CONSENSUS STATEMENT

HEART FAILURE RELATED CARDIOGENIC SHOCK: AN ISHLT CONSENSUS CONFERENCE CONTENT SUMMARY

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ABSTRACT

In recent years, there have been significant advancements in the understanding, risk-stratification, and treatment of cardiogenic shock (CS). Despite improved pharmacologic and device-based therapies for CS, short-term mortality remains as high as 50%. Most recent efforts in research have focused on CS related to acute myocardial infarction, even though heart failure related CS (HF-CS) accounts for >50% of CS cases. There is a paucity of high-quality evidence to support standardized clinical practices in approach to HF-CS. In addition, there is an unmet need to identify disease-specific diagnostic and risk-stratification strategies upon admission, which might ultimately guide the choice of therapies, and thereby improve outcomes and optimize resource allocation. The heterogeneity in defining CS, patient phenotypes, treatment goals and therapies has resulted in difficulty comparing published reports and standardized treatment algorithms. An International Society for Heart and Lung Transplantation (ISHLT) consensus conference was organized to better define, diagnose, and manage HF-CS. There were 54 participants (advanced heart failure and interventional cardiologists, cardiothoracic surgeons, critical care cardiologists, intensivists, pharmacists, and allied health professionals), with vast clinical and published experience in CS, representing

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42 centers worldwide. State-of-the-art HF-CS presentations occurred with subsequent breakout sessions planned in an attempt to reach consensus on various issues, including but not limited to models of CS care delivery, patient presentations in HF-CS, and strategies in HF-CS management. This consensus report summarizes the contemporary literature review on HF-CS presented in the first half of the conference (part 1), while the accompanying document (part 2) covers the breakout sessions where the previously agreed upon clinical issues were discussed with an aim to get to a consensus.
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cardiogenic shock; mechanical circulatory support; consensus statement; heart failure shock; global perspective

INTRODUCTION

Cardiogenic shock (CS) presents a significant challenge to the medical community, and no consensus exists regarding the best practices in initial triage, evaluation, and management. While several etiologies can cause CS, most commonly, it may be associated with decompensated heart failure (HF-CS) or acute myocardial infarction (AMI-CS). With improving treatments for AMI and chronic HF, more patients survive to develop HF-CS as the final common pathway of deterioration for patients with impaired ventricular function. Despite improved pharmacologic and device-based therapies for CS, mortality remains as high as 50%.[1] Most of the guidance in published literature refers to AMI-CS due to the existing trial evidence. Data from American and European multicenter registries have recently highlighted a rising prevalence of HF-CS.[2,3] In the absence of randomized controlled trials enrolling HF-CS patients, there are significant gaps in knowledge of risk assessment, use of temporary mechanical circulatory support (tMCS) device therapies, and treatment goals in patients presenting with HF-CS.[4] As a result, mortality and morbidity associated with HF-CS have remained high.

An international consensus conference commissioned by the International Society for Heart and Lung Transplantation (ISHLT) took place on April 26, 2022, in Boston, Massachusetts, USA, to ascertain the current practices in the management of HF-CS. The conference was attended by 54 participants from 42 centers in 11 countries. Key opinion leaders in the fields of interventional and heart failure cardiology, critical care, cardiothoracic surgery, and pharmacy were invited to participate (see appendix). Of note, in-person attendance was limited from Asia, Australia, and other international sites due to the ongoing COVID-19 pandemic.

Within that context, the participants were organized into three task forces, with section leaders to address three key topics related to HF-CS:

Task Force 1: (Chairs: Phyllis Billia and Varinder Randhawa) "*Focus on Centers: Models of CS care*" with discussions on systems of care in CS, with global perspectives on implementation and integration CS care, teams, and networks.

Task Force 2: (Chairs: Sharon Chih and Christopher Barnett) "*Focus on Patients: Presentations in HF-CS*" with discussions on the approach to the initial evaluation of patients in HF-CS, phenotypes, risk-stratification, and goals of treatment.

Task Force 3: (Chairs: Stephan Ensminger and Jaime Hernandez Montfort) "*Focus on Management: Strategies in HF-CS management*" with discussions on management of HF-CS, hemodynamic mechanisms, and escalation/de-escalation strategies using tMCS.

The morning session at the conference consisted of presentations from each of the three task forces who had multiple discussions via teleconference in the months before the in-person meeting. The afternoon session included breakout sessions where the previously agreed upon clinical issues were discussed with an aim to get to a consensus. This manuscript focuses on the presentations delivered in the morning, while the accompanying document covers the consensus report from the breakout sessions. Given the rapidly evolving literature, this publication is not intended to be a state-of-the-art review. Instead, this document encapsulates knowledge from the three task force perspectives and is the basis from which the consensus conclusions were derived. Since the conference, scientific statements and guidelines on various aspects of HF-CS and tMCS have been published, and these too have been summarized herein. Throughout the document, CS refers specifically to HF-CS since this is the area of the slightest evidence and where expert consensus in the absence of robust trial data is urgently needed.

