



Cardiogenic Shock: Updated Approach to Management

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Objectives

- Review definitions of cardiogenic shock (CS)
- Discuss pathophysiology and various hemodynamic presentations of CS
- Discuss noninvasive and invasive testing for evaluating CS
- Review management procedures of CS
- Future direction with respect to managing CS

Defining CS

- Low-cardiac-output state that results in life-threatening end-organ hypoperfusion and hypoxia
- Acute MI with LV dysfunction the most common reason for CS
- Clinical presentation
 - Persistent hypotension unresponsive to volume replacement
 - Clinical features of end-organ hypoperfusion requiring intervention with pharmacological or mechanical support

Various Definitions of CS

Clinical Definition	SHOCK Trial ^{9*}	IABP-SHOCK II [†]	ESC HF Guidelines ¹⁵
Cardiac disorder that results in both clinical and biochemical evidence of tissue hypoperfusion	<p>Clinical criteria: SBP <90 mmHg for ≥30 min OR Support to maintain SBP ≥90 mmHg AND End-organ hypoperfusion (urine output <30 mL/h or cool extremities)</p> <p>Hemodynamic criteria: CI of ≤2.2 L·min⁻¹·m⁻² AND PCWP ≥15 mmHg</p>	<p>Clinical criteria: SBP <90 mmHg for ≥30 min OR Catecholamines to maintain SBP >90 mmHg AND Clinical pulmonary congestion AND Impaired end-organ perfusion (altered mental status, cold/clammy skin and extremities, urine output <30 mL/h, or lactate >2.0 mmol/L)</p>	<p>SBP <90 mmHg with adequate volume and clinical or laboratory signs of hypoperfusion</p> <p>Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure</p> <p>Laboratory hypoperfusion: Metabolic acidosis, elevated serum lactate, elevated serum creatinine</p>

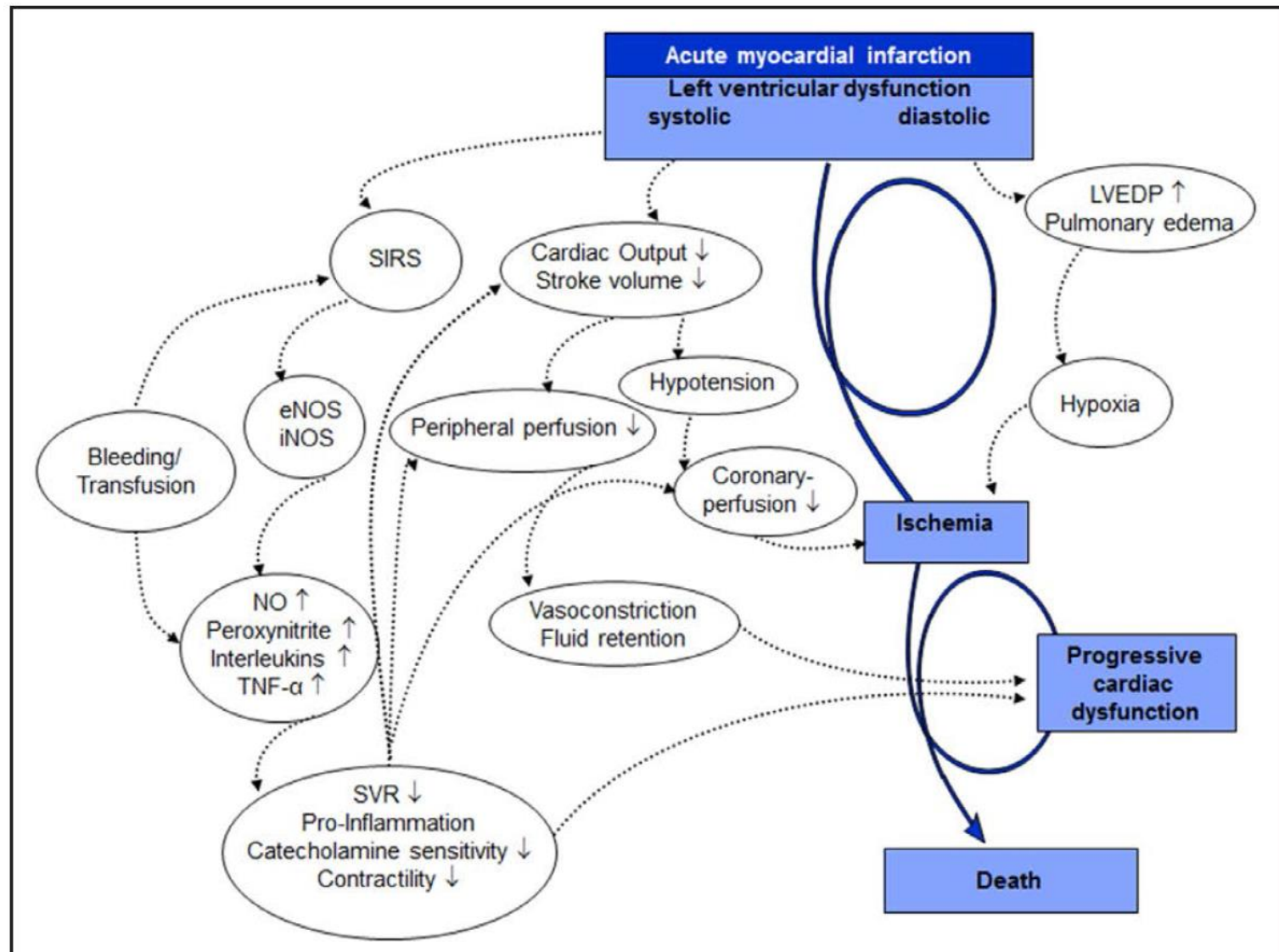
CI indicates cardiac index; CS, cardiogenic shock; ESC, European Society of Cardiology; HF, heart failure; IABP-SHOCK II, Intraaortic Balloon Pump in Cardiogenic Shock II; LV, left ventricular; MI, myocardial infarction; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; and SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock.

