

Review Article

Cardiogenic Shock Due to ST Elevation Myocardial Infarction: How Far Are We?

Rohit Mody^{1*}, Debabrata Dash², Bhavya Mody³, Aditya Saholi⁴ and Shubham Sachdeva⁵

¹Department of Cardiology, MAX Super specialty hospital, Bathinda, Punjab, India.

ORCID - <https://orcid.org/0000-0001-8977-5803>

²Department of Cardiology, Zulekha Hospital, AL Zahra Street, Sharjah - 457, UAE.

ORCID - <https://orcid.org/0000-0003-1354-3808>

³Department of Medicine, Kasturba medical college, Manipal, Karnataka, India.

ORCID - <https://orcid.org/0000-0001-8944-9418>

⁴Department of Cardiology, Adesh Institute of Medical Sciences, Bathinda, Punjab, India.

ORCID - <https://orcid.org/0000-0001-7545-5833>

⁵Department of Medicine, MAX Super specialty hospital, Bathinda, Punjab, India.

ORCID - <https://orcid.org/0000-0001-5052-5102>

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***Corresponding author:** Rohit Mody, Department of Cardiology, MAX Super specialty hospital, Bathinda, Punjab, India. Tel: +91-9888925988; E mail: drmody_2k@yahoo.com

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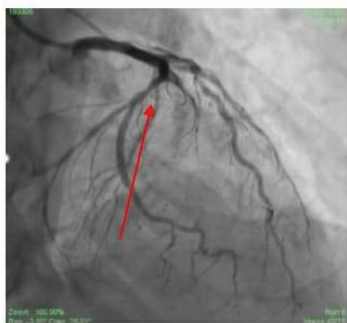
Abstract

Cardiogenic shock (CS) due to acute ST-elevation myocardial infarction is a complex state of low cardiac output and hemodynamic instability that transmutes to hypoperfusion of various body tissues leading to multi-organ dysfunction and death. Mortality rates due to CS remain high despite many recent advances in treatment. In the management of CS, early revascularization is the mainstay of the treatment. The patient can be stabilized using fluids, vasopressors or inotropes, mechanical circulatory support, and general intensive care techniques. Due to only few randomized trials on CS patients, there is lack of concrete evidence supporting various treatment modalities, except for revascularization. Thus, CS and its management is a topic with more controversies than conclusions regarding the optimal treatment and management.

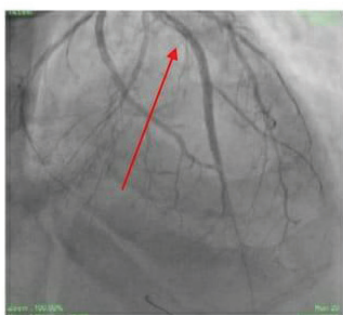
Article Highlights

- Cardiogenic shock due to acute STEMI is a syndrome of low cardiac output and hemodynamic instability that leads to hypoperfusion of organs leading to their dysfunction and eventually death.
- Mortality rates still exceed 40%.
- Early timely revascularization remains the mainstay of treatment. The role of only culprit vessel angioplasty needs further evaluation.

There is a growing evidence that in select patients, the role of MCS is increasing. Various RCTs are the need of the hour.



LAD 100% with clot



Revascularised

CS is a state of low cardiac output and hemodynamic instability leading to hypoperfusion of various body tissues. The mortality rate still exceeds 40%.

Norepinephrine is considered first line vasopressor agent. Pulmonary artery catheterization leads to early identification. Early and timely revascularization is the mainstay of treatment.

Consulting a team of various specialists is recommended for severe CS for use of MCS. Various RCTs is the need of hour.

Graphical Abstract: (A) Anterior segment mass (B) CT scan of orbit (C) Histological stain showing mixed spindle B and pigmented epithelioid cells (D) Appearance of eye after excision of anterior segment mass.

