Cardiogenic Shock

Pathogenesis, Classification, and Management

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KEYWORDS

• Cardiogenic shock • Acute myocardial infarction • Acute heart failure
• Cardiac critical care

KEY POINTS

- Cardiogenic shock is a heterogeneous and often fatal condition of critically low cardiac output and hypoperfusion typically caused by myocardial infarction or decompensated cardiomyopathy.
- Cardiogenic shock manifests a spectrum of severity quantified by the SCAI Shock Classification, necessitating tailored hemodynamic support using vasopressors, inotropes and mechanical circulatory support.
- Comprehensive cardiogenic shock patient evaluation incorporates shock severity, phenotype, and risk modifiers to predict survival and individualize the use of mechanical circulatory support.
- Early stabilization of cardiogenic shock patients to rapidly restore tissue perfusion may mitigate end-organ injury and prevent progression to refractory hemo-metabolic shock.

INTRODUCTION

Cardiogenic shock (CS) is a life-threatening syndrome of cardiac dysfunction and systemic hypoperfusion, with rising incidence and persistently high mortality rates.[1,2] CS accounts for a substantial proportion of admissions to the cardiac intensive care unit (CICU), particularly among patients who do not survive hospitalization.[3–5] An evolving literature has highlighted the complexity of CS as a clinical syndrome, necessitating individualized patient care guided by a limited evidence base. In this narrative review, we will discuss the epidemiology, pathophysiology, clinical manifestations, risk stratification, and medical management of CS.

EPIDEMIOLOGY

Based on recent registry data from the United States (US), CS accounts for an estimated 408/100,000 hospitalizations with an average in-hospital mortality rate of

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37%.[6] European data suggest in-hospital mortality ranging from 30% to 60%.[2] Historically, CS occurred primarily due to acute myocardial infarction (AMI), but growing access to timely revascularization has reduced the proportion of AMI cases complicated by CS (AMI-CS) to 5% to 7% in ST-elevation MI (STEMI) and 2% to 4% in non-ST-elevation MI (NSTEMI).[7] However, CS patients account for most in-hospital deaths in the AMI population.[8] In parallel, the incidence of heart failure–related CS (HF-CS) has increased, outnumbering AMI as a cause of CS in several studies.[3,6,9,10] Despite improvements during the 1990s and 2000s,[11] CS in-hospital mortality rates have plateaued at 30% to 40% over the past decade.[2,7] Importantly, there are significant race, ethnicity, and gender-based disparities in care access and outcomes.[12–14] Female, Black, and Hispanic patients with CS have higher risk of mortality and are less likely to receive revascularization or mechanical circulatory support (MCS).[13,14] Furthermore, CS patients in randomized clinical trials (RCTs) have been predominantly Caucasian males with AMI-CS.

DEFINITIONS

Classically, CS has been defined by sustained hypotension (eg, systolic blood pressure [SBP] < 90 mm Hg or requirement for vasoactive medications) with tissue hypoperfusion due to low cardiac output (eg, cardiac index [CI] < 2.2 L/min/m^2) and congestion (eg, pulmonary capillary wedge pressure [PCWP] $\geq$ 15 mm Hg or pulmonary congestion on imaging).[11,15,16] However, CS is a clinical diagnosis usually made without hemodynamic data, and hypotension may not be present in all patients with a low cardiac output, hypoperfusion, and congestion.[3] Thus, recent consensus statements have defined CS more broadly as the presence of hypoperfusion due to ineffective cardiac output with an adequate preload (ie, normal or elevated ventricular filling pressures) (**Fig. 1**).[1,2,17] Hypoperfusion has been increasingly recognized as the defining criterion for shock, such that patients meeting all other features of CS without hypotension may be classified as "normotensive CS" (hypoperfusion without hypotension).[17,18] Patients with normotensive CS have higher mortality than hypotensive

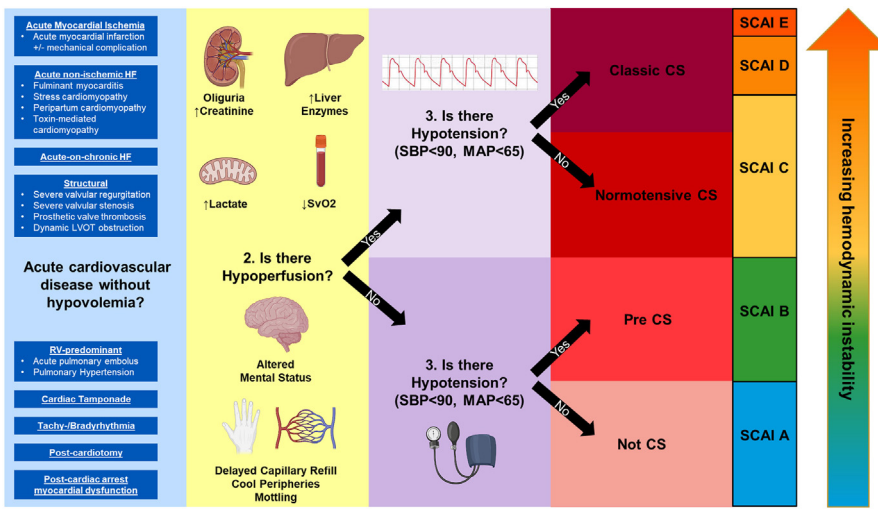

Fig. 1. Common etiologies and definitions of cardiogenic shock (CS), normotensive CS, and pre-CS, with corresponding Society for Cardiovascular Angiography and Interventions (SCAI) Stage Classification.

patients without hypoperfusion ("pre-shock") and similar adjusted mortality relative to hypotensive "classic" CS.[18,19] Patients with acute cardiac disease and hypoperfusion without hypovolemia or an alternative etiology can be given a presumptive diagnosis of CS.