CURRENT STATE-OF-THE-ART PRACTICES IN HF-CS

Section 1: Systems of care in HF-CS

Global perspective on implementation and integration of CS care

CS has a worldwide prevalence with a very high morbidity and mortality regardless of geographic location and across varying levels of access to care. As interventions and technologies improve, care systems for CS patients must evolve as well. Best practices in HF-CS management should be framed within the context of a health care system's capacities, aiming to promote global CS diagnostic awareness and to provide simple yet vital interventions to support patient stabilization.

Patient outcomes are impacted by rapid recognition and prompt institution of CS interventions, including transfer to a tertiary care center. The initial site of CS presentation for the vast majority of patients is at rural or community hospitals.[5,6] While research has supported using shock teams with triage and management protocols,[7–10] such specialized care structures are still globally rare and limited to tertiary and quaternary care centers[6] (Table 1A). There is considerable resource variation across centers regarding available support devices and specialists. For instance, in a 2020 survey addressing variability in caring for patients with CS, 45% of clinicians reported practicing at sites without advanced HF capabilities, 16% practiced at sites without on-site cardiothoracic surgery and 6% practiced at sites that did not offer 24/7 coronary intervention coverage – and these respondents practiced in well-resourced healthcare systems.[11] Moreover, the CS population remains very heterogeneous, requiring multi-dimensional levels of care.[12] Several centers have also created mobile shock and extracorporeal membrane oxygenation (ECMO) programs that operate under the purview of multi-disciplinary shock team members.[13,14] Mnemonics or acronyms (e.g. CALL-SHOCK) have been used to facilitate provider CS awareness and recall of CS diagnostic features, incorporating key clinical characteristics and laboratory abnormalities suggestive of multisystem organ dysfunction.[15] The Society for Cardiac Angiography and Intervention (SCAI) staging for CS has provided a common taxonomy to allow assessment of shock severity across clinical specialties and institutions.[16]

Table 1A Tiers of Shock Centers and Shock Team Composition.

	Tier 4	Tier 3	Tier 2	Tier 1
Description	Non-PCI capable	24/7 Cath Lab Can do tMCS (IABP, Impella)	Tier 3 + CT surgery VA-ECMO Dedicated CCU	Tier 2+: LVAD/HT
CS goals	Identify CS Pharmacologic support and transfer	Identify and Stabilize CS +/– PCI +/– Initiate tMCS Identify refractory CS and transfer	Identify, Stabilize, and Manage CS PCI Initiate, Manage, and Escalate tMCS Bridge to Recovery Identify Refractory CS and Transfer	Identify, Stabilize, and Manage CS PCI Initiate, Manage, and Escalate tMCS Bridge to Recovery LVAD, OHT
Shock Team Needed	No	Yes (if patients will stay after tMCS implantation) +/– Consultation with Tier 2/1 Team	Yes	Yes
Shock Team Members		IC Intensivist	IC Intensivist HF CTS	IC Intensivist HF CTS
Notes	Needs relationships w/higher tier centers	Wide variation Needs relationships w/Tier 2		

CCU, cardiac intensive care unit; CS, Cardiogenic shock; CTS, cardiothoracic surgery; ECMO, extracorporeal membrane oxygenation; HF, heart failure; HT, heart transplantation; IABP, intra-aortic balloon pump; IC, interventional cardiology; LVAD, left ventricular assist device; PCI, percutaneous intervention; tMCS, temporary mechanical circulatory support.

Table 1B Suggested Role of Multi-Disciplinary Shock Team Members.

Role	Team members
Identifying shock	Often pre-shock team involvement
Establishing shock severity	IC/HF/CTS/Intensivist
Determining tMCS candidacy	IC/HF/CTS +/– Intensivist
tMCS insertion	IC/CTS +/– HF
tMCS weaning/escalation management	IC/HF/CTS/Intensivist
Management of tMCS complications	IC/CTS + consultants
ICU management and care coordination	IC/HF/CTS/Intensivist
Non cardiac organ dysfunction	IC/HF/CTS/Intensivist + consultants
Determining candidacy for durable heart replacement therapies	HF/CTS
End of life care/discussions	IC/HF/CTS/Intensivist + palliative care

CTS, cardiothoracic surgery; HF, heart failure; IC, interventional cardiology; tMCS, temporary mechanical circulatory support.

Multidisciplinary shock teams

Multidisciplinary shock teams have evolved in response to the changing landscape and increased complexity surrounding care of CS patients. A 'shock team' aims to facilitate the rapid identification of CS, phenotyping, decision-making, treatment plan, and implementation, as well as ongoing patient and device evaluation.[7] Several centers have demonstrated improvements in survival with the institution of multidisciplinary CS teams.[7,10,17] A recent analysis of the multi-institutional Critical Care Cardiology Trials Network (CCCTN) reported an improved ICU survival for centers with and without shock teams (mortality of 23% vs. 29% respectively, adjusted OR: 0.72; 95% CI: 0.55–0.94; $p = 0.016$) in North American centers.[18] However, interpretation and application of the findings remain limited due to the nonrandomized nature, use of historical controls from a specific geographical area.