Introduction

Recent data suggest that mortality improvement among ST-elevation myocardial infarction (STEMI) have staggered in recent years [1]. CS complicates acute myocardial infarction (AMI) in approximately 10% of patients [2]. Recent registries have shown different incidences, which are decreased in some and increased in others [2]. CS caused by STEMI remains one of the most difficult conditions to manage [3]. Mortality rates are high, with up to one-half of all the patients dying before hospital discharge [4]. Timely reperfusion with a primary percutaneous intervention (PCI) is a class I recommendation in American heart association (AHA) guidelines for managing patients with STEMI complicated by CS [4]. Despite continued improvement in the door-to-balloon time since implementation of the guideline [5], mortality rates remain high. In this article, we shed light on the various approaches to manage and overcome the hurdles limiting the recovery rate of CS. At least 80% of CS cases are attributed to AMI-induced left ventricular failure (LVF). The other causes include mechanical complications of AMI, which are less frequent like ventricular septal rupture, free wall rupture, and acute severe mitral regurgitation - in less than 13% of the cases [6].

Definition of Cardiogenic Shock in Acute MI

Cardiogenic Shock, here, is a state of end-organ hypoperfusion and hypoxia due to left ventricular failure and its complications [7]. The diagnosis of CS can be made on clinical grounds when there is persistent hypotension despite the administration of IV fluids. Evidence of organ hypoperfusion such as cold extremities decreased urine output, impaired consciousness is also usually present. In addition to that, elevated arterial lactate levels reflect reduced tissue perfusion. Some important trials for CS have been conducted worldwide. Parameters used to define CS in different trials are given in (Table 1).

In search of a common language for defining disease severity, the

Society for Cardiovascular Angiography, and Interventions (SCAI) recently put forth a 5-stage (A-E) classification system for CS [9] (Figure 1). Recently, a simple index called the Shock Index has been used for prognostication of patients of CS. It is defined as the heart rate on arrival, divided by systolic blood pressure, and normally lies between 0.5 and 0.7 for healthy adults. Furthermore, multiplying this shock index with age gives us age shock index [10].

Management and Treatment

Emergency Department

Quick and effective emergency department management is of utmost importance for early recognition and treatment of CS. In AMI-CS, this includes performing and interpreting a 12-lead electrocardiography (ECG) by the emergency medical officer as soon as possible and immediate transfer to a catheterization lab-equipped hospital. In the emergency department, CS diagnosis can be facilitated by physical examination, ECG, laboratory evaluation, and (when available) point-of-care echocardiography [11]. SCAI has developed a new five-stage classification system for CS severity, as shown in Figure 1. The patients in SCAI stages A and B are generally shifted to the catheterization lab without delay. However, the patients with stages C and D who need initial stabilization in the form of mechanical ventilation, vasopressors, etc., also should be transferred to the catheterization lab as soon as possible [12]. As evidenced, with SCAI stages C, D, and E, mortality increases from 12.4% to 40.4%, to 67.0%, respectively [13].

This classification system helps us choose the right candidates for mechanical circulatory support (MCS). In patients with SCAI stage E or end-stage CS in whom aggressive therapies may be futile, palliative care consultation and discussions with health care surrogates regarding goals of care may be warranted [14]. As soon as the patient arrives, the shock index should be calculated. A patient with a higher index value should be

managed aggressively, as it is associated with higher chances of CS, atrial and ventricular tachyarrhythmia, and thus higher mortality rates.

As established by the SHOCK trial, early PCI is the gold standard treatment in CS postAMI [8]. Early revascularization, as compared to early medical stabilization, resulted in a reduction in mortality rates at 6 months, 1-year, and 6-year follow-up but could not lower 30-day mortality rates and failed to meet the trial's primary goals [8, 15]. Failure to meet the primary endpoint of a trial usually results in the null hypothesis. Despite this, early PCI remains the first-line treatment modality as long-term follow-ups have revealed a

mortality reduction from the previous 70–80% to 40–50%. This provides the basis for the current class 1B recommendations for early PCI in CS due to AMI in the European Society of Cardiology (ESC) and US guidelines (Figure 2) [16-18]. Furthermore, studies claim that outcomes worsen with delay in revascularization and vice versa [12, 19]. Hence, these patients should be transferred without any delay to a PCI-capable center which 24/7 availability of services. Many trials have not backed a positive effect of administration of a fibrinolytic in CS. However, if an early invasive approach cannot be completed, a fibrinolytic may be considered in AMI-CS (Figure 2).



Figure 1: Cardiogenic shock pyramid according to a recent proposal. Five categories of cardiogenic shock [9].
 Stage A: 'At risk' for cardiogenic shock.
 Stage B: 'Beginning' of cardiogenic shock.
 Stage C: 'Classic' cardiogenic shock.
 Stage D: 'Doom' stage.
 Stage E: Patients in 'Extremis'.

