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REVIEW

Treatment of Cardiogenic Shock: Inotropes, Vasopressors and Machines

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Abstract

Cardiogenic shock (CS) is associated with significant mortality. Advances in pharmacological therapies and mechanical circulatory support (MCS) devices have markedly improved the therapeutic approach to CS, though treatment efficacy and safety vary. The recent DanGer shock trial showed a significant reduction in 6-month mortality for CS patients due to acute myocardial infarction. Future randomised trials should evaluate a phenotype-guided pharmaco-MCS approach to the management of CS. This paper summarises contemporary pharmacological and MCS treatments for patients with CS.

Key words: cardiogenic shock; mechanical circulatory support; inotropes

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Introduction

Etiology and Pathophysiology of Cardiogenic Shock (CS)

Cardiogenic shock (CS) is a life-threatening condition with short-term (in-hospital or 30-day) mortality exceeding 30% across the literature (Chioncel et al, 2011; Chioncel et al, 2020; Maggioni et al, 2010). There are three components to the diagnosis of CS: an underlying cardiac pathology, circulatory failure related to the cardiac pathology and evidence of hypoperfusion due to circulatory failure.

The acute coronary syndrome is the archetypal cause of CS, but recent studies have increasingly recognised other causes of CS, including end-stage heart failure due to non-ischaemic cardiomyopathy, fulminant and other inflammatory myocarditis, and valvular heart disease (Kolte et al, 2016; Shah et al, 2018). The underlying etiology is a major determinant of the CS phenotype, indication for treatment, clinical course and potential outcomes. For example, revascularization is indicated in CS due to acute myocardial infarction. Full recovery is likely in acute fulminant myocarditis if the patient survives CS, but 'heart replacement therapy' may be indicated in CS due to end-stage cardiomyopathy (Vahdatpour et al, 2019). Irrespective of the underlying etiology, reduction in cardiac output is the dominant pathophysiology of circulatory failure in CS. Global oxygen delivery is a function of cardiac output of blood oxygen content. Global oxygen delivery diminishes due to the compromised cardiac output and may become inadequate to maintain tissue/organ

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perfusion, leading to clinical and metabolic features of hypoperfusion. Prompt correction of low cardiac output and improved oxygen delivery is necessary to avoid multi-organ failure and death from CS.

Markers of Cardiogenic Shock

Sustained hypotension is commonly used as evidence of circulatory failure (The European Society of Cardiology guidelines have defined sustained hypotension as systolic blood pressure <90 mmHg for over 30 minutes or the necessity for vasoactive drugs to maintain blood pressure), but it is also recognised that CS may present without hypotension due to arterial vasoconstriction. Other features of circulatory failure include elevated cardiac filling pressures and low cardiac output (if measured). Evidence of hypoperfusion may be clinical (cold extremities, skin mottling, mental confusion, oliguria) or biochemical indicators such as metabolic acidosis and elevated blood lactate levels (Chioncel et al, 2020).

Classification of Cardiogenic Shock

The diagnosis of CS should be followed by phenotyping, which includes characterisation of acuity/severity and pathophysiology. The Society for Cardiovascular Angiography and Interventions (SCAI) classification is commonly used to describe the acuity/severity of CS from A (at risk of CS) to E (extremis). The pathophysiology of CS involves the assessment of left, right or biventricular function, and the systemic and pulmonary circulations (pulmonary vascular resistance). The underlying aetiology, acuity/severity and pathophysiology guide the management of CS, including the use of mechanical circulatory support (MCS) (Baran et al, 2019).

Management of Cardiogenic Shock

The haemodynamic management of cardiogenic shock can be divided into four phases: Recognition/Rescue, Optimization, Stabilization, and Exit/De-escalation (ROSE) (Fig. 1) (Lim et al, 2024). Inotropes and vasopressors are pharmacological agents employed to achieve hemodynamic stability in the Rescue and Optimisation phases and mitigate the progression of CS. This review will discuss contemporary pharmacological and mechanical support in CS.

Pharmacological Therapy in Cardiogenic Shock

At its most basic, inotropes are pharmacological agents that enhance cardiac contractility to increase cardiac output and vasopressors induce arterial/arteriolar vasoconstriction to increase arterial blood pressure (Bloom et al, 2023; Cooper, 2008; Russell, 2019). Table 1 provides a summary of the vasoactive drugs utilised in the management of cardiogenic shock.