PATHOGENESIS

Initiation

CS can be precipitated by many etiologies and may develop acutely or subacutely (see **Fig. 1**). AMI is the archetypal model used to understand the pathophysiology of CS.[20] Ischemic myocyte necrosis and myocardial stunning cause an acute reduction in ventricular contractility. The resulting drop in stroke volume, cardiac output, and blood pressure triggers compensatory tachycardia and neurohormonal activation with arteriolar and venous constriction (**Fig. 2**). This raises afterload, worsens myocardial energy debt, and increases stressed blood volume (SBV), causing increased ventricular filling pressures and congestion.[20,21] The bi-directional relationship between

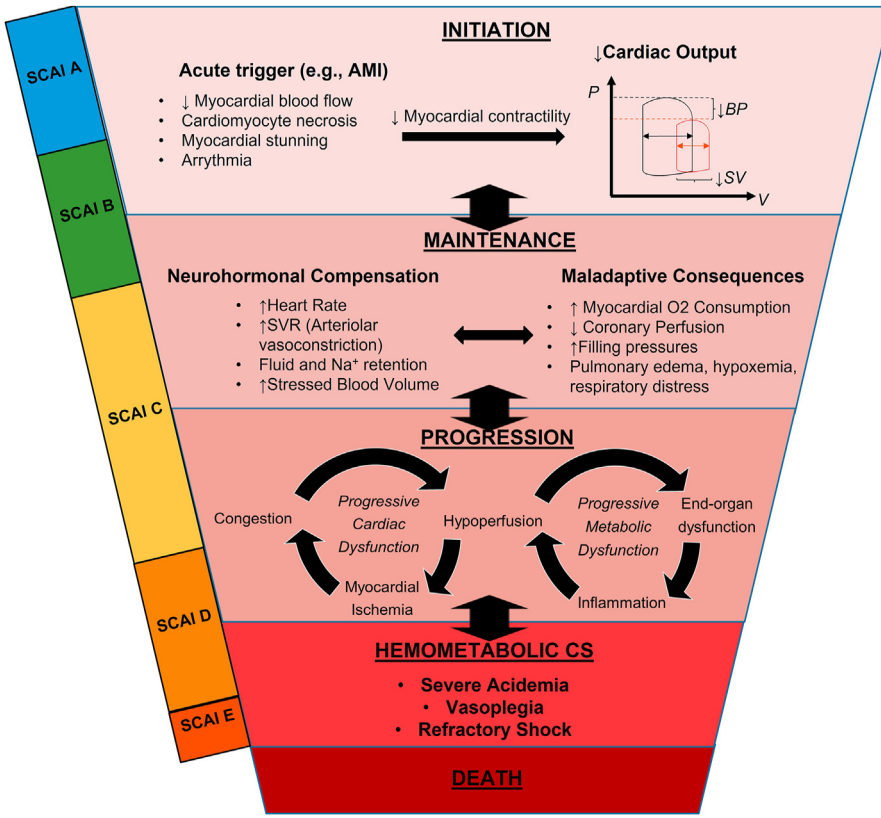

Fig. 2. An abrupt drop in myocardial contractility (eg, due to acute myocardial infarction [AMI]) causes reduced blood pressure (BP) and stroke volume (SV), triggering a reflex increase in heart rate and systemic vascular resistance (SVR), which propagates myocardial ischemia via increased myocardial oxygen consumption (MvO2). A vicious cycle of hypoperfusion, end-organ dysfunction, and inflammation ensues, leading ultimately to refractory hemometabolic shock and death.

myocardial dysfunction and congestion results in progressive systemic hypoperfusion and hypotension. By comparison to AMI-CS, which has a clear inciting event, congestion and resultant end-organ dysfunction occur earlier during the insidious worsening of chronic myocardial dysfunction that characterizes chronic HF-CS, and congestion can rapidly and reversibly worsen cardiac performance in these patients. Indeed, acute-on-chronic organ injury (eg, acute kidney injury [AKI]) may precipitate the transition from compensated to decompensated chronic HF, known as "acute renocardiac syndrome."[22,23] Furthermore, the pathogenesis of *de novo*/acute HF-CS is distinct from that of decompensated chronic HF with CS.[24] Recent evidence suggests higher shock severity and in-hospital mortality in acute HF-CS, possibly related to the absence of ventricular dilation (which can help preserve stroke volume during ventricular systolic dysfunction) and chronic compensatory mechanisms to low CO.[24,25]

Maintenance

CS is maintained by a vicious cycle of worsening hemodynamics, end-organ damage, inflammation, and metabolic derangement due to tissue hypoperfusion (see **Fig. 2**). Hypotension coupled with tachycardia and coronary hypoperfusion may induce myocardial ischemia that aggravates cardiac dysfunction independent from the original trigger of CS. Renal and hepatic dysfunction commonly result from hypotension, venous congestion, systemic inflammation, and iatrogenic organ toxicity and can contribute to worsening CS via metabolic acidosis, fluid retention, electrolyte abnormalities, and direct uremic myocardial injury.[26,27] Microcirculatory dysfunction contributes to the development of end-organ injury and persistent hypoperfusion despite the restoration of adequate macrohemodynamic parameters.[28] Systemic inflammation commonly develops in CS, resulting from either infectious (eg, sepsis or endotoxemia from gut translocation) or noninfectious processes (eg, tissue hypoxia or ischemia-reperfusion injury as it occurs after CA or in AMI-CS), resulting in a mixed cardiogenic-vasodilatory shock phenotype with worse outcomes.[29,30]

Progression to Hemometabolic Cardiogenic Shock

Multiorgan failure is a major cause of death in patients with CS, along with refractory shock and anoxic brain injury after CA.[31,32] Metabolic acidosis resulting from hypoperfusion and decreased acid clearance (due to kidney and liver dysfunction) is a central feature of worsening CS that may further aggravate myocardial compromise, end-organ injury, vasoplegia, and systemic inflammation. Serum lactate is a critical biomarker of hypoperfusion and, along with other markers of acidosis, is a powerful predictor of mortality in CS.[33] The phenotype of severe CS with multiorgan failure and acidosis, termed hemometabolic shock, has been associated with significantly higher mortality in multiple cohorts.[33,34] Crucially, once established, hemometabolic shock may be refractory to hemodynamic stabilization (eg, using MCS), leading to a vicious cycle of progressive CS and death (see **Fig. 2**).