Patients with CS receiving intensive care treatments often present with mixed shock and may require invasive cardiac hemodynamic management, advanced respiratory therapies, or renal replacement therapies.[19] It is appropriate that palliative care are involved early during the course of CS or when specific criteria are present.[20] Hence, shock team composition varies by institution based on local expertise and specialty availability (Table 1B). Centers with shock teams also demonstrated increased use of pulmonary artery catheters (PAC), less tMCS use overall but higher utilization of durable MCS and heart transplantation.[18,21–23]

SECTION 2: APPROACH TO PATIENTS PRESENTING IN HF-CS

Initial assessment and prognostication in HF-CS

The initial patient clinical assessment should be rapid, focusing on the patient vital signs and the critical components of a clinical examination that will assist in establishing the diagnosis of HF-CS and assessing their tissue perfusion, mental status, and volume status. Emphasis is placed on identifying the underlying triggers, evaluating the severity of acute HF, and recognizing end-organ injuries.

Defining HF-CS

There is lack of a standardized nomenclature and definition of HF-CS. (Table 2) The definition of CS used in clinical trials has been associated with AMI-CS. It includes systolic blood pressure $<$ 90 mm Hg for ≥30 minutes (or support to maintain blood pressure), a cardiac index ≤ 2.2 liter·min^{-1}·m^{-2}, pulmonary capillary wedge pressure ≥ 15 mm Hg, and markers of end-organ hypoperfusion (urine output $<$ 30 ml/h or $<$ 0.3–0.5 ml/kg/h, altered mental status, cool extremities, lactate $>$ 2 mmol/liter).[7,8,10,24–26] Compared with AMI-CS, HF-CS often presents with exaggerated hemodynamic derangements representing congestion instead of hypotension, making the clinical assessment of shock severity challenging.[4] Hence criteria that define the HF-CS syndrome are

Table 2 Definitions of Cardiogenic Shock in Literature.

AHA/ACC/ HFSA 2022	Hypotension: SBP < 90 mm Hg for >30 min OR mean BP < 60 mm Hg for >30 min OR requirement of vasopressors to maintain SBP ≥ 90 mm Hg or mean BP ≥ 60 mm Hg Hypoperfusion: Poor mentation, cold extremities/livedo reticularis, urine output <30 ml/h, lactate >2 mmol/liter
ESC 2021	Diagnosis of cardiogenic shock mandates the presence of clinical signs of hypoperfusion (cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure). Biochemical manifestations of hypoperfusion (elevated serum creatinine and lactate, metabolic acidosis). Hypoperfusion is not always accompanied by hypotension
CSWG	One of the following: ● Sustained episode of SBP ≤90 mm Hg for ≥30 min or need for vasoactive agents to maintain BP. ● CI < 2.2 liter/min/m^2 due to cardiac dysfunction. ● Use of temporary MCS.
CCCTN	All of the following: ● Sustained episode of SBP <90 mm Hg for ≥30 min or need for vasoactive agents to maintain BP; AND ● Evidence of end-organ hypoperfusion (altered mental state, oliguria, acute kidney/ hepatic injury, OR lactate >2 mmol/liter) ● If available, CI < 1.8 or < 2.2 liter/min/m^2 (on inotrope) with elevated filling pressures.
Mayo Clinic (SCAI C)	Hypoperfusion defined by the presence of any of the following: ● Lactate >2 mmol/liter. ● Urine output <720 ml during the first 24 hour. ● Creatinine increase ≥0.3 mg/dL during the first 24 hour.

AHA/ACC/HFSA, American Heart Association/American College of Cardiology/Heart Failure Society of America; CI, cardiac index; CCCTN, Critical Care Cardiology Trials Network; CSWG, Cardiogenic Shock Working Group; ESC, European Society of Cardiology; MCS, mechanical circulatory support; SBP, systolic blood pressure.

circulatory failure attributable to cardiac dysfunction that results in abnormal tissue perfusion: in other words, congestion with or without hypotension.[27] Hyperlactatemia and organ dysfunction are often used as objective evidence of tissue hypoperfusion, demarcating the continuum of decompensated HF and CS. However, it is important to emphasize that a single data point gleaned during patient evaluation is insufficient to diagnose or rule out CS. Additionally, the accuracy of individual criterion will vary based on the presence or absence of pre-existing cardiac dysfunction HF. For example, a cut-off of systolic blood pressure < 90 mm Hg is commonly applied in clinical studies for dichotomization,[8] but was in fact derived only from expert consensus[16,28] and can potentially (falsely) capture stable individuals with chronic systolic HF. Similarly, defining CS based on a combination of hypotension and organ dysfunction, such as abnormal liver and/or renal function, can also capture patients with decompensated HF who do not manifest CS.[29] Lastly, hypotension may be absent in patients presenting with CS, especially in younger individuals who have the ability to compensate with high vascular tone. Heart rate thresholds to assist with CS diagnosis are also challenging to assign, as patients with CS may present with inappropriate bradycardic, compensatory sinus tachycardia, or tachyarrhythmias.