Norepinephrine

Norepinephrine predominantly targets alpha-1 receptors, promoting vasoconstriction and subsequently elevating blood pressure. Norepinephrine has weak beta-1 receptor affinity, resulting in some inotropic effects (Bloom et al, 2023; Cooper,

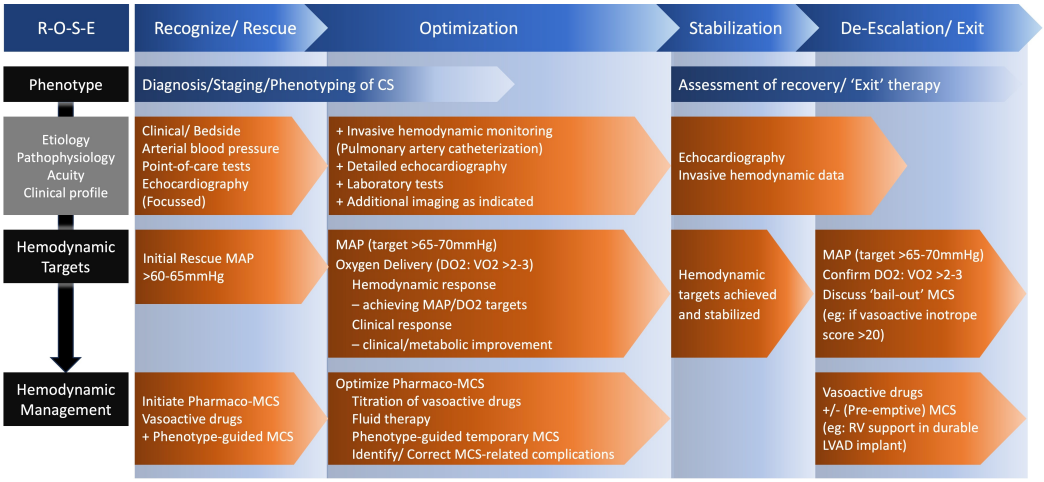

Fig. 1. The four phases of cardiogenic shock. ROSE, Recognition/Rescue, Optimization, Stabilization, and Exit/De-escalation; CS, cardiogenic shock; MCS, mechanical circulatory support; LVAD, Left Ventricular Assist Device; MAP, mean arterial pressure; DO2, oxygen delivery; VO2, oxygen consumption. Data from "Hemodynamic management of cardiogenic shock in the intensive care unit" by Lim HS et al is licensed under CC BY 4.0.

2008; Russell, 2019). In the Sepsis Occurrence in Acutely Ill Patients (SOAP-II) trial, which compared dopamine and norepinephrine (Zampieri et al, 2024), there was no significant difference in mortality rates between the dopamine and norepinephrine cohorts (52.5% in the dopamine group versus 48.5% in the norepinephrine group, $p = 0.10$), but the incidence of arrhythmic events was significantly higher in the dopamine group (24.1% vs 12.4%, $p < 0.001$). A meta-analysis similarly showed a reduced risk of arrhythmic events and a lower 28-day mortality rate compared to dopamine (relative risk (RR) 1.611 [95% confidence interval (CI) 1.219–2.129]; $p < 0.001$) (Rui et al, 2017).

Epinephrine

Epinephrine increases systemic vascular resistance, cardiac output, and blood pressure. However, its use is often constrained by associated adverse effects, including myocardial ischemia, arrhythmias, hyperlactatemia, and splanchnic ischemia (Bistola et al, 2019). A prospective randomized study that compared epinephrine and norepinephrine-dobutamine combination in 30 patients with CS reported similar hemodynamic effects; but epinephrine was linked to higher incidence of lactic acidosis, arrhythmias, and inadequate gastric mucosa perfusion (Levy et al, 2011). In a prospective double-blind randomized study of patients with acute myocardial infarction-induced CS (AMI-CS), norepinephrine and epinephrine produced comparable effects on arterial blood pressure and cardiac index, but epinephrine resulted in higher heart rates and blood lactate levels, although it required a shorter duration of inotropic support ($p < 0.001$) (Levy et al, 2018). A meta-analysis of fourteen cohort studies and 2583 patients reported that the incidence of mortality in epinephrine was threefold higher compared to other drug regimens (Léopold et al, 2018).

Table 1. Summary of the main medications used for cardiogenic shock.