CLASSIFICATION

Classification by Hemodynamics

Traditional hemodynamic classification systems for CS have focused on (1) congestion and vascular tone ("dry/wet" vs "warm/cold", **Fig. 3**); and (2) left ventricle (LV)-predominant versus right ventricle (RV)-predominant versus biventricular CS.[1,35] These distinct hemodynamic phenotypes may be defined using clinical and echocardiographic findings or a pulmonary artery catheter (PAC) (**Table 1**). Defining the

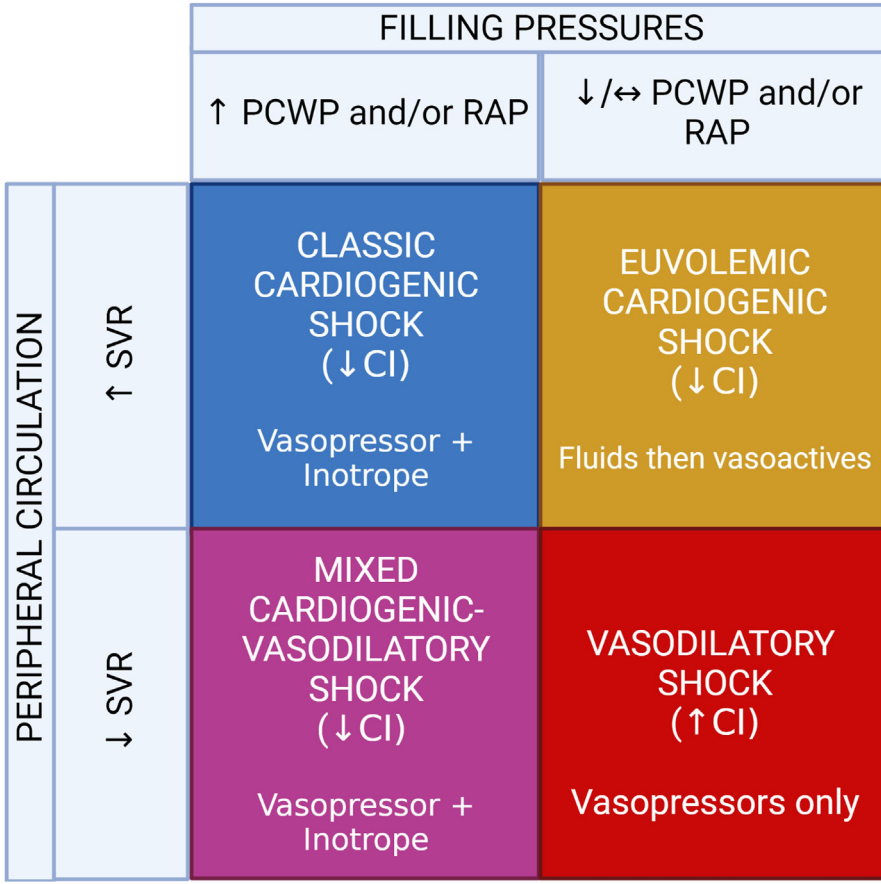

Fig. 3. Hemodynamic classification of cardiogenic shock (CS) through evaluation of the systemic vascular resistance (SVR) and filling pressures (pulmonary capillary wedge pressure [PCPW] and/or right atrial pressure [RAP]).

Table 1
Hemodynamic profiles in cardiogenic shock–patients may have signs of LV congestion, RV congestion, or both

Diagnostic modality	Evidence of LV Congestion	Evidence of RV Congestion
Physical examination & chest X-ray	• Pulmonary rales • S3 gallop • Pulmonary edema	• Elevated JVP/JVD/HJR • Ascites and peripheral edema
Echocardiography/ lung ultrasound	• Elevated mitral E/e' ratio • Bilateral pulmonary B lines	• Dilated/noncollapsible IVC & internal jugular vein • Abnormal hepatic and portal vein flow pattern • Interventricular septal flattening/ paradoxical motion
Hemodynamics	• Elevated PWP >18 mm Hg	• Elevated CVP/RAP >14 mm Hg

Abbreviations: HJR, hepatojugular reflux; IVC, inferior vena cava; JVD, jugular venous distention; JVP, jugular venous pressure; LV, left ventricle; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RV, right ventricular.

hemodynamic phenotype can guide fluid resuscitation, diuresis, and choice of vasoactive therapy, while delineating the severity of RV and LV dysfunction may help inform diagnosis, prognosis, pharmacotherapy, and MCS (including eligibility for left ventricular assist device [LVAD]).[35] Echocardiographic and hemodynamic correlates of RV dysfunction are predictive of adverse outcomes while mixed vasodilatory-cardiogenic CS often necessitates escalating vasopressor requirements with attendant poor outcomes.[29,36,37] PAC-guided management has not been prospectively tested in patients with CS although previous RCTs have failed to show a survival advantage in acute decompensated HF or ICU patients.[38,39] More recent observational data suggest a survival advantage in patients with complete PAC-derived hemodynamic data, particularly in the setting of MCS.[40] Invasive hemodynamic data are essential in evaluating candidacy for cardiac transplantation or durable ventricular assist devices (VADs).[22]