*In setting of MI complicated by predominantly LV dysfunction.

†In setting of acute MI

CGS Pathophysiology

- Systemic inflammation triggered by acute cardiac injury may cause pathological vasodilatation
- Endothelial and inducible nitric oxide (NO) synthase may play major role in production of high NO levels, along with peroxynitrite (cardiotoxic and has negative inotropic effect)



Uncommon CS Manifestations

- Normotensive CS
 - 5% of patients in SHOCK
 - Comparable CI's, PWCP's, and LV EF but higher SVR compared with hypotensive patients with CS
- RV CS
 - 5.3% reported prevalence among patients with MI-induced CS
 - Hemodynamically defined as CVP: PCWP ratio ≥ 0.8
 - Cohort characterized by relatively higher CVP's, LV EF, and lower pulmonary artery systolic pressures

Pathogenesis

- As many as 81% of patients presenting with CS have an underlying acute coronary syndrome (ACS)
 - Testing should include an ECG within 10 minutes of presentation
- Chronic HF can present in acute decompensated state; may account for up to 30% of CS cases

Trends in Outcomes and Therapies

- Analysis of Nationwide Inpatient Sample Database between 2003 and 2010 reported increase in prevalence of CS from 6% to 10% in overall population and from 7% to 12% among patients > 75 yrs old presenting with STEMI
- In-hospital mortality decreased from 45% to 34%
- Mortality rates remained high (55%) in patients > 75 years of age

Prognostic Models

- In general ICU setting, APACHE-II and SAPS-II scores are commonly used
 - APACHE =II includes 13 physiological variables and is designed to be used in first 24 hours after patient >16 years is admitted to the ICU
 - SAPS-II includes 12 physiological variables and 3 disease-related variables
- Among patients with ACS complicated by CS, the GRACE score has good discrimination and calibration for in-hospital and long-term mortality

Long-Term Outcomes

- Among patients with ACS-associated CS who had revascularization and survived to discharge, majority (62%) were alive 6 years later (SHOCK trial)
- Considerable morbidity- 1 year all-cause and HF re-hospitalization rates were 59% and 33%, respectively