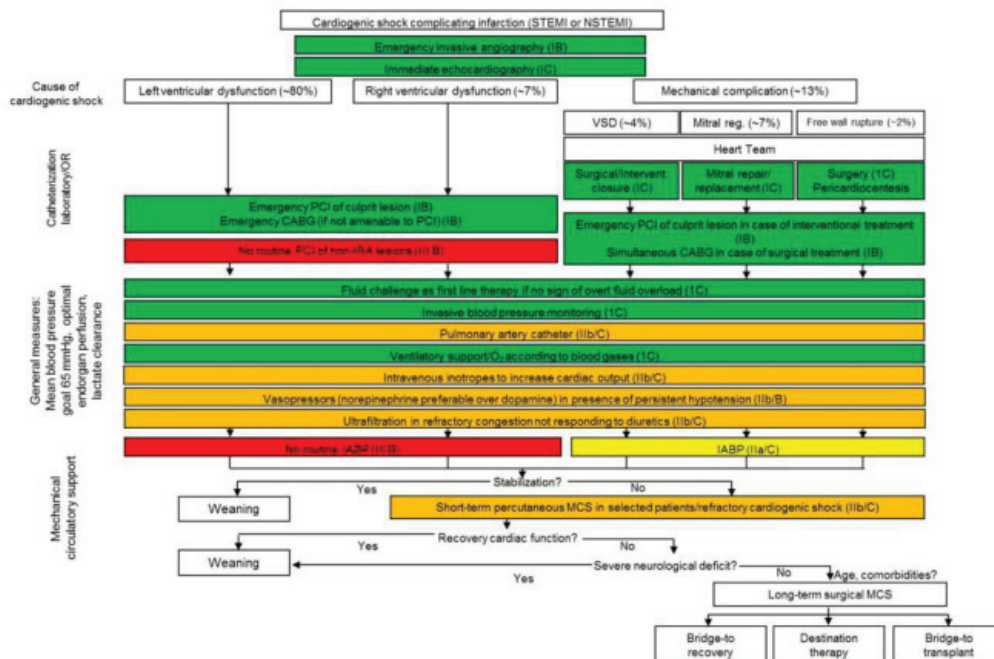


Figure 2: Flow chart for patients with cardiogenic shock complicating acute myocardial infarction. According to the most recent European Society of Cardiology guidelines. Class I recommendations are depicted in green. Class IIa recommendations are depicted in yellow. Class IIb recommendations are depicted in orange. Class III recommendations are depicted in red [16-18].

Revascularization Strategies

The incidence of multi-vessel coronary artery disease (CAD) in patients with AMI-CS is 70%. However, only a few of them undergo coronary artery bypass grafting (CABG). Observational data suggest that PCI and CABG have similar mortality rates in AMI-CS [20]. Notwithstanding the established benefits of complete revascularization in AMI, the optimal management of non-infarct-related artery lesions in AMI-CS remains unclear [21]. The CULPRITSHOCK (Culprit Lesion Only PCI versus Multi-vessel PCI in Cardiogenic Shock) trial is the only study that addresses this question, and it has demonstrated lower rates of 30-day death with culprit-vessel PCI versus multi-vessel intervention [46]. A recent sub-study of the National Cardiogenic Shock Initiative showed that mortality, incidence of acute kidney supported by MCS. Ad hoc multi-vessel PCI in AMI-CS currently receives a Class IIb guideline recommendation²³.

CICU Management of Cardiogenic shock

Treatment of CS is not a simple feat, and to optimally treat a patient and tackle the complications, we need a cardiac intensive care unit (ICU) [7] As we have already mentioned, CS can lead to multi-organ dysfunction syndrome (MODS), and for avoidance and management of such complications, cardiac ICUs are a necessity. Management of such patients requires a collaborative approach. If invasive ventilation is required, the tidal volume should be kept under 6 ml/kg body weight to prevent barotrauma to the lungs which may lead to further complications like pneumothorax. Non-invasive ventilation (NIV) might be used in patients in whom intubation is to be delayed [24]. The first organ to be compromised due to reduced perfusion is the kidneys. So, regular renal function tests (RFT), including serial serum urea and creatinine measurements, are of utmost importance. As indicated by these and other investigations like arterial blood gases (pH below 6.0 mmol/L), renal replacement therapy should be initiated in case of acute renal failure.