Early recognition of CS

Rapid recognition of CS is imperative for patient survival. Delays in shock recognition and management can lead to progressive myocardial systolic and diastolic dysfunction, instigation of the systemic inflammatory response system, and end-organ failure.[30,31] After assessing patient vitals, clinical assessment of tissue perfusion (coolness vs warmth) and congestion profile is integral for rapidly triaging these patients. Forrester first developed a clinical classification scheme for the assessing patients with AMI-CS, which has since been translated into the advanced HF population.[32,33] This simple scheme has been widely adopted into practice and offers a valuable construct for the initial evaluation of patients with acute HF but is alone inadequate for directing therapeutic management of HF-CS. While shock cannot be ruled out in patients who are warm to touch, coolness with skin mottling contributes to the diagnosis of CS.[34] Additionally, serial assessment of urine output and patient's mental status are critical for assisting with the CS diagnosis. A Glasgow coma score (GCS) of < 15 may be used as the threshold for abnormal mentation, although any somnolence or waxing and waning mentation should raise concern.

Initial fundamental testing

Table 3 outlines the critical tests integral for establishing a CS diagnosis and risk assessment. These include markers of generalized systemic hypoperfusion (plasma or whole blood lactate, serum bicarbonate, acidosis) and more specific markers of cardiac (troponin), renal (serum creatinine), or hepatic (alanine aminotransferase, aspartate aminotransferase, bilirubin) injury as well as providing an assessment of oxygen-carrying capacity and bleeding risk (hemoglobin, INR).

While not widely available across lower-resourced healthcare systems, lactate levels (either venous or arterial) are now considered integral to the assessment of CS severity and characterization of hemometabolic derangements[35,36]. A precise threshold for lactate elevation cannot be ascribed due to variability in assay values and the inability to differentiate lactate elevation secondary to decreased perfusion, reduced hepatic clearance or tissue hypoxia.[37] Nonetheless, a high lactate in a patient with other clinical signs and symptoms of CS should provoke further and rapid investigation. Serial lactate levels to quantify lactate clearance[38] is increasingly validated as the optimal prognostic marker and index of adequate resuscitation in CS with greater early (6–8 hours)[39,40] and later (24 hours)[40,41] clearance as well as threshold values[39] being associated with outcomes, including mortality. Beyond lactate, the severity of acidosis quantified by anion gap, pH, bicarbonate and base excess is associated with shock severity, non-cardiovascular organ failures and in-hospital mortality[36].

Given that shock can present with mixed etiology (e.g., sepsis in the presence of low LVEF and other vasoplegic or distributive shock states), it is important to differentiate between CS and other forms of shock. Evaluating mixed venous saturation and systemic vascular resistance, underlying infections (consider cultures, imaging and procalcitonin) in the context of patient presentation is helpful.

Prognostication and risk-stratification in CS

In the past 5 decades, over 30 outcome-prediction scores, indirectly aimed to quantify CS risk severity, have been developed. Most risk scores, however, have been validated in the setting of AMI-CS or are pertinent to patients

Table 3 Shock Labs at Baseline and for Re-Profiling.

HF-CS DYNAMIC RE-PROFILING PILLARS (Every 12-24h or if clinical changes)			
Clinical variables	**Investigations**	**Echography parameters**	**Hemodynamic assessment**
Physical examination • Mental status/ Consciousness • Perfusion • Urinary output • JVP • Cardiorespiratory examination Vital Signs • Blood pressure • Pulse pressure • Heart rate • Temperature • Respiratory rate • Oxygen saturation	• Electrocardiogram • Chest X ray • Lactate • Arterial blood gas • NTproBNP/BNP • Troponin • Coagulation • Comprehensive metabolic panel • Complete blood count *Optional* • *Procalcitonin* • *Microbiologic cultures*	• Diameters LV/RV • LVEF • TAPSE • PASP/IVC • LVOT VTI • Valvulopathies • Pericardial effusion *Optional:* • *Lateral mitral annulus peak systolic velocity* • *RVEF/S' Tricuspid annulus*	• RAP • PAP (s/d,m) • PCWP • CI/CO • SVO2 • CPO • SVR • TPG • LVSWi • RVSWi • PAPi

BNP, brain natriuretic peptide; CPO, cardiac power output; JVP, jugular venous pressure; LV and RVSWi, left and right ventricular stroke work index; LVEF, left ventricular ejection fraction; LVOT VTI, left ventricular outflow tract obstruction velocity time integral; PAPi, pulmonary artery pressure index; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVEF, right ventricular ejection fraction; SVR, systemic vascular resistance; TAPSE, Tricuspid Annular Plane Systolic Excursion; TPG, transpulmonary gradient.

with CS who are supported by tMCS devices.[42] Hence, available risk scores have important limitations that restrict their generalizability and routine use at the bedside, especially for those in HF-CS.[7,26] Moreover, they do not account for the dynamic clinical trajectory of the CS patient and fail to include complex hemodynamics and/or the presence of contemporary tMCS devices.