Agents	Mechanism	Dose range	Adverse effect
Norepinephrine	Alpha agonist (+) Beta agonist	0.05–0.20 µg/kg/min	Tachycardia Hypertension
Epinephrine	Alpha agonist (++) Beta agonist	0.01–0.3 µg/kg/min	Myocardial ischaemia Arrhythmia Hypertension Pulmonary congestion
Dopamine	Dose-dependent Acts on alpha, beta and dopaminergic receptors	Lower dose: 1–2 µg/kg/min Intermediate dose: 5–15 µg/kg/min Higher dose: >15 µg/kg/min	Increased incidence of arrhythmias Higher risks of ICU mortality and hospital mortality as dose increases
Dobutamine	Beta agonist	5–20 µg/kg/min	May contribute to hypotension
Milirinone	Phosphodiesterase 3 inhibitor	0.125–0.35 microg/kg/min	Induce arrhythmia and cardiac ischaemia Hypotension
Levosimendan	Calcium sensitiser	0.05–0.4 µg/kg/min	Hypotension AF, tachycardia Hypocardia

The number of '+' indicates the effect size. AF, atrial fibrillation; ICU, intensive care unit.

Dopamine

Dopamine, a precursor to norepinephrine and epinephrine, exhibits dose-dependent cardiac effects through its interaction with different receptors. At lower doses (1–2 µg/kg/min), dopamine primarily induces vasodilation in the renal and splanchnic systems due to its affinity for dopaminergic receptors. However, studies have not demonstrated significant benefits on renal hypoperfusion in patients with CS (Amado et al, 2016; Bloom et al, 2023; Cooper, 2008; Russell, 2019). At intermediate doses (5–15 µg/kg/min), dopamine activates both alpha- and beta-adrenergic receptors, enhancing myocardial contractility and blood flow. At higher doses (>15 µg/kg/min), its effects are predominantly mediated by alpha-1 stimulation (vasoconstriction). The SOAP-II trial showed an increased incidence of arrhythmic events in patients treated with dopamine (used as vasoconstrictor) compared to norepinephrine, and may be associated with higher mortality in patients with CS ($p = 0.03$) (Zampieri et al, 2024). A retrospective study suggested that dopamine at doses exceeding 15 µg/kg/min significantly elevated the risk of hospital mortality (Gao and Zhang, 2021). A comparative study between dopamine and dobutamine showed that dopamine increased left ventricular filling pressure more than dobutamine at 5 µg/kg/min ($p < 0.001$) and 10 µg/kg/min ($p < 0.05$) (Francis et al, 1982).

Dobutamine

Dobutamine primarily enhances cardiac output by increasing myocardial contractility. The effect on arterial blood pressure may be negligible, but hypotension due to vasodilatation is well-recognised. Several studies in the literature have suggested an association between dobutamine use and higher hospital mortality. A retrospective cohort study reported that while dobutamine significantly decreased intensive care unit (ICU) mortality, it was linked to increased hospital mortality (Gao and Zhang, 2021). Additionally, an observational study indicated that in patients at SCAI stages B and C, the use of dobutamine resulted in a 15% increased risk of mortality for each 1 µg/kg/min increment in dosage (Nandkeolyar et al, 2021). Despite these findings, dobutamine remains a recommended inotrope for improving myocardial contractility, often administered concurrently with norepinephrine. The combination of norepinephrine-dobutamine was associated with lower heart rates and blood lactate levels compared to epinephrine (Levy et al, 2011).

Milrinone

Milrinone, a phosphodiesterase inhibitor, is a positive inotrope and a peripheral vasodilator (Amado et al, 2016; Bistola et al, 2019), enhancing cardiac output and decreasing arterial blood pressure. In observational studies, all-cause mortality was lower with milrinone compared to dobutamine (odds ratio 1.19, 95% CI 1.02–1.39; $p = 0.02$) (Abdel-Razek et al, 2023). The Cardiovascular Percutaneous Intervention Trial Dobutamine Compared with Milrinone (CAPITAL-DOREMI) trial compared dobutamine vs milrinone in patients with CS (Mathew et al, 2021). There was no significant difference in in-hospital mortality between the two groups (37% in the milrinone group and 43% in the dobutamine group; RR, 0.85; 95% CI, 0.60–1.21)

(Mathew et al, 2021). The ongoing CAPITAL-DOREMI 2 trial aims to assess the safety and efficacy of inotrope therapy (dobutamine or milrinone) versus placebo in treating CS patients.