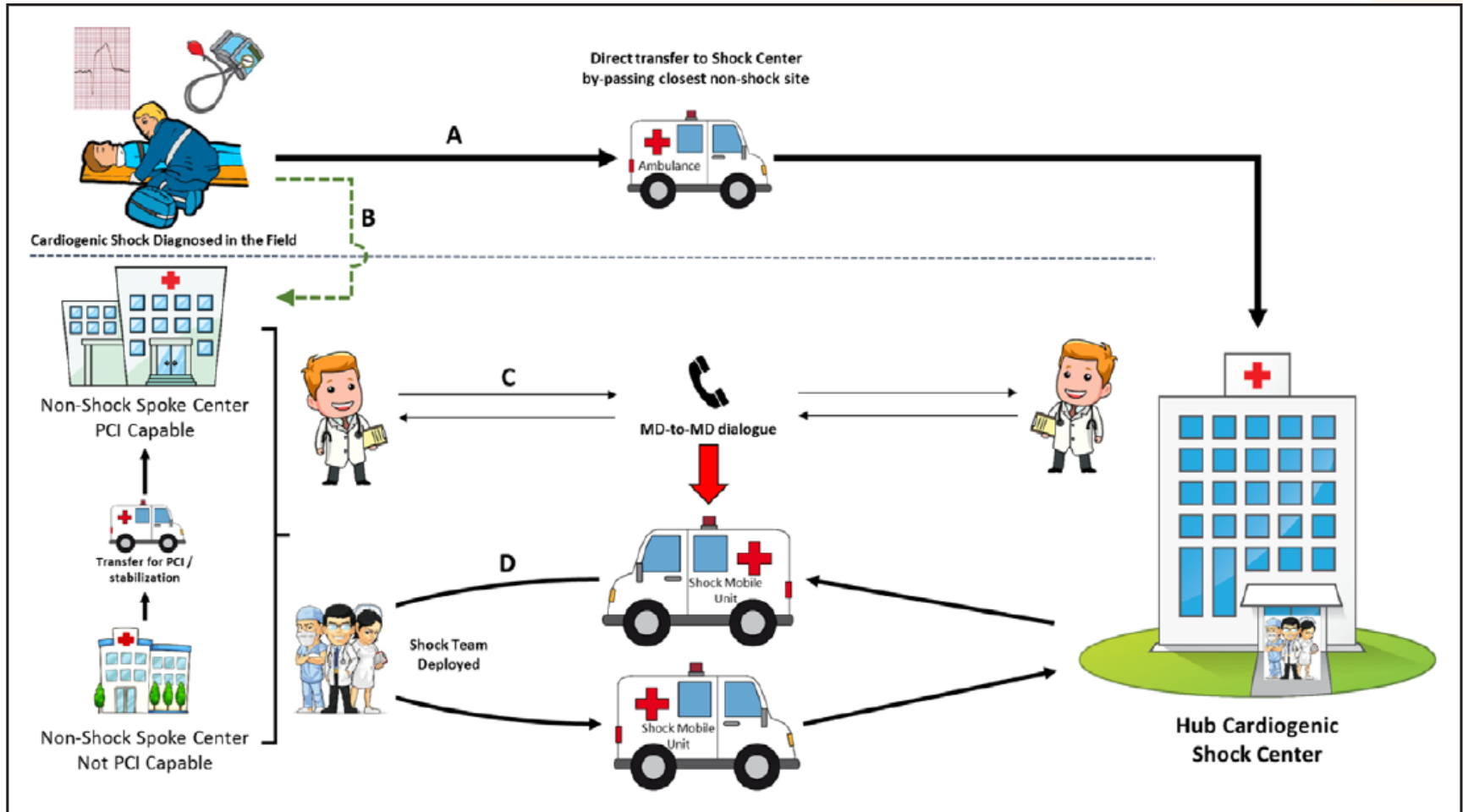
Clinical Volume and Patient Outcomes

- Hospital and medical provider volumes consistently and positively associated with survival in medical and surgical care.
- Meta-analysis of 15 PCI studies and 7 CABG studies, including >1 million patients from >2000 hospitals reported lower in-hospital mortality in large-volume (>600 cases) PCI and CABG centers
- Study from Nationwide Inpatient Sample reported that hospitals treating >107 cases/yr more frequently provided early revascularization, VAD's, ECMO, and hemodialysis