The SCAI staging system[43] discriminates for both short- and long-term mortality[44,45] including in patients with HF-CS[46] that has been validated in single and multicenter cohorts.[47] It was designed to track shock severity across all phases of hospital care, not limited to admission or initial assessment. Assessment of SCAI stage and serial changes may identify CS patients at high risk of either mortality or deterioration where early discussions regarding potential transfer to a shock center are indicated.[20,48] The CSWG-SCAI classification further improved clinical application of the staging system by providing clear definitions for hypotension, hypoperfusion and treatment intensity.[27] It provided new insights into the trajectory of hospitalized CS patients, focusing on an association of in-hospital mortality with both baseline and maximal SCAI stages. Significantly among the HF-CS population, key differences in presentation and clinical trajectories have been described for the HF-CS population as native heart survival, heart replacement therapies (durable left ventricular assist device/ LVAD or heart transplantation) or in-hospital mortality.[24,49] Using the CCCTN data, both clinician and algorithm-based applications of the 2019 SCAI stages identify a stepwise gradient of mortality risk; however, clinician-staging may better allocate higher0risk patients into advanced SCAI stages.[50] Updated algorithmic staging using the 2022 SCAI criteria and vasoactive-inotropic score further refines risk stratification.

Some known mortality in HF-CS include older age,[51,52] frailty,[53,54] and comorbid diseases·[54] Whilst age cut-offs have been proposed to select patients suitable for tMCS,[55] no consensus exists on the best method of evaluating frailty or age cut-offs in HF-CS.[12] Cardiac arrest, when accompanied by coma following return of a spontaneous circulation or evidence of established anoxic brain injury, is arguably the most potent predictor of outcome in CS and an adverse effect modifier.[49,56,57] However, early prognostication with cardiac arrest is challenging and not recommended until at least 72 hours post-targeted temperature management.[58] The use of peak inotrope and vasopressor dosing and calculation of vasoactive indices including the vasoactive inotropic score coupled with serum lactate levels, may guide the timing of transition to tMCS, but their clinical utility is poorly validated.[59]

Assessment of hemodynamic parameters using right heart catheterization/ PAC or echocardiography is desirable to define the severity of CS and guide initial therapy.[60] In fact, early use of PAC within 6 hours of presentation has been associated with lower mortality in HF-CS.[61] The major limitation of invasive hemodynamic monitoring tools is their availability coupled with expert interpretation. Despite recent data supporting the role of PAC in the phenotyping and management of CS,[60,62] hemodynamic data is rarely available during the early phase of hospital admission and resuscitation, and is mainly limited to academic and advanced HF centers.[62] Often, even in the presence of PAC, complete assessment using all the hemodynamic variables are not performed which has also been shown to impact in-hospital mortality across all SCAI stages.[60] Echocardiography is the standard, non-invasive tool in the acute setting. Quantitative assessment of left ventricular ejection fraction (LVEF) has historically been used and is prognostic at thresholds less than 40%,[63,64] but has limitations.[64] Doppler measurements, specifically the left ventricular outflow tract velocity time integral (VTI)[64] and left ventricular stroke work index[65] appear to have prognostic value beyond left ventricular ejection fraction (LVEF), in a general CICU population. The stoke volume index calculated using the LVOT VTI is an important measurement of forward flow and values $< 35\,ml/m^2$ are associated with higher hospital mortality independent of calculated cardiac index, which is likely driven by compensatory tachycardia.[66] The presence of right ventricular dysfunction, although common in the HF population, is associated with worse outcomes when assessed by PAC[46] or echocardiography,[67] although the latter technique has lesser sensitivity in detecting RV failure.

Phenotyping-CS

There is increasing emphasis on defining the specific phenotype of CS at each time point according to: (1) Type of ventricular dysfunction (right-, left- or bi-ventricular); (2) Presence of concomitant respiratory failure; (3) Etiology and type or acuity of HF; and (4) Shock severity based on hemodynamics and metabolic derangements, systemic inflammatory response, and vasopressor toxicity. Two clinical entities can be recognized within the subset of patients with CS based on the clinical presentation[1]: worsening chronic or advanced HF associated with reduced or preserved LVEF and[2] de novo HF, which may or may not evolve into a chronic HF state after the index

presentation.[49,68] While a distinction based on these two modes of presentation has relevance for in-hospital and post-discharge management, such a classification has limited utility in directing therapeutic intervention at the time of hospital presentation.