Classification by Shock Severity

Defining CS severity can facilitate tailoring the degree of hemodynamic support to the degree of circulatory compromise. The Society for Cardiovascular Angiography and Intervention (SCAI) shock classification system was conceived to capture the broad spectrum of CS severity (see **Fig. 1**, **Table 2**).[17] Similar paradigms exist in chronic HF; the INTERMACS profile and the United Network for Organ Sharing (UNOS) classification can define the severity for CS to allow patient selection for VAD and heart transplantation, respectively.[22] While patients with CS are captured in INTERMACS profiles 1–3, or UNOS status 1–3, the SCAI classification system provides additional gradation.[22] The prognostic value of the SCAI Shock Classification has been validated in a broad range of CS cohorts, encompassing AMI-CS, HF-CS, out-of-hospital cardiac arrest (OHCA) survivors, and those receiving venoarterial extracorporeal membrane oxygenator (VA-ECMO).[41–43] The SCAI Shock classification may even aid patient selection for coronary angiography after out-of-hospital cardiac arrest (CA).[44]

Other Classification Systems

Traditional clinical scoring systems to predict the risk of death in CS cohorts have generally incorporated nonmodifiable risk factors rather than markers of shock severity.[45,46] The recently derived CLIP score (*C*ystatin-C, *L*actate, *I*nterleukin-6, N-terminal pro-B-type natriuretic peptide [NT-proBN*P*]) used biomarkers to predict risk in AMI-CS populations, outperforming clinical risk scores.[47] Zweck and colleagues[34] performed unsupervised machine learning based on laboratory biomarkers to describe 3 CS subphenotypes with unique characteristics and mortality risk: (1) noncongested (younger patients with a lower illness severity); (2) cardiorenal (older patients with renal dysfunction, pulmonary congestion, and anemia); and (3) cardiometabolic (high illness severity with right-sided congestion and multiorgan dysfunction). These phenotypes succeeded in separating patients according to demographic, hemodynamic, echocardiographic, and laboratory data across CS etiologies, emphasizing the heterogeneity within syndromically defined CS populations.[34,48]

Integrating Cardiogenic Shock Classification Systems

A 3-axis model for CS evaluation and prognostication was recently proposed to capture the interaction between demographics, etiology, shock severity, biomarkers, and hemodynamics (**Fig. 4**).[17] Integrating the SCAI Shock Classification with a conventional risk score may improve risk stratification.[46]

Table 2
Assessment of SCAI stage and implications for management

		SCAI A	SCAI B	SCAI C	SCAI D	SCAI E
Assessment	Hypoperfusion	No	No	Yes	Yes	Yes
	Hypotension	No	Not necessarily	Not necessarily	Yes	Yes
	Descriptors	"At risk" Risk factors (eg, AMI) but no current CS signs	"Beginning" Relative tachycardia or hypotension without hypoperfusion	"Classic" Persistent hypoperfusion despite correcting hypovolemia.	"Deteriorating" Worsening despite initial management	"Extremis" Near circulatory collapse or refractory shock despite multiple interventions
Management	Vasoactive agents	None	Consider depending on BP	Usually required. NE + dobutamine first line	Escalating doses or multiple drugs usually required	High doses of multiple drugs usually required
	Hemodynamic monitoring	Noninvasive	Consider arterial line	Place arterial line Consider PAC	Place arterial line and PAC	Place arterial line and PAC
	Temporary MCS	No	No	Evaluate need and candidacy	Initiate if eligible Limited role for IABP. Consider axial flow pump or ECMO.	Initiate if eligible Consider ECMO Palliation if ineligible
Triage	Level of care	Ward or ICU	Consider ICU	ICU Shock team	ICU Shock team	ICU Shock team
	Location of care	Local center/ "Spoke"	Consider transfer to regional hub if high-risk features	Transfer to regional hub	Transfer to regional hub	Likely not stable for transport Consider mobile ECMO for transfer
	Transplant/durable VAD evaluation	No	Depending on etiology (eg, HF-CS)	If limited reversibility anticipated	Yes	Yes if end-organ function stabilizes

Abbreviations: AMI, acute myocardial infarction; BP, blood pressure; CS, cardiogenic shock; CS, heart failure–related CS; ECMO, extracorporeal membrane oxygenation; HF-IABP, intra-aortic balloon pump; ICU, intensive care unit; MCS, mechanical circulatory support; NE, norepinephrine; PAC, pulmonary artery catheter; SCAI, Society for Cardiovascular Angiography and Intervention; VAD, ventricular assist device.