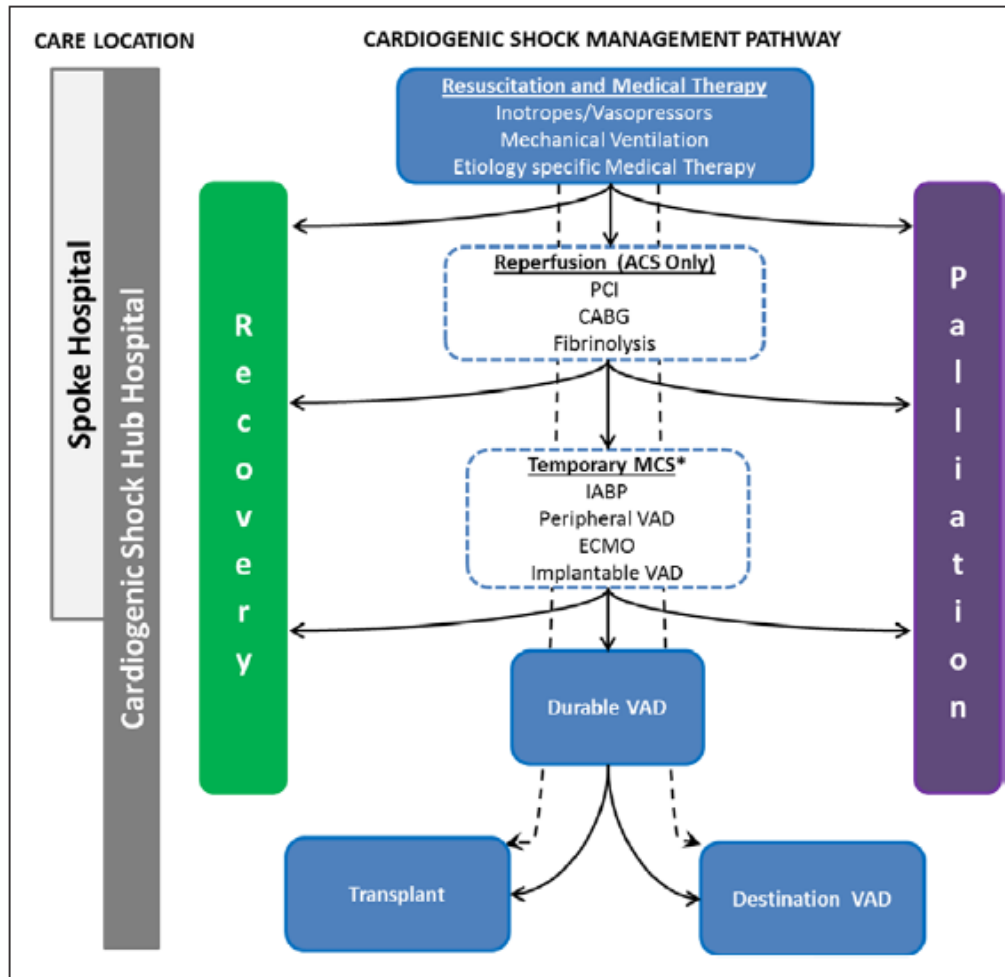
CS Center Characteristics

Hospital	Critical Care Unit	Medical and Technological Capabilities	Onsite Medical Consultants	Professional Consultants	Academic Characteristics
Tertiary care center	CICU or ICU	24-h/7-d Primary PCI	Cardiology: interventionalists, echocardiographers, advanced HF/transplantation specialists Electrophysiology	Pharmacy	CS research or participation in national registries
			Palliative care		
			Neurology		
High-volume cardiovascular center	24-h/7-d In-house unit coverage by MD, PA, NP, or resident	Cardiac surgery	Cardiologist-intensivists or intensive care	Social work	Quality improvement and auditing
	1:1 Nurse-to-patient ratio	IABP	Cardiac surgery	Respiratory therapist	Trainee education
	Vasoactive infusions	Percutaneous VAD	Nephrology	Physical therapy	
	Mechanical ventilation	Implantable VAD	Palliative care	Occupational therapy	
	Invasive cardiac and hemodynamic monitoring	ECMO: mobile ECMO team and eCPR capabilities		Dietician	
	CRRT	Echocardiography		Pharmacy	
	Temporary transvenous pacing			Social work	