Phenotypes can be integrated into standard measures of CS severity, while sub-phenotyping can identify specific treatable underlying disease processes.[69] Using six variables driving mortality in their clustering algorithm, Zweck et al. derived three CS phenotypes (or clusters): non-congested, cardiorenal and cardiometabolic.[70] These phenotypes were subsequently validated in a mixed CICU population to predict both in-hospital and 1-year mortality.[71] Despite the significant heterogeneity of treatment effect that may exist between phenotypes in this population, sub-phenotyping using machine learning can facilitate precision medicine in this field.

SECTION 3: APPROACH TO MANAGEMENT OF HF-CS

Hemodynamic mechanisms of HF-CS

The pathophysiology of HF-CS often differs significantly from that of AMI-CS in that HF-CS often present with lower mixed venous oxygen saturations yet better oxygen extraction than AMI-CS. Via compensatory enhanced anaerobic metabolism, the HF-CS patient has had time for renal adaptation with better ability to buffer the acid during CS onset, leading to less acute pH derangement than patients with AMI-CS.[72] Additionally, the chronically dysfunctional HF-CS ventricle functions at higher right and left-sided filling pressures, both increasing following the onset of shock. Thus, in HF-CS, volume elevation often instigates dysfunction and improving the Frank-Starling relationship tends to improve cardiac output. Therefore, patients presenting with HF-CS require rapid assessment of volume status, aiming to reduce right and left heart congestion through diuresis (or ultrafiltration in non-responders) and to promote ventricular unloading with inotropes or tMCS. The use of neurohormonal antagonists and beta-blockers may contribute to hemodynamic deterioration and thus should be avoided in CS. In those without severe hypotension, vasodilators may be used to reduce ventricular afterload. Failing pharmacologic strategies, afterload reduction and ventricular decongestion can be achieved through the most readily available mechanisms at each center, including intra-aortic balloon pump or other forms of tMCS.

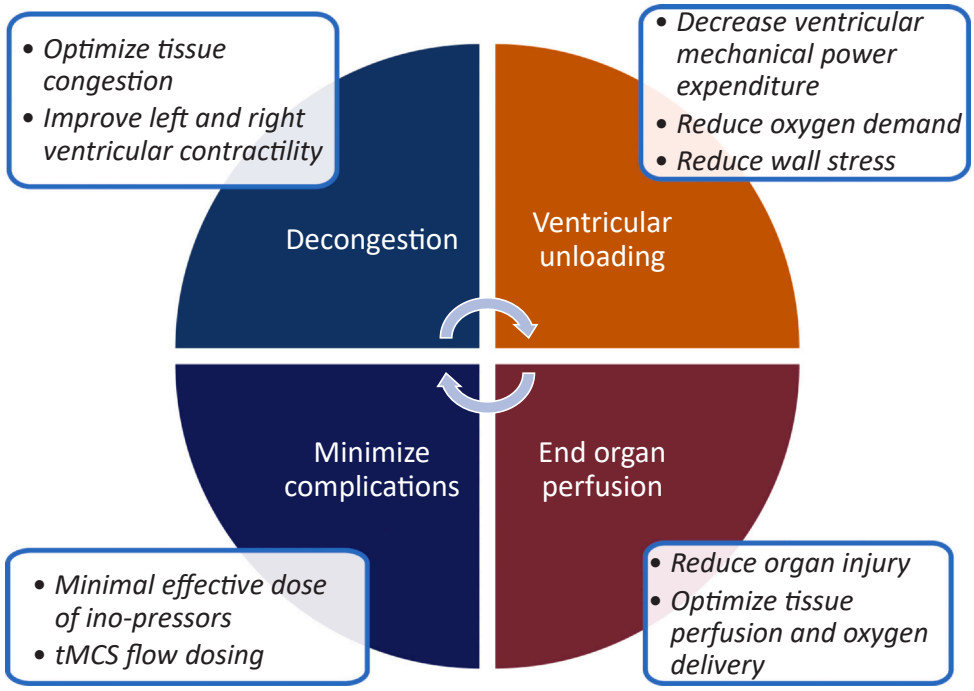
Transitions in temporary MCS support in HF-CS: Focus on MCS devices

Intravenous inotropes and vasopressors remain the most important therapies in the initial management of HF-CS. Norepinephrine may be the preferred first-line agent to treat hypotension in HF-CS while assessment is ongoing, targeting the lowest perfusing MAP.[20] For inotropy, dobutamine and milrinone are often used, although both had an equivalent impact on short-term mortality.[73] Both can potentiate myocardial oxygen demand and have vasodilatory properties.

If a patient presents in an advanced stage of CS (> SCAI stage B), tMCS should be considered early, in appropriate cases. Reversible or transient etiologies that are contributory to the shock state (e.g. rapid atrial or ventricular arrhythmias, peri-partum state, valvular pathology, stress-induced cardiomyopathy) should be rapidly assessed for and corrected as possible. Likelihood of recovery and potential candidacy for heart transplantation or durable LVAD should be considered in the decision-making on the appropriateness of tMCS, as tMCS is a bridging therapy.