Levosimendan

Levosimendan exhibits inotropic properties by increasing the sensitivity of troponin C to intracellular calcium within the myocardium, but also induces peripheral vasodilation and hypotension (Nieminen et al, 2013). One small randomised trial found that levosimendan improved cardiac index and cardiac power output over a 24-hour treatment period compared to dobutamine in patients with AMI-CS (García-González et al, 2006). Small studies have shown no significant statistical difference in long-term survival between levosimendan and other inotropic medications. One randomised trial of patients with CS reported no significant differences in outcomes between the levosimendan and control groups over 12 months (p = 0.24) (Samimi-Fard et al, 2008). An observational study also found no difference in 30-day mortality rates (p = 0.93) or 1-year mortality rates (p = 0.87) between the levosimendan and control groups (Omerovic et al, 2010).

Clinical Guidance

The current body of evidence, largely comprising observational studies, provides limited support for the superiority of one inotropic agent over another. Current European Society of Cardiology (McDonagh et al, 2021) and the American Heart Association (van Diepen et al, 2017) guidelines recommend norepinephrine as the first-line vasopressor due to its lower arrhythmic risk (dose ranging from 0.05–0.20 µg/kg/min). Dobutamine may be administered concurrently with norepinephrine to enhance cardiac contractility.

Mechanical Circulatory Support

Mechanical circulatory support (MCS) has emerged as a pivotal therapeutic modality in addressing this imbalance between oxygen delivery and consumption in CS. These devices range from relatively small percutaneous devices such as the intra-aortic balloon pump to surgical assist devices (Table 2). Mechanical circulatory support devices have been evaluated in patients with CS in a number of clinical trials (Table 3).

Intra Aortic Balloon Pump (IABP)

The intra-aortic balloon pump (IABP) functions to enhance organ perfusion by decreasing cardiac afterload and augmenting diastolic aortic pressure, thereby improving diastolic blood flow. The device's balloon inflates and deflates from electrocardiogram (ECG) triggers and reduces left ventricle (LV) afterload and myocardial oxygen demand (Musa et al, 2017). The IABP is favoured for its simplicity and ease of insertion. Contraindications for IABP use include severe aortic regurgitation, aortic dissection, and severe peripheral artery disease (Ferguson et al, 2001; Musa et al, 2017). The Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II) Trial investigated

Table 2. Summary of mechanical circulatory support devices.

Device	Insertion time	Ventricular support	Level of support	Ischaemic risk	Bleeding risk
IABP	<10 minutes	LV offloading	About 0.5 L/min	<5%	5–10%
Impella CP	10–20 minutes	LV support	About 3.5 L/min	5–10%	10–20%
Impella 5.5	30–60 minutes	LV support	About 5.5 L/min	<5%	8–10%
Tandem heart	30–60 minutes	Direct LV offloading	About 4 L/min	5–10%	40–50%
VA-ECMO	10–20 minutes	Biventricular support	Over 5 L/min	5–10%	20–40%
Surgical assist devices	60–90 minutes	Left, Right or Biventricular support	Over 5 L/min	5–10%	15–30%

IABP, intra-aortic balloon pump; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; LV, left ventricle; CP, cardiac power.

Table 3. Clinical trials in mechanical circulatory support.

Trial name	Patient groups	Intervention	Outcomes
IABP-SHOCK II	CS due to acute myocardial infarction	IABP vs no IABP	No significant difference in 30-day mortality
ALTSHOCK 2	CS due to acute decompensated heart failure	IABP vs vasoactive treatments	Ongoing trial
DanGer Shock	CS due to acute myocardial infarction	Impella vs no Impella	12.7% improvement in 6-month survival with Impella
ULYSS	CS due to acute myocardial infarction	Impella vs medical treatment	Ongoing trial
Recover IV	CS due to acute myocardial infarction	PCI with or without Impella	Ongoing trial
ECLS-SHOCK	CS due to acute myocardial infarction	ECLS vs medical treatment	No significant difference in 30-day mortality
ECMO-CS	CS of different aetiologies	immediate VA-ECMO vs standard use	No significant difference in 30-day mortality
ECLS-SHOCK I	CS due to acute myocardial infarction	ECLS vs no ECLS	Reduction in 12-month all-cause mortality No significant difference in 30-day mortality
EURO SHOCK	CS due to acute myocardial infarction	VA-ECMO vs standard therapy	No significant difference in 30-day and 12-month mortality