Proposed Regional System of Care for CS



Cardiogenic Shock Management Pathway



Management of CS

- Coronary reperfusion the mainstay evidence-based therapeutic intervention for patients with acute MI presenting with CS
- When early invasive approach cannot be completed in timely fashion, fibrinolysis can be considered in CS associated with STEMI
- CULPRIT-SHOCK trial compared culprit vessel-only PCI with immediate multivessel PCI, showed the former to be better with respect to all-cause mortality at 30 days

Medical Management of CS Patient

- Management of CS requires primary care team to coordinate the multidisciplinary delivery of patient monitoring, pharmacological therapies, and mechanical technologies
- Critical Care Unit Monitoring
 - **Central venous catheter (CVC) insertion-** can allow for administration of vasoactive medications and monitoring of CVP and mixed venous O₂
 - **Pulmonary artery catheter (PAC)-** can confirm presence and severity of CS, involvement of RV, vascular resistance of pulmonary and systemic arterial beds

Mean Arterial Pressure

- In general, goals of therapy should focus instead on restoring and maintaining satisfactory tissue perfusion
- Commonly used MAP targets (65 mm Hg) are often extrapolated from non-CS populations
- Hemodynamic monitoring should complement (not replace) other markers of end-organ perfusion in CS
 - Arterial lactate, mixed venous O₂, urine output, creatinine, liver function tests, mental status, temperature, etc.

Vasopressors and Inotropes

- Vasoactive medications are often used in management of patients with CS
- Despite frequent use, few clinical outcome data are available to guide the initial selection of vasoactive therapies in patients with CS

Mechanism of Action of Common Vasoactive Medications

Medication	Usual Infusion Dose	Receptor Binding				Hemodynamic Effects
		α_1	β_1	β_2	Dopamine	
Vasopressor/inotropes						
Dopamine	0.5–2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	–	+	–	+++	$\uparrow\text{CO}$
	5–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+	+++	+	++	$\uparrow\uparrow\text{CO}$, $\uparrow\text{SVR}$
	10–20 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+++	++	–	++	$\uparrow\uparrow\text{SVR}$, $\uparrow\text{CO}$
Norepinephrine	0.05–0.4 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	++++	++	+	–	$\uparrow\uparrow\text{SVR}$, $\uparrow\text{CO}$
Epinephrine	0.01–0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	++++	++++	+++	–	$\uparrow\uparrow\text{CO}$, $\uparrow\uparrow\text{SVR}$
Phenylephrine	0.1–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+++	–	–	–	$\uparrow\uparrow\text{SVR}$
Vasopressin	0.02–0.04 U/min	Stimulates V_1 receptors in vascular smooth muscle				$\uparrow\uparrow\text{SVR}$, $\leftrightarrow\text{PVR}$
Inodilators						
Dobutamine	2.5–20 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+	++++	++	–	$\uparrow\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Isoproterenol	2.0–20 $\mu\text{g}/\text{min}$	–	++++	+++	–	$\uparrow\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Milrinone	0.125–0.75 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Enoximone	2–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Levosimendan	0.05–0.2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Myofilament Ca^{2+} sensitizer, PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$

Management Considerations in Types of CS

Cause or Presentation of CS	Vasoactive Management Considerations	Hemodynamic Rationale
Classic wet and cold	Norepinephrine or dopamine ¹⁴⁴ Inotropic agent ^{210,211*}	This subtype has low CI and high SVR. Consider hemodynamic stabilization with norepinephrine (preferred in ↑HR or arrhythmias) or dopamine (↓HR preferred but associated with higher risk of arrhythmias) Consider addition of inotropic agent when stabilized and after revascularization (MI only)
Euvolemic cold and dry	Norepinephrine or dopamine ¹⁴⁴ Inotropic agent ^{210,211} Small fluid boluses	Consider hemodynamic stabilization with norepinephrine (preferred in ↑HR or arrhythmias) or dopamine (↓HR preferred but associated with higher risk of arrhythmias) Consider addition of inotropic agent when stabilized and after revascularization (MI only) LVEDP may be low, and patients may tolerate fluid boluses
Vasodilatory warm and wet or mixed cardiogenic and vasodilatory	Norepinephrine Consider hemodynamics-guided therapy	This subtype has low SVR
RV shock	Fluid boluses ^{144,145} Norepinephrine, dopamine, or vasopressin ^{144,212,213} Inotropic agents ^{144*} Inhaled pulmonary vasodilators ²¹⁴	Hemodynamic goals include maintaining preload, lowering RV afterload (PVR), treating absolute or relative bradycardias, and maintaining atrioventricular synchrony Dopamine (↓HR preferred but associated with arrhythmia risk) Vasopressin may raise SVR and have neutral effect on PVR Consider adding or transitioning to inotrope after initial hemodynamic stabilization and revascularization
Normotensive shock	Inotropic agent or vasopressor	Initial inotropic therapy may be appropriate given that this subtype has SBP >90 mmHg and relatively high SVR