The choice of therapies should be tailored to the degree of HF-CS hemodynamic derangement as well as availability of therapeutic options at the treating facility.[4] MCS devices differ based on their mechanism, level of cardiac support provided, contraindications, and potential complications. Careful patient selection and comprehensive intensive care by an experienced team are essential to successful outcomes in patients with CS supported on tMCS.[74] Just as premature use may expose a patient to undue risks and complications, delayed initiation may be suboptimal, or even futile. The ideal deployment should occur after other, less invasive treatments have been considered or exhausted, but before the onset of significant end-organ dysfunction. The goals of tMCS deployment should ideally be defined before implementation and include hemodynamic stabilization and restoration of systemic perfusion (Figure 1). Currently there is minimal data to guide the use and

Figure 1 The goals of tMCS deployment include hemodynamic stabilization and restoration of systemic perfusion. tMCS, temporary mechanical circulatory support.



timing of use of MCS devices in CS, with recommendations predominantly informed by observational registries in the absence of randomized trial data.

Our consensus conference focused on three key issues:

1. *Dynamic re-profiling of patients in HF-CS*: Risk assessment in CS should not be restricted to time of initial presentation only, re-profiling must occur in an ongoing fashion throughout the patient's hospital stay. Escalation of SCAI stage from baseline is common, and the time to escalation varies significantly by baseline SCAI stage.[27] In addition to baseline SCAI stages, maximal SCAI stage achieved during hospitalization is also directly associated with an increase mortality. The dynamic CS spectrum as a continuum including three central aspects: CS severity, CS phenotypes and etiologies, and risk modifiers & comorbidities has been emphasized in the updated SCAI CS classification.[75]
2. *Tailored and timely implantation of tMCS*: The selection of the best tMCS device for a given patient depends on individualized patient factors, the level of hemodynamic support needed, the goal of tMCS, and physician/institutional expertise with the different tMCS devices.[76] Key patient factors important for device selection include the etiology of CS, expected treatment course, patient comorbidities, end-organ function, invasive hemodynamic measurements, and echocardiographic features. Invasiveness and cost of tMCS devices emphasize the need to evaluate when and in whom these devices may be most effective in improving patient outcomes, considering that each tMCS device may have a different risk-benefit profile for different patients at different stages of CS. Identification of predictors of response to tMCS may allow tailored therapy and reserve use of more powerful tMCS devices for patients with more advanced stages of CS.
3. *Escalation and de-escalation strategies of tMCS*: There are different algorithms for transitions from medical management to tMCS,[76] but a standardized protocol is lacking. Generally, early transition when possible is associated with better outcomes. As tMCS are always a bridging strategy for recovery, advanced heart failure therapies, or palliative care, risk predictive factors for worse outcomes in the setting of transitions from tMCS to durable LVAD or heart transplantation have been identified.[77,78] If the center managing these patients does not offer advanced heart failure therapies, early referral to such a center should be expedited to avoid 'narrowing the window of eligibility' for advanced options. Weaning tMCS should be considered after the achievement of hemodynamic stability, and metabolic/end-organ recovery has been established.

Table 4 Goals of Treatment Monitoring for Perfusion and Unloading.

	Perfusion	Unloading
Clinical	• Resting HR ≥ 100 bpm • SBP < 90 mm Hg • MAP < 65 mm Hg • End-organ dysfunction from kidney, liver, brain, gut, heart • Lactate > 2.2 mmol/liter • pH < 7.3	• LV: Dyspnea, orthopnea, hypoxia, chest pain, pulmonary edema by exam or imaging; or by echo LV dilation, right-shifted ventricular septum, or > mild MR • RV: Elevated jugular venous pressure, peripheral edema, congestive hepatopathy or renal vascular congestion; or by echo RV dilation, left-shifted ventricular septum, or > mild TR
Hemodynamic	• Total Cardiac Index (heart + pump) < 2.2 liter/min/m^2	• LV: LVEDP, LAP, or PCWP > 15 mm Hg; mean PAP > 25 mm Hg • RV: RVEDP or RAP > 10 mm Hg