IABP-SHOCK II, Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock; ALTSHOCK 2, Early intra-aortic balloon pump in acute decompensated heart failure complicated by cardiogenic shock; DanGer Shock, Danish-German Cardiogenic Shock trial; ULYSS, Ulysses Cardiogenic Shock study; ECLS-SHOCK, Extracorporeal Life Support in Infarct-Related Cardiogenic Shock; ECMO-CS, Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; PCI, percutaneous coronary intervention.

outcomes of IABP in AMI-CS. showed no significant difference in 30-day all-cause mortality with IABP in AMI-CS (RR 0.96, 95% CI 0.79–1.17, $p = 0.69$) (Thiele et al, 2012). Long-term follow-up at six years confirmed no reduction in mortality with IABP use in AMI-CS (Schrage et al, 2019). As a result, the European Society of Cardiology guidelines have advised against its routine use of IABP in AMI-CS due to the lack of mortality benefit (Byrne et al, 2023). The American College of Cardiology/American Heart Association guidelines recommend using IABP as a temporary stabilising measure for patients who fail to achieve hemodynamic stability with pharmacological treatment (Rossini et al, 2021). The ongoing Altshock-2 trial will evaluate IABP in CS due to acute decompensated heart failure (Morici et al, 2021).

Left Ventricular Assist Device (LVAD)

Impella

The Impella (Abiomed, Danvers, MA, USA) device is a catheter-mounted micro-axial blood pump that provides ventricular support. The current left-sided support Impella devices are the Imeplla CP and Impella 5.5. The devices work by lowering the LV end-diastolic pressure which reduces the left ventricular well stress, in turn reducing infarct size in acute myocardial infarction. Left ventricular thrombus and mechanical aortic valve prostheses, and severe aortic regurgitation are contraindications to Impella. Complications include bleeding, limb ischemia, and haemolysis, which may necessitate transfusion or device repositioning (Musa et al, 2017; National Institute for, Health, and Excellence Care, 2016; Zein et al, 2022).

The DanGer Shock trial demonstrated that the use of the Impella CP in selected patients with AMI-CS reduced all-cause mortality at 180 days (45.8% in the Impella group compared to 58.5% in the standard care group, hazard ratio 0.74; 95% CI 0.55–0.99; $p = 0.04$). The 12.7% absolute reduction in mortality with Impella CP indicates a number needed to treat to prevent 1 death of 8 (Møller et al, 2024). However, the reduction in mortality was associated with an increased risk of complications, including bleeding and hemolysis. Other ongoing studies include the Recover IV trial, to assess whether Impella support during percutaneous coronary intervention in AMI-CS patients, as well as the ULYSS trial to assess whether Impella should be used on top of standard medical therapy in patients undergoing AMI-CS (Masiero et al, 2024). Previous comparative studies have reported no significant difference in mortality between Impella and IABP in CS. The Impella LP2.5 vs. IABP in Cardiogenic Shock (ISAR-SHOCK) trial reported a 30-day mortality rate of 46% in both groups (Seyfarth et al, 2008). The Imella Left Ventricular Assist Device Study in Cardiogenic Shock (IMEPLLA STIC) trial in 2020 also reported no significant statistical change to the cardiac power index after 12 hours (IABP group: cardiac power index (ΔCPI) = 0.08 $\pm$ 0.08 W/m^2; Impella LP 5.0 + IABP group: ΔCPI = –0.02 $\pm$ 0.25 W/m^2; $p = 0.40$) (Bochaton et al, 2020). The Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction (IMPRESS) trial found no statistical difference in survival between IABP and Impella in patients with AMI-

CS (Karami et al, 2021). These studies suggest the need for more nuanced selection of patients with CS for Impella support and meticulous attention to potential complications associated with the device. The International Society for Heart and Lung Transplantation (ISHLT) guidelines recognise the Impella device as an option for haemodynamic support for patients with AMI-CS to facilitate myocardial recovery (Class II B evidence C) (Saeed et al, 2023).

TandemHeart Device

Similarly, the TandemHeart (LivaNova) is a percutaneous centrifugal Left Ventricular Assist Device (LVAD) that drains blood from the left atrium via a transseptal atrial cannula and pumps the blood back into the descending aorta. The result is an increase in cardiac output and cardiac power while reducing left ventricular end-diastolic pressure and myocardial oxygen consumption (Megaly et al, 2023).