Valvular Associated CGS

Aortic stenosis	Phenylephrine or vasopressin In patients with reduced LVEF, echocardiography- or PAC-guided dobutamine titration	Shock caused by aortic stenosis is an afterload-dependent state Inotropy may not improve hemodynamics if LVEF is preserved Definitive therapies will be defined by underlying cause and may include surgical aortic valve replacement or balloon valvuloplasty and/or transcatheter aortic valve replacement
Aortic regurgitation	Dopamine Temporary pacing	Maintaining an elevated HR may shorten diastolic filling time and reduce LVEDP Definitive therapies will be defined by underlying cause and may include surgical aortic valve replacement
Mitral stenosis	Phenylephrine or vasopressin Esmolol or amiodarone	Shock resulting from mitral stenosis is a preload-dependent state Avoiding chronotropic agents, slowing the HR (and thereby increasing diastolic filling time), and maintaining atrioventricular synchrony may improve preload Definitive therapies will be defined by underlying cause and may include surgical mitral valve replacement or balloon valvuloplasty
Mitral regurgitation	Norepinephrine or dopamine Inotropic agents* Temporary MCS, including IABP ¹⁴⁴	After hemodynamic stabilization with vasopressor, consider addition of inotropic agent Afterload reduction may help reduce LVEDP IABP may reduce regurgitation fraction by reducing afterload and increasing CI Definitive therapies will be defined by underlying cause and may include surgical mitral valve replacement/repair and percutaneous edge-to-edge repair

Care Bundles and Prevention of Critical Care Complications

- Critically ill patients are at higher risk of ventilator-associated pneumonia, delirium, ICU-acquired weakness, central-line associated bloodstream infections (CLABSI), stress ulcers, and venous thromboembolism
- Bundles of best-practice prevention strategies can help reduce complications and improve outcomes in critically ill patients

Prevention Bundles for CS Patients

- ABCDE bundle (awakening and breathing coordination, delirium monitoring/management, and early exercise mobility)
- Ventilator bundle
- Central line bundle
- Stress ulcer prophylaxis
- Deep vein thrombosis prophylaxis

Mechanical Ventilation

- Insufficient evidence to recommend specific ventilation modes, strategies, or end points in CS population
- Clinicians should be aware of few basic physiological interactions when managing CS patients on MV

Positive End-Expiratory Pressure (PEEP)

- Airway (and alveolar) pressure above atmospheric pressure at conclusion of expiratory phase
- Improves gas exchange, lung recruitment, airway patency
- Can counterbalance hydrostatic forces that lead to pulmonary edema
- Can reduce LV afterload by decreasing transthoracic pulmonary pressures
- In patients with ↓ RV function, can reduce pulmonary vascular resistance and thereby increase CI

Continuous Renal Replacement Therapy

- Among patients with CS, a reported 13% to 28% develop acute kidney injury
- Up to 20% require renal replacement therapy
- CS patients often do not tolerate fluid shifts with intermittent hemodialysis
- CRRT is more commonly used (allows for more gradual removal of fluid and toxins)
- Can be considered with stage 2 AKI (defined as increase in serum creatinine ≥ 2.0 times baseline and urine output < 0.5 ml/kg/h for ≥ 12 hours)

Mechanical Circulatory Support and Cardiac Transplantation

- MCS can be classified into temporary or durable devices
 - Temporary devices are inserted either percutaneously or surgically
 - Insertion of temporary MCS as bridge to decision can permit hemodynamic optimization, allow reversal of CS-mediated end-organ failure, and provide additional time for medical and social assessment
 - Durable MCS devices (surgically implanted) can be used as a bridge to recovery, as BTT, or as destination therapy