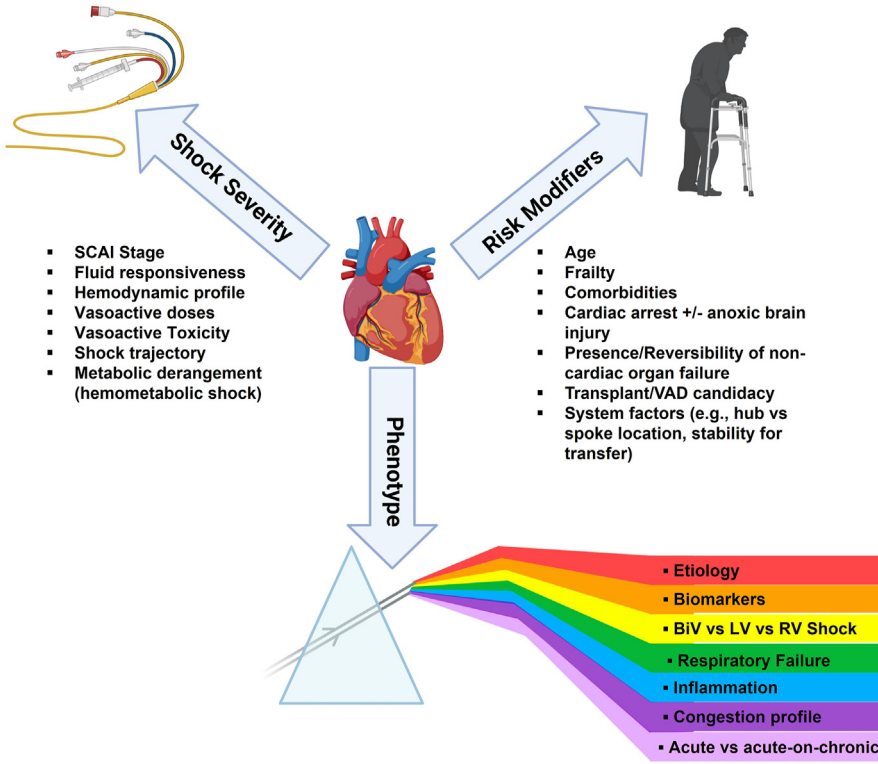

Fig. 4. The 3-axis model of CS. Each axis contributes to the cumulative estimation of risk but informs clinical decision-making in different ways—shock severity determines the need to escalate hemodynamic support, phenotype guides the type of hemodynamic support, and risk modifiers influence candidacy for advanced support modalities.

INITIAL STABILIZATION

General Principles

Three core principles underlie the initial CS investigation and management: (1) stabilize airway, breathing, and circulation; (2) identify and reverse the underlying etiology; (3) triage the need for advanced hemodynamic support with timely initiation if appropriate[49] (**Fig. 5**, **Table 3**). These steps should take place simultaneously and require multidisciplinary involvement. The use of a "shock team" to individualize care on a case-by-case basis has been associated with improved outcomes.[9,50] Consensus statements and recent evidence advocate for a hub-and-spoke approach with early triage and transfer to high-volume, high-resource regional centers.[1,51]

Ventilation and Oxygenation

Patients with CS may experience reduced consciousness due to brain hypoperfusion or anoxic brain injury following CA; securing the airway to ensure ventilation and prevent aspiration is therefore essential. The deleterious hemodynamic effects of hypoxia and respiratory distress are magnified in patients with CS, in whom the respiratory muscles may utilize a substantial portion of an already low CO.[52] Therefore, restoring normoxia using supplemental oxygen and decreasing work of breathing with additional respiratory support may improve hemodynamics. The effects of positive

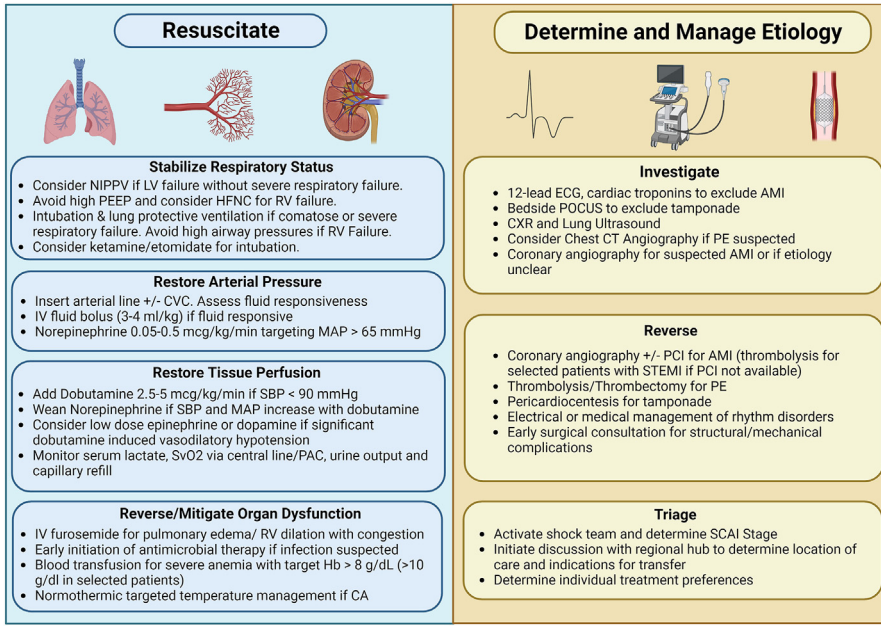

Fig. 5. Management priorities in the first hour ("golden hour") of CS management. Importantly, resuscitation and etiology-based management should occur simultaneously. AMI, acute myocardial infarction; CA, cardiac arrest; CVC, central venous catheter; ECG, electrocardiogram; Hb, hemoglobin; LV, left ventricular; MAP, mean arterial pressure; NIPPV, noninvasive positive-pressure ventilation; PCI, percutaneous coronary intervention; PE, pulmonary embolism; PEEP, positive end-expiratory pressure; POCUS, point-of-care ultrasound; RV, right ventricular; SBP, systolic blood pressure; SvO_2, central venous oxygen saturation; TTE, transthoracic echocardiogram.

pressure ventilation on hemodynamics in patients with CS can differ based on the phenotype of RV and LV function. In LV failure, positive pressure ventilation may improve hemodynamics through a reduction in LV preload and afterload; however, high airway pressures may be deleterious in RV failure by increasing RV preload and afterload, compromising RV performance.[52] For this reason, we favor a trial of noninvasive positive pressure ventilation in conscious patients with LV-predominant CS (particularly with pulmonary edema); by contrast, we prefer high-flow nasal cannula oxygen in conscious patients with RV-predominant CS whenever feasible to avoid high airway pressures.[52] When employing mechanical ventilation in patients with CS (eg, due to severe respiratory failure or coma), CICU care providers should consider a lung-protective ventilation strategy and avoid hyperoxia.[52] Patients with any phenotype of CS are at a substantial risk of hemodynamic deterioration during intubation, necessitating a careful approach to induction of anesthesia and preemptive hemodynamic support.

