothoracic surgeon, critical care physician, and specialists in ECMO perfusion, nursing, nutrition and rehabilitation who are knowledgeable in the trajectory of CS and the multiple advance treatment options for patients in various stages of CS.¹³

The goal of the shock team is to make time-sensitive decisions about the most appropriate interventions depending on the patient's status, from the escalation of vasoactive drugs to short-term tMCS in the acute shock phase. Equally important is the simultaneous assessment of eligibility for advanced therapies such as heart transplantation or durable MCS based on an exhaustive search of contraindications, including significant psychosocial barriers or the presence of other life-threatening conditions (eg, metastatic cancer, irreversible multiorgan failure) that would preclude candidacy.¹⁴ Although stabilizing the patient is of primary importance, assessment for advanced therapies (eg, evaluating social support, history of compliance, contraindications, diabetes) may occur in parallel.

CONCLUSIONS

Cardiogenic shock in patients with advanced heart failure remains a challenging condition to manage given its heterogeneity, lack of a universal definition, blunted hemodynamic response, and lack of an immediate resolution

compared to patients with STEMI. With little data to guide us, evolving efforts to unify consensus in definitions and stratification could provide the first platform for future research.

KEY POINTS

- Current definitions and phenotypes of cardiogenic shock are unclear and less predictable for patients with acute and chronic advanced heart failure (HF).
- Recognition of baseline laboratory values in patients with acute or chronic HF is vital to interpreting the severity of disease.
- Patients with acute or chronic HF are less likely to respond to medical interventions and more likely to need temporary mechanical circulatory support (tMCS) due to exhausted reserves.
- Trials of tMCS typically include patients with cardiogenic shock from post-acute myocardial infarction and less likely to include those with end-stage HF because their higher burden of comorbidities and lower survival rate make it difficult to extrapolate their outcomes to the acute and chronic HF population.
- Classification of cardiogenic shock, as defined by the Society for Cardiovascular Angiography and Interventions consensus document, could provide a platform for future research in the cardiogenic shock patient population.

Conflict of Interest Disclosure:

Dr. Hall is an advisor for Abbott US, Abiomed, CareDx, Evaheart, Inc., and Syncardia Systems and serves on the speakers bureau for Novartis and CareDx.

Keywords:

cardiogenic shock, advanced heart failure, stage D heart failure, end-stage heart failure

REFERENCES

1. Yancy CW, Jessup M, Bozkurt B, et al.; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 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 Oct 15;62(16):e147-239.
2. Harjola VP, Lassus J, Sionis A, et al. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail*. 2015 May;17(5):501-9.
3. Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiología Intervencionista; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. *J Am Coll Cardiol*. 2015 May 19;65(19):2140-1.
4. Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012 Oct 4;367(14):1287-96.
5. van Diepen S, Katz JN, Albert NM, et al. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation*. 2017 Oct 17;136(16):e232-e268.
6. Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. *J Heart Lung Transplant*. 2009;28(6):535-541.
7. Baran DA, Grines CL, Bailey S, 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 Jul 1;94(1):29-37.
8. 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 Jul-Aug;14(4):288-93.
9. Stretch R, Sauer CM, Yuh DD, Bonde P. National trends in the utilization of short-term mechanical circulatory support: incidence, outcomes, and cost analysis. *J Am Coll Cardiol*. 2014 Oct 7;64(14):1407-15.
10. Kapur NK, Davila CD, Jumean MF. Integrating Interventional Cardiology and Heart Failure Management for Cardiogenic Shock. *Interv Cardiol Clin*. 2017 Jul;6(3):481-5.
11. Estep JD, Cordero-Reyes AM, Bhimaraj A, et al. Percutaneous Placement of an Intra-Aortic Balloon Pump in the Left Axillary/Subclavian Position Provides Safe, Ambulatory Long-Term Support as Bridge to Heart Transplantation. *JACC Heart Fail*. 2013 Oct;1(5):382-8.
12. Hall SA, Uriel N, Carey SA, et al. Use of a Percutaneous Temporary Circulatory Support Device as a Bridge to Decision During Acute Decompensation of Advanced Heart Failure. *Heart Lung Transplant*. 2018 Jan;37(1):100-6.
13. Vallabhajosyula S, Barsness GW, Vallabhajosyula S. Multidisciplinary teams for cardiogenic shock. *Aging (Albany NY)*. 2019 Jul 17;11(14):4774-6.
14. Bellumkonda L, Gul B, Masri SC. Evolving Concepts in Diagnosis and Management of Cardiogenic Shock. *Am J Cardiol*. 2018 Sep 15;122(6):1104-10.