Temporary MCS devices

- Intra-aortic balloon pump (IABP)
- TandemHeart
- Micro-Axial Impella 2.5, CP, and 5.0
- CentriMag ventricular assist system
- Data on percutaneous MCS devices in CS are still quite limited
- One meta analysis in 2009 showed patients with percutaneous MCS had higher CI, higher MAP, lower PCWP's, and more frequent bleeding complications with no difference in mortality

- In USpella registry of patients with CS treated with Impella devices before PCI, MCS placement resulted in improved survival to hospital discharge
- No available trial results for iVAC and HeartMate Percutaneous Heart Pump with respect to CS and mortality

IABP

- Still most widely used MCS device in CS
- 7F to 8F catheter positioned in the descending thoracic aorta, distal to L subclavian artery
- Timed to inflate during diastole, increasing coronary perfusion
- Prior to 2012, IABP use was Class I recommendation
- Due to IABP-SHOCK II trial, IABP use has been downgraded to Class IIIA recommendation for routine use in CS

Extracorporeal Membrane Oxygenation (ECMO)

- Veno-venous (VV) ECMO- used to support patients with isolated respiratory failure and no significant cardiac dysfunction
- Veno-arterial (VA) ECMO- used to support both cardiovascular and respiratory systems; **preferred system in CS patients**
- Relative contraindications- advanced age (>75 years), life expectancy <1 year, severe PVD, advanced liver disease, contraindications to systemic anticoagulation, and neurological injury

VA ECMO Complications

- Distal limb ischemia
- Thromboembolism/stroke
- Bleeding/hemolysis
- Infection
- Aortic valve insufficiency
- Resultant increase in LV afterload, which may to inadequate unloading of LV

ECMO Outcomes

- Per ELSO (Extracorporeal Life Support Organization) registry, 56% of patient survived to decannulation from ECMO, 41% survived to discharged (when ECMO used for cardiac reason)
- Patients with potentially reversible cause of CS (e.g. acute myocarditis) do better
- Patients with postcardiotomy CS do worse
- No randomized trials assessing ECMO effectiveness with respect to CS

	IABP	TandemHeart™	Impella™ 2.5/CP	Impella™ 5.0	ECMO
Mechanism	Pulsatile	Centrifugal (continuous)	Axial (continuous)	Axial (continuous)	Centrifugal (continuous)
CO or Flow	↑ CO 0-0.5 L/min	Flow ~ 4.0 L/min	Flow 2.5-4.0 L/min	Flow up to 5.0 L/min	Flow >4.0 L/min
Size	7-8 Fr	Arterial: 15-19 Fr Venous: 21 Fr	12-14 Fr	21 Fr	Arterial: 14-19 Fr Venous: 17-24 Fr
Advantage(s)	Readily available Familiarity Rapid insertion Easy to adjust No extracorporeal blood	Independent of rhythm Robust CO support	Independent of rhythm Easy insertion No extracorporeal blood	Robust support No extracorporeal blood	Independent of rhythm Robust CO support Pulmonary support
Disadvantage(s)	Minimal ↑CO Requires stable rhythm No effect on mean BP or lactate	Difficult insertion Requires transseptal puncture Vascular complications	Vascular complications Hemolysis	Vascular complications Hemolysis Requires surgical insertion	Vascular complications May not unload heart (may need venting) Regional hypoxemia

Abbreviations: CO, Cardiac Output; ECMO, extra-corporeal membrane oxygenation; Fr, French; IABP, intra-aortic balloon pump

CentriMag ventricular assist system

- Ventricular assist device that can be used in either univentricular or biventricular fashion (for short-term)
- Central cannulation performed via median sternotomy
- Device consists of magnetically levitated rotor with ability to deliver flows up to 10 L/min
- Inflow cannula placed either in left atrium or into LV apex; outflow cannula sutured into ascending aorta
- For RV support, inflow sewn into right atrium, and outflow cannula placed in main PA

Durable Ventricular Assist Devices

- Durable MCS can be implanted in a bridge to recovery, bridge to a bridge, BTT, or destination therapy strategy in appropriately selected patients with CS
- Current devices are continuous-flow devices and include an inflow cannula placed into LV cavity and outflow graft sutured into ascending aorta
- HeartMate II and HeartWare HVAD make up >95% of all FDA-approved durable MCS devices currently implanted