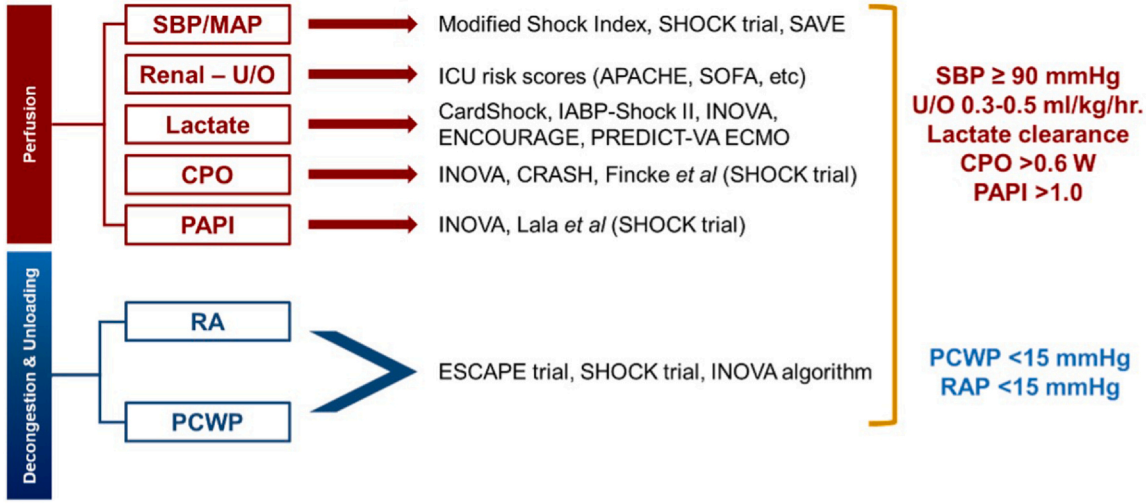
LV, left ventricular; LVEDP, left ventricular end diastolic pressure; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; RV, right ventricular; RVEDP, right ventricular end diastolic pressure; SBP, systolic blood pressure.

When weaning tMCS is not possible, transitioning to advanced heart failure therapies or palliative care should be considered. If not already done, early transfer of these patients to an LVAD- or transplant-capable hospital should be pursued. This allows centers time to assess patients' medical and psychosocial background to exclude contraindications that would preclude candidacy for advanced therapies. Palliative care teams may help with transitions of care in the absence of hemometabolic recovery and when advanced therapies are not an option in the absence of heart recovery. Early involvement of palliative care in the clinical course of the patient with CS is appropriate to clarify the goals and limits of care and to provide support to patients and caregivers.

Management and flow dosage in temporary MCS

Each tMCS platform has unique management parameters of interest.[79] Several common themes exist across devices related to the choice of optimal device output (i.e., flow-dosing) and the prevention and management of tMCS-related complications. Broadly, tMCS devices provide two main functions: (1) perfusion, to recover end-organ function and (2) ventricular unloading to reduce left ventricular wall-stress so that pulmonary congestion is minimized, and the probability of myocardial recovery is maximized.[80,81] Invasive hemodynamic monitoring is critical in HF-CS to fully characterize perfusion and unloading deficits, particularly in advanced shock SCAI stages

Figure 2 Suggested parameters for perfusion and de-congestion/unloading goals in HF-CS. CPO, cardiac power output; HF-CS, heart failure-cardiogenic shock; MAP, mean arterial pressure; PAPI, pulmonary artery pulsatility index, PCWP, pulmonary capillary wedge pressure; RA, right atrial pressure; SBP, systolic blood pressure; U/O, urine output.



D and E.[60] Table 4 and Figure 2 provide a list of useful perfusion and unloading parameters. However, interpatient variability and baseline parameters before shock development may dictate different patient-specific cutoffs.

The trajectory of clinical, biochemical and hemodynamic variables is likely to be more meaningful than isolated snapshots. Evidence of impaired perfusion and/or unloading would generally warrant increasing device flow. Similarly, flow requirements exceeding device capability warrant consideration of a change in device configuration, higher flow tMCS, HRT or whether additional pathophysiology, such as sepsis is present. Conversely, higher flow may lead to greater flow-mediated complications. Therefore, achieving perfusion and unloading targets using the minimal required flow is desirable. Optimizing device settings and flow should be done in conjunction with medical therapy through the achievement of euvolemia, management of arrhythmias and adequate dose of vasopressors and inotropes.

Multiple complications are associated with tMCS use that may adversely impact patient outcomes and increase mortality risk.[82] In general, the risk of complications accumulates over time, so the benefits of continued tMCS use must be weighed against the risk of complications. Many tMCS configurations restrict mobility, which can accelerate deconditioning in HF-CS, where issues with cachexia, sarcopenia, and frailty are frequently present. Mobility can be a critical factor in outcomes after shock recovery and/or advanced heart failure therapies so deliberate attention must be paid to maximize mobility where possible through the use of insertion sites different from the femoral access.[83]

CONCLUSION

HF-CS remains a challenging and heterogenous syndrome. With a dearth of high-quality published data, current best practice reflects broad principles of care that may optimize patient outcomes independent of resource availability across all healthcare systems. Central to these principles are: (1) the role of team-based care and decision making; (2) utilizing a battery of serial clinical, laboratory, imaging and hemodynamic data to inform and revise clinical decision making, particularly around escalation to tMCS; (3) the role of risk-stratification to inform the expediency of intervention and escalation/de-escalation; and (4) the importance of a nuanced, patient- and institution-specific strategy, maximizing potential gains from tMCS while minimizing complications. Ongoing current and forthcoming investigation in the HF-CS patient population are enthusiastically anticipated to better inform future practice.

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APPENDIX

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