Currently, there are no multi-centre randomised clinical trials evaluating the effectiveness of TandemHeart in patients with CS. However, there are some small observational studies supporting the potential of this device. A prospective observational study demonstrated improved hemodynamic benefits in patients with CS, with a 74% 30-day survival and a 66% 180-day survival (Megaly et al, 2023).

Extracorporeal Life Support (ECLS)

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO), also known as extracorporeal life support (ECLS) offers cardiac and respiratory support for patients with CS. This system includes a venous drainage cannula, typically inserted into the femoral vein, to draw venous blood into a pump, which pumps the blood through an oxygenator. The membrane oxygenator decarboxylates and oxygenates the venous blood, which is then returned to systemic circulation via a cannula into the artery (usually femoral artery). ECLS can generate flows of over 5 L/min and is capable of providing significant haemodynamic support even in the absence of native heart function (e.g., cardiac arrest) (Musa et al, 2017; Shekar et al, 2014). Despite its life-saving potential, ECLS is associated with significant risks, including limb ischemia, thromboembolism, haemolysis, infection, and pulmonary oedema due to left ventricular distension (Musa et al, 2017). The Out-of-Hospital cardiac arrest & SmartphonE RespOndErS trial (HEROES) trial reported that 21.1% of patients experienced bleeding complications. Thus, the success of ECLS heavily depends on meticulous patient selection and management (Willers et al, 2022).

The ECLS-SHOCK I study reported the 12-month all-cause mortality in the ECLS group as 19% compared to 38% in the control group, albeit with a small sample size of only 42 patients (Lackermair et al, 2021). The ECLS-SHOCK trial evaluated ECLS in 420 patients with AMI-CS. There was no significant difference in all-cause mortality at 30 days mortality and the ECLS group had a higher incidence of complications such as severe bleeding (23.4% vs 9.6%) (Thiele et al, 2023). Similarly, the smaller ECMO-CS trial comparing immediate ECLS vs later or downstream use of the device in patients with severe cardiogenic shock reported no significant difference in 30-day mortality (10.3.% vs 13.6%; risk difference, –3.2 [95% CI, –15.0–8.5]) or serious adverse events (60.3% vs 61.0%; risk difference,

–0.7 [95% CI, –18.4–17.0]) (Ostadal et al, 2023). Current guidelines recommend short-term MCS including ECLS, as a bridge to decision, recovery, or transplantation (Class IIa, Level C) (McDonagh et al, 2021). The ISHLT guidelines advocate MCS in patients at high risk of 1-year mortality, emphasizing the need for comprehensive neurological assessment before ECLS (Feldman et al, 2013; Saeed et al, 2023).