Initial Hemodynamic Stabilization

Rapidly restoring MAP, CO, and systemic perfusion are primary hemodynamic goals in CS management to disrupt the vicious cycle of worsening shock. Careful intravenous crystalloid boluses (eg, 3–4 mL/kg) may be appropriate in noncongested patients, as patients with CS require higher-than-normal cardiac filling pressures for adequate

Table 3
Etiology-guided management in CS

Etiology	CS Management Considerations
AMI-CS	• Dual anti-platelet therapy and anticoagulation • Emergent culprit-vessel revascularization • Consider thrombolytics for STEMI if timely PCI is unavailable • Expedited echocardiography to detect mechanical complications, with urgent surgical consultation • Limited role for IABP without mechanical complications
HF-CS	• Assess reversibility of myocardial dysfunction if acute-on-chronic HF-CS/end-stage HF • Consider immunosuppression in selected cases (eg, giant cell myocarditis, immune-checkpoint inhibitor toxicity) • Consider use of MCS as a bridge to LVAD/transplant → anecdotally better response to IABP support than AMI-CS • Early involvement of advanced HF and transplantation team to guide exit strategy
RV-predominant CS	• Correct hypoxia and hypercapnia • Avoid elevated airway pressures in ventilated patients • Consider High-Flow Nasal Oxygen for hypoxia • Consider inhaled nitric oxide (even if no pulmonary hypertension) • Consider systemic pulmonary vasodilators for pulmonary arterial hypertension (selected patients) • Consider milrinone if inotropy required • Vasopressor therapy (eg, vasopressin given its selectivity for systemic vasculature) to keep systemic BP above PA pressure
Post-Cardiotomy CS	• Exclude cardiac tamponade (echocardiogram may be insensitive to localized post-operative hemopericardium) • Consider coronary angiography to exclude native coronary artery or bypass graft occlusion • Milrinone or inhaled NO to optimize RV afterload if RV dysfunction present • Vasopressin for vasoplegia • Escalation to MCS often required (central VA ECMO commonly used)

Abbreviations: AMI-CS, acute myocardial infarction cardiogenic shock; ECMO, extra-corporeal membrane oxygenation; HF-CS, heart failure cardiogenic shock; MCS, mechanical circulatory support; NO, nitric oxide; PA, pulmonary artery; STEMI, ST elevation myocardial infarction.

forward flow.[49] Pharmacotherapy using vasopressors and inotropes is recommended for initial hemodynamic stabilization (see **Fig. 5**, **Table 4**).[1] Norepinephrine (NE) is widely used as the first-line vasopressor to raise arterial pressure in CS via peripheral vasoconstriction given its more favorable safety profile (lower arrhythmogenicity), with RCT data supporting its use over epinephrine and dopamine.[53,54] Blood pressure targets in CS remain uncertain, and a MAP >65 mm Hg and/or SBP >90 mm Hg are widely targeted; placement of an arterial catheter is recommended.[55]

Following restoration of MAP, an inotrope may be added to improve cardiac output if there is persistent systemic hypoperfusion, especially if SBP remains <90 mm Hg. Dobutamine is often used as a first-line inotrope given its relatively short duration of action, while milrinone may provide greater RV afterload reduction in patients with RV-predominant CS.[56] The DOREMI RCT compared dobutamine and milrinone as first-line inotropes in predominantly HF-CS, finding no difference between groups with respect to survival, efficacy, or safety.[57] While both drugs may cause peripheral vasodilation and hypotension,

Table 4
Commonly used vasopressors and inotropes in CS

Drug	Standard Doses Ranges	Pharmacologic Mechanism	Hemodynamic Effect	Suggestions for Use
Vasopressors				
Norepinephrine	0.05–0.5 μg/kg/min	α > β agonism	↑SVR ↑HR, ↑Inotropy	First-line vasopressor in most forms of CS including mixed shock Toxicity: Tachycardia/digital ischemia, increased LV afterload
Epinephrine	0.01–0.2 μg/kg/min	β > α agonism	↑SVR ↑HR, ↑Inotropy	Bradyrhythmias or second-line vasopressor/inotrope Increased toxicity compared to NE (OptimaCC trial) Low doses (up to 0.1 μg/kg/min) may be considered for inotropic support in patients with reduced vascular tone Toxicity: arrythmia, lactic acidosis, tachycardia
Vasopressin	0.02–0.04 U/min	V1 agonism	↑SVR	Vasopressor for severe vasoplegia (mixed shock) or RV failure Generally contraindicated in CS due to LV failure unless CO is normalized
Dopamine	*Low*: 2–5 μg/kg/min *Intermediate*: 5–10 μg/kg/min *High*: 10–20 μg/kg/min	*Low*: D > β1 > α *High*: α > β1 > D	*Low*: ↑Inotropy *High*: ↑SVR	Bradyrrhythmias or second-line inotrope (not recommended as a vasopressor) Increased mortality compared to NE when used at high doses (SOAP trial) Low doses (up to 5 μg/kg/min) may be considered for inotropic support in patients with reduced vascular tone
Inodilators				
Dobutamine	2.5–20 μg/kg/min	β1 Agonism	↑HR ↑Inotropy ↓ = SVR	First-line inotrope in CS. Short half-life Toxicity: Tachycardia, vasodilation, arrhythmia. concomitant Beta blocker use may theoretically limit efficacy
Milrinone	0.125–0.75 μg/kg/min	PDE-3 inhibitor	↑Inotropy ↓SVR ↓PVR	Equivalent to dobutamine for outcomes and toxicity (DOREMI) Consider in RV shock given ↓ PVR Can be combined with beta-agonist Toxicity: Vasodilation may be poorly tolerated. Longer half-life