INTERMACS

- Implantation of durable MCS and mortality related to patient's clinical status, which is determined by INTERMACS scoring
- Implantation of durable MCS in patients with INTERMACS 1 or 2 associated with substantially higher mortality compared with lower-acuity patients

Level	Description	Time to MCS
1	“Crashing and burning” – critical cardiogenic shock	Within hours
2	“Progressive decline” – inotrope dependence with continuing deterioration	Within a few days
3	“Stable but inotrope-dependent” – describes clinical stability on mild-moderate doses of intravenous inotropes (patients stable on temporary circulatory support without inotropes are within this profile)	Within a few weeks
4	“Recurrent advanced heart failure” – “recurrent” rather than “refractory” decompensation	Within weeks to months
5	“Exertion intolerant” – describes patients who are comfortable at rest but are intolerant of exercise	Variable
6	“Exertion limited” – a patient who is able to do some mild activity but fatigue results within a few minutes or any meaningful physical exertion	Variable
7	“Advanced NYHA 3” – describes patients who are clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent	Not a candidate for MCS

Heart Transplantation

- Remains the preferred option for patients requiring biventricular MCS
- Up to 44% of MCS device implantations in INTERMACS profile 1 and 2 are performed with BTT strategy
- Low number of available organs coupled with unpredictable donor availability make transplantation in acute setting of CS an unreliable primary therapy

Palliative Care in CS

- Palliative care can reduce physical and emotional distress, improve quality of life, and complement curative therapy in advanced HF
- Despite burdensome symptoms and multiple comorbidities, only 6% to 8% are referred for palliative care services during hospitalization
- Reasons for low referral rates include limited knowledge about role of palliative care and uncertainty about differences between standard HF care and palliative care

Initiation of Palliative Care Discussion

- Predictors of all-cause death in advanced HF population include :
 - Low EF
 - Low SBP
 - Low hemoglobin
 - Low Na⁺ level
 - High creatinine
 - High NT-BNP level
 - High NYHA class
 - Inpatient Status
 - History of ischemic heart disease
 - Atrial fibrillation
 - HF ≥ 6 months
 - Heart rate > 70 bpm
 - Not being treated with RAAS or β-blocker

Future Directions

- Research on addressing clinical knowledge-treatment gaps needed in managing CS
- Development of risk stratification tools that can be used to aid in treatment decisions
- Revascularization rates in patients with CS with MI remain low (50%-70%) in registries.
 - Improvement in revascularization rates may increase CS survival

Summary Points

- Before routine use of early revascularization, MI-associated CS had in-hospital mortality >80%
 - After advent of revascularization, mortality is 27-51% (remains high)
- Common physiology among all subtypes of CS is low cardiac index (CI), but ventricular preload (PCWP or CVP), volume, and systemic vascular resistance may vary
- All patients with CS should be evaluated with ECG, CXR, and echocardiogram

Summary

- Direct relationship between in-hospital mortality and hospital volume
 - Mortality as high as 42% in hospitals treating <27 cases per year, per Nationwide Inpatient Sample
 - Establishing systems of care with high-volume hospitals as hubs has potential to improve patient outcomes
- Early revascularization (either PCI or CABG) should be key for all suitable patients with ACS-related CS, including those with uncertain neuro status or who have received prior fibrinolysis

Summary

- Pulmonary artery catheterization remains an important tool for diagnosis and management of CS
- Norepinephrine (Levophed) is associated with fewer arrhythmias and may be the vasopressor of choice in many CS patients
- Temporary over durable MCS as first-line option should be considered when immediate stabilization is needed to enable recovery of the heart

Summary

- Long-term/durable MCS devices can be considered primary devices in patients with CS who are not likely to recover without long-term MCS support, have capacity for meaningful recovery, and do not have irreversible organ dysfunction, systemic infections, or other contra-indications
- All patients being evaluated for durable MCS should be evaluated for cardiac transplantation
- Palliative care benefits and limitations should be discussed throughout the entire process of managing patients with CS (including at start)

Conclusions

- CS is a multifactorial and hemodynamically diverse high-acuity illness that is frequently associated with multisystem organ failure.
- Complexity of CS requires widespread application of best-care practice standards and a coordinated regionalized approach to CS
- Further research and new medical treatment options are needed to address significant patient morbidity and mortality associated with this condition

Thank You