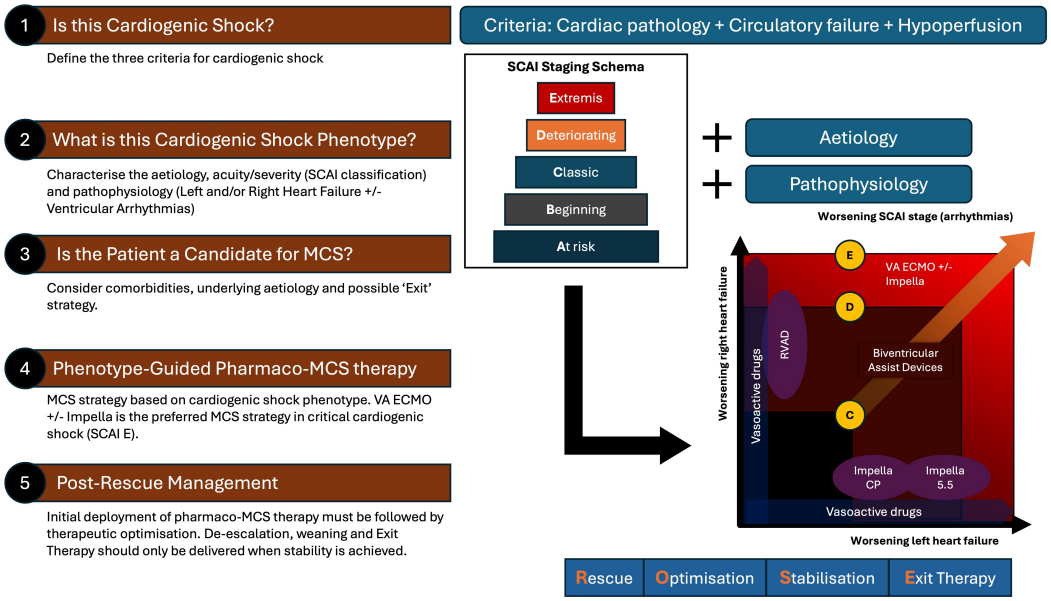

Fig. 2. Initial approach to CS with a 5-step algorithm. If the patient is a candidate for temporary MCS, the CS phenotype is the primary consideration to guide the deployment of pharmaco-MCS. Secondary considerations include vascular access, prior sternotomy (if surgical approaches are considered) and anaesthetic considerations. Not shown here (and beyond the scope of this review) is the additional pharmaco-MCS considerations in patients with CS and respiratory compromise. Data from "Hemodynamic management of cardiogenic shock in the intensive care unit" by Lim HS et al is licensed under CC BY 4.0.

Temporary Ventricular Assist Devices (VAD)

Temporary ventricular assist devices (VAD) with the use of centrifugal flow pumps (Centrimag devices) can be implanted surgically to provide full biventricular support in patients with CS (blood flow of up to 10 L/min). It is primarily used as a bridge to recovery, transplantation, or decision-making for long-term treatment options. The Centrimag device features a magnetically levitated motor that operates without mechanical bearings or seals, reducing the risk of blood-related complications (Amado et al, 2016). Current guidelines suggest short-term use of CentriMag for 30 days but these devices have been used for longer duration of support over several months to bridge patients to heart transplantation. There are no randomized controlled trials for surgical VADs in CS (National Institute for, Health, and Excellence Care, 2017). The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) 1 study, a retrospective analysis, examined the survival rates of cardiogenic shock patients using CentriMag as a bridge to decision. Among

Table 4. Case vignettes.

Case 1	
Clinical presentation	A 22-year-old female presented with new-onset biventricular dysfunction (LV ejection fraction 20%) following a week of flu-like illness. Blood pressure was 96/78 mmHg but she had signs of mottling and oliguria. Arterial blood lactate was 4.6 mmol/L.
Therapeutic approach	A pulmonary artery catheter was inserted to characterize the hemodynamic profile. Pulmonary artery pressure of 36/26 mmHg and central venous pressure of 15 mmHg indicated severe low output state and severe right heart failure. Thermodilution confirmed a low cardiac index of 1.2 L/min/m^2 at a heart rate of 146/min. She was started on dobutamine and milrinone. Her cardiac index failed to increase with inotropes, and she deteriorated rapidly. Decision was made to support her with VA-ECMO. The VA-ECMO 'run' was uncomplicated and she made a full recovery after 7 days.
Comments	Although not hypotensive (systolic blood pressure >90 mmHg), this patient had clear signs of hypoperfusion. In the context of severe cardiac dysfunction, these clinical features are consistent with the syndrome of cardiogenic shock. The clinical course is typical of acute fulminant myocarditis. With such a low baseline cardiac index, it was unlikely that inotropes would be sufficient to restore oxygen delivery. Continuous monitoring with pulmonary artery catheter could guide timely escalation of support. VA-ECMO was used in this case due to the rapid deterioration and biventricular failure.
Case 2	
Clinical presentation	Acute myocardial infarction and PCI to proximal right coronary artery. Recurrence of chest pain and re-infarction 12 hours after PCI. Stent thrombosis confirmed on angiography and coronary blood flow restored. However, progressively more hypotensive with signs of hypoperfusion.
Therapeutic approach	Echocardiography in the cath lab showed extensive areas of inferior/inferolateral akinesia but no pericardial effusion or tamponade. The patient was started on metaraminol and an Impella CP was inserted but the patient continued to deteriorate. The Impella device failed to achieve adequate flow due to repeated 'suction' events.
Comments	The patient had evolving right heart failure due to acute right ventricular infarction. The failing right heart was not able to produce sufficient cardiac output to 'preload' the left ventricle and the Impella CP, resulting in 'suction' events. The Impella CP, providing only left ventricular support was inappropriate MCS modality in this case. This case highlights the importance of characterizing the pathophysiological phenotype (right, left or biventricular failure) to guide the use of MCS devices.