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Table 4
(*continued*)

Drug	Standard Doses Ranges	Pharmacologic Mechanism	Hemodynamic Effect	Suggestions for Use
Isoproterenol	2–20 μg/min	β1 and β2 Agonism	↑↑HR ↑Inotropy ↓SVR	Bradyrrhythmia Toxicity: Use may be limited by hypotension due to ↓ SVR.
Levosimendan	0.05–2 μg/kg/min	PDE-3 Inhibitor Ca^{2+} Sensitizer	↑Inotropy ↓SVR ↓PVR	Not available in USA. Comparatively lower increase in myocardial O_2 consumption.

Abbreviations: CO, cardiac output; CS, cardiogenic shock; HR, heart rate; LV, left ventricle; NE, norepinephrine; PVR, pulmonary vascular resistance; RV, right ventricle; SOAP, sepsis occurrence in acutely ill patients; SVR, systemic vascular resistance.

the effects of milrinone on blood pressure tend to be more prolonged and profound (particularly in patients with reduced creatinine clearance).[56] Among patients presenting with normotensive CS, IV vasodilators (eg, nitroprusside) are typically the first-line therapy to avoid inotrope-associated toxicity. Withholding beta-blockers and other HF guideline-directed medical therapy (GDMT) is essential in CS and pre-CS during the acute phase or when vasopressors are indicated.

Improvements in mental status, capillary refill, peripheral temperature, and urine output suggest response to therapy. Serial lactate measurements are useful, and lactate clearance is an independent predictor of mortality.[58] In CS, low mixed venous oxygen saturations (SvO_2) reflect increased peripheral oxygen extraction in the setting of low CO, and increases in SvO_2 have been correlated with improved outcomes, especially in HF-CS.[59] A low cardiac power output (typically <0.6 Watts, where $CPO = \frac{MAP \times CO}{451}$) is associated with worse outcomes in AMI-CS, while a low pulmonary artery pulsatility index (typically <1.5, where $PAPI = \frac{PA\ Systolic\ Pressure - PA\ diastolic\ pressure}{Right\ Atrial\ Pressure}$) may suggest RV dysfunction requiring RV support.[35,36]

MCS may be considered in CS patients with toxicity or inadequate response to vasoactive medications as a bridge to recovery, durable VAD, or heart transplant. The limited RCT data regarding MCS in CS have not demonstrated clear improvements in outcomes, suggesting that these devices should be used on a case-by-case basis (ideally after a shock team discussion). A full review of MCS is beyond the scope of this document but has been covered elsewhere in this issue.

Organ Support

Because the development and reversibility of noncardiac organ failure is an important determinant of outcomes in CS, organ support is essential for CS management (see **Fig. 5**). For oliguric patients with CS and congestion, restoration of renal perfusion by optimizing CO, MAP, and SvO_2 is the primary task; after this, an IV furosemide challenge of 1.5-2 mg/kg or more can be given, and failure to respond to this will identify patients (ie, nonresponders) at elevated risk of needing renal replacement therapy (RRT).[26] The timing and threshold for initiating RRT in patients with AKI and CS is an area of ongoing debate; hence, the decision to initiate RRT should be individualized given that several specific situations may arise in CS, which have not been tested in RCTs, and the requirement for RRT is a poor prognostic marker.[26,60] Patients with CS and severe congestion may require pre-emptive initiation of RRT if their urinary output on maximal diuretic doses is inadequate to maintain even or negative fluid balance, and continuous RRT modalities are often needed in vasopressor-dependent CS.[26]

ETIOLOGY-GUIDED MANAGEMENT

Initial Investigations

Identifying and reversing the underlying etiology for CS should be prioritized concurrently with initial resuscitation (see **Fig. 5**).[1] A 12-lead electrocardiogram, serial troponin measurement, and chest radiography are essential investigations, along with bedside echocardiography to rapidly exclude cardiac tamponade and assess biventricular function.[49] Coronary angiography should be pursued urgently in patients with suspected AMI-CS and should be considered electively in most patients with cardiomyopathy of unclear etiology.[7]

Acute Myocardial Infarction Cases Complicated by Cardiogenic Shock

Emergent culprit-vessel revascularization is the only intervention for AMI-CS that has improved survival in RCTs.[15] For patients with multivessel coronary disease,

immediate multivessel revascularization was associated with harm compared with the initial culprit-vessel-only revascularization with delayed non–culprit-vessel revascularization.[61] Ischemia-reperfusion injury can aggravate myocardial dysfunction after revascularization of the culprit vessel, while chronically hibernating myocardium often demonstrates delayed recovery of contractility in nonculprit territories.

Heart Failure Cases Complicated by Cardiogenic Shock

HF-CS is distinguished from low-output HF by the presence of hypoperfusion, and often hemodynamic parameters are inadequate to distinguish HF-CS from end-stage HF. Reversal of congestion itself may improve myocardial performance, particularly with right ventricular dysfunction. Patients with HF-CS often have underlying end-stage HF and are more likely to require bridging to durable VAD or heart transplant than patients with AMI-CS, so candidacy for heart transplantation or durable VAD implantation should be evaluated early in HF-CS.[22,62] As such, a lower threshold for instituting aggressive hemodynamic support including MCS may be appropriate.[24] Although the use of an intra-aortic balloon pump (IABP) is not recommended in AMI-CS due to lower efficacy and no evidence of improved outcomes, in our experience, patients with HF-CS may have a more favorable response to IABP as a bridge to definitive therapy.[63]