Table 4. Continued.

Case 3	
Clinical presentation	A man with ARVC presented with VT storm, resulting in 30 ICD shocks, despite amiodarone, lignocaine and esmolol. He developed refractory VT and became increasingly unstable with escalating doses of norepinephrine due to hypotension.
Therapeutic approach	The patient underwent successful implantation of an Impella 5.5 via surgical cutdown to the right axillary artery (left-sided ICD) and percutaneous right ventricular assist device. The biventricular assist devices provided full hemodynamic support despite the persistent VT. The patient was successfully bridged to heart transplantation.
Comments	Inotropes are ineffective and potentially even contraindicated in patients with recurrent ventricular arrhythmias. Ventricular assist devices are capable of providing full hemodynamic support, such that perfusion can be maintained even in refractory ventricular arrhythmias.

ARVC, arrhythmogenic right ventricular cardiomyopathy; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary intervention; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VT, ventricular tachycardia. Note: The cases were fictional to highlight specific aspects of cardiogenic shock management.

63 patients, 58% were discharged from the hospital, with a five-year survival rate of 46% (Mehta and Venkateswaran, 2020). A systematic review on CentriMag evaluated its efficacy as a temporary VAD. Survival rates on support were 82% (95% CI 70–92) and 63% (95% CI 46–76) in patients with pericardiotomy cardiogenic shock. Bleeding is the most significant complication, affecting up to 28% of cases, alongside risks of infection, thrombosis, and haemolysis (Borisenko et al, 2014).

Case Vignettes and Treatment Algorithms

Faced with a range of pharmacological agents and temporary MCS devices, the therapeutic approach to a patient with CS can be daunting. The following 5-step algorithm could aid the approach and initial management of a patient with CS (Fig. 2).

Step 1: Recognising CS. Features of CS should be actively sought or excluded in any patient with features of circulatory compromise.

Step 2: Characterise the phenotype: aetiology, acuity/severity (SCAI stages) and pathophysiological phenotype.

Step 3: Assess candidacy for temporary MCS. The possible 'Exit strategy' must be considered prior to MCS.

Step 4: Phenotype-guided pharmaco-MCS therapy.

Step 5: Post-Rescue management—Optimisation, Stabilisation and Exit therapy.

A series of case vignettes are provided in Table 4 to illustrate some of the therapeutic considerations in CS (The cases were fictional to highlight specific aspects of cardiogenic shock management).

Limitations and Future Direction

Firstly, most clinical trials of CS to date have only included patients with AMI-CS. It is not clear if the results of these clinical trials can be extrapolated to patients with CS due to other causes, especially if recovery is less likely and bridging to 'heart replacement therapy' is the dominant outcome (Warren et al, 2024). Few patients in the clinical trials were bridged to heart transplantation or durable LVADs and more data are needed to define the optimal bridging strategy.

Secondly, clinical trials of MCS have largely been device-centric. The combined use of vasoactive drugs with MCS devices have not been well studied. There is growing recognition that better characterisation and phenotyping of CS is necessary for a more tailored delivery of pharmaco-MCS therapy to improve clinical outcomes. Biomarkers and proteomic profiling may aid the diagnosis and management of CS (Patel et al, 2024). The integration of biomarkers and proteomic profiling could improve the precision in treatment that could enhance both the diagnosis and management of CS by identifying specific patient subgroups who might benefit from tailored therapies.

Conclusion

There has been significant progress in the management of CS. Temporary MCS has, for the first time been shown to reduce mortality in patients with AMI-CS. But challenges remain, most notably the complications related to MCS and the high residual risk of mortality. More studies are needed to guide the use of pharmaco-MCS treatment in patients with CS.

Key Points

- Cardiogenic shock (CS) is associated with significant mortality. Advances in pharmacological agents and mechanical circulatory support (MCS) have improved clinical outcomes but residual mortality remains high.
- In the absence of randomised controlled trials, the pharmaco-MCS therapy should be guided by the CS phenotype.
- There is little data to suggest the superiority of one inotropic agent over another.
- The DanGer Shock trial demonstrated that the use of the Impella pump increased six-month survival rates in patients with acute myocardial infarction-induced CS.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

EYKC and HSL designed the review. EYKC was responsible for literature search, drafting of manuscript, design tables and figures. HSL was responsible for drafting and revision of manuscript, tables and figures. Both authors contributed to the important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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