Right Ventricle Shock

RV-predominant CS may be caused by an acute or chronic process directly affecting the RV myocardium (eg, right ventricular infarction) and/or causing pulmonary hypertension (ie, cor pulmonale).[64] After addressing reversible etiologies, management depends on optimizing RV preload and afterload without compromising arterial pressure or LV loading conditions.[64] While RV failure is commonly described as a preload-dependent condition, most patients with acute-on-chronic RV failure are already congested, and excessive fluid administration may be harmful by increasing RV dilation and afterload necessitating assessment of RV preload before fluid administration.[64] Given the sensitivity of RV stroke volume to afterload, factors that increase pulmonary vascular resistance such as hypoxia, hypercapnia, and elevated airway pressures in ventilated patients should be avoided. Selective pulmonary vasodilators may be considered in some patients, while milrinone and vasopressin may be beneficial given their pulmonary vasodilatory properties. Inhaled nitric oxide can be effective in selected patients with RV failure even without pulmonary hypertension.

Postcardiotomy Shock

Postcardiotomy shock describes either the inability to wean from cardiopulmonary bypass or the onset of CS in the postoperative period following cardiac surgery.[65] Vasoplegia is often superimposed due to postoperative systemic inflammation and may respond to vasopressin. RV dysfunction is a common contributor to postcardiotomy CS (particularly after VAD implantation), and the use of milrinone or inhaled nitric oxide may be considered.[65]

Cardiac Arrest

At least a third of CS hospitalizations are complicated by CA, which may precipitate or worsen CS and is associated with poorer outcomes at each SCAI shock stage.[17] Concomitant CA has several important implications for management at each stage of the CS care pathway, most importantly in patients who are comatose and may have anoxic brain injury (**Table 5**).[66] Targeted temperature management (TTM) is still

Table 5
CA-specific considerations in CS management

CS Care Setting	CA-Specific Considerations
Emergency department	• ECG to screen for STEMI • Unsedated neurological examination if possible to determine presence of coma • Consider head CT if comatose • Refer for early coronary angiography if AMI-CS
Catheterization laboratory	• Culprit vessel revascularization only • Early invasive hemodynamic monitoring with PAC implantation • Consider MCS implantation for persistent shock in patients without clear evidence of severe brain injury
CICU	• Lung protective ventilation • Initiation of normothermic TTM (goal 37.5°C) • Control of hyperglycemia and electrolyte abnormalities • No evidence for different BP goals than other CS patients • Monitoring for evolution from cardiogenic to vasoplegic shock/mixed shock phenotype • Empiric antibiotics for fevers • Close monitoring for seizure activity or myoclonus, consider continuous EEG monitoring • Involvement of neurology for structured neuroprognostication following anoxic brain injury (typically after 72 hours) • Early involvement of brain injury/rehabilitation team and ICD if indicated for survivors

Abbreviations: AMI, acute myocardial infarction; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; ECMO, extra-corporeal membrane oxygenation; EEG, electro-encephalogram; MCS, mechanical circulatory support; PAC, pulmonary artery catheter; ROSC, return of spontaneous circulation; TTM, targeted temperature management.

believed to be important for mitigating brain injury in comatose patients after CA although RCTs have not shown a benefit from hypothermic TTM to a goal temperature of 33°C when compared to either normothermic TTM targeting 36°C or strict avoidance of pyrexia (ie, maintaining temperature <37.8°C).[67] Given the possible adverse hemodynamic effects of induced hypothermia (particularly at 33°C), a TTM strategy of aggressive fever prevention to maintain core temperature to <37.5°C is reasonable.[66] Optimal patient selection for MCS or coronary intervention in patients with CS and CA remains uncertain given that severe anoxic brain injury may obviate any benefits of these therapies in many patients.[44,68]

SHARED DECISION-MAKING IN CARDIOGENIC SHOCK

Many patients with CS will die during their hospital stay, while hospital survivors may experience subacute deterioration with frequent readmissions following discharge due to persistent HF.[69] Decisions made in the CICU (eg, durable LVAD implantation) may have permanent implications for patients' lives. Given the morbidity, symptom burden, and decisional complexity associated with CS, palliative care involvement should be considered in all patients and can occur concurrently with aggressive care. Decision-making in CS patients is difficult due to the acuity of critical care

decision-making, decisional incapacity, and the inherent uncertainty of clinical prognostication.

SUMMARY

CS is a life-threatening syndrome manifesting a wide spectrum of etiologic, hemodynamic, and biochemical features. Once established, CS progresses via a series of maladaptive, self-perpetuating processes which can rapidly result in refractory shock and irreversible multiorgan failure. Hence, achieving a good outcome depends on early recognition, rapid reversal of the underlying cause, and prompt initiation of hemodynamic support.

CLINICS CARE POINTS

- Cardiogenic shock (CS) epidemiology is changing, with heart failure-CS (HF-CS) outnumbering acute myocardial infarction-CS (AMI-CS) in many centers.
- Patients with acute cardiac dysfunction and hypoperfusion despite adequate preload may be given a presumptive diagnosis of CS.
- The Society for Cardiovascular Angiography and Intervention (SCAI) Shock Classification can grade the severity of CS to allow tailored hemodynamic support and facilitate decision-making.
- CS may progress rapidly via a series of vicious cycles, requiring early hemodynamic stabilization prior to the onset of refractory shock and multiorgan failure.
- Restoring the mean arterial pressure, cardiac output, and systemic perfusion are primary goals in CS management; hemodynamic data derived from the pulmonary arterial catheter may guide resuscitation and triage for advanced therapies.
- Early reversal of the underlying etiology is central to CS management; culprit vessel revascularization for AMI-CS remains the only intervention proven via a randomized clinical trial to reduce mortality in CS.

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