Another important organ to be involved is the liver. In patients with CS, the right ventricle gets congested because of the backpressure, leading to a detrimental effect on the liver, as evidenced by the elevated liver function tests (LFT). LFTs are altered in more than half of CS patients [24]. Liver hypoperfusion is confirmed by the elevation of transaminases (AST and ALT). This derangement in LFTs indicates an increased risk of mortality [26]. Liver perfusion can be optimized by stabilizing the perfusion pressure. A tight glycemic control should also be emphasized with a target blood glucose level between 140 – 180 mg/Dl [27]. General recommendations for critically ill patients, which includes stress ulcer prophylaxis (histamine-2 antagonists, antacids, sucralfate, etc.) and thromboembolism prophylaxis (low molecular weight heparins, etc.) are also to be enforced.

As per the nutrition recommendations, a recent RCT focusing on shocks of all kinds, including CS, was published. According to the trial results, early isocaloric enteral nutrition (iEN) started within one day of hospitalization was not superior to parenteral nutrition. Rather, it was associated with a higher risk of GI complications. For hemodynamic monitoring in assessing and treating patients in CS, the jury is still out. For patients who are unresponsive to initial therapy, we should consider using pulmonary artery catheter (PAC) early in the treatment course [7, 24]. Since the advent of PAC, we have found various hemodynamic profiles where the patient's prognosis depends on the RV performance. Hence, using MCS has emerged as an important modality of management. The variables and calculations for the management of CS, including but not limited to pulmonary artery pulsatility index, have been reviewed recently [28]. The overall CICU management of CS is summarized in (Figure 3) [29].

Mechanical circulatory support

Mechanical circulatory support (MCS) devices are increasingly used in CS to stabilize hemodynamics [30], although exactly when, whether, and how to incorporate them in shock care remain controversial [7]. Potential benefits of MCS include reduction of LV stroke work, intracardiac filling pressures, and enhancement of coronary and end-organ perfusion [31]. Device selection should be guided by the acuity of illness, CS phenotype, degree of circulatory and ventricular support required, vascular access or anatomy, and operator- or center-specific procedural volume and expertise (Figure 4) [29]. Understanding how each platform alters ventricular pressure-volume relationships is critical to implementing the optimal strategy [31].

Although axial and centrifugal-flow devices may improve hemodynamics compared with the intra-aortic balloon pump, no survival benefit has yet been demonstrated [32]. Also, recent observational data from the CathPCI and Chest Pain-MI registries and the Premier Healthcare database show wide variations in axial flow device use across the United States and raise safety concerns, particularly major bleeding, stroke, and mortality^{33,34}. Emerging data from dedicated shock center registries suggest that when MCS devices are deployed selectively using early invasive hemodynamics and standardized multidisciplinary treatment algorithms, improvements in survival may be achieved [35-37]. In patients with prohibitive iliofemoral vasculature, expertise in alternative access is the key. The axillary artery has been demonstrated to be a suitable conduit for intra-aortic balloon pump and Impella (Abiomed, Danvers, Massachusetts) in patients with CS, as it may also facilitate earlier ambulation and improved nutritional status for patients requiring prolonged circulatory support while awaiting cardiac replacement therapy [38].

Our current practice is to deploy MCS selectively in suitable patients with acute severe or refractory CS after expedited consultation with the multidisciplinary shock team, consisting of an interventional cardiologist, cardiothoracic surgeon, and cardiac intensivist, and advanced heart failure specialist. Lactate levels, cardiac power output, and pulmonary arterial pulsatility index facilitate MCS selection and weaning strategies. MCS can be used as a bridge to myocardial recovery, cardiac replacement therapy, or a temporizing measure to assess a patient's candidacy for a durable ventricular assist device or cardiac transplantation. Strict adherence to best vascular access and closure practices, familiarity with device troubleshooting, and multidisciplinary care in a level 1 CICU are critical components of optimal care [39].

Controversies of mechanical circulatory support

The controversies surrounding the use of mechanical devices are still present, like the ideal timing of device insertion. If MCS is used early at the onset of CS, probably, MODS can be avoided. On the other hand, early use might increase the complications due to invasive therapy. Hence, appropriate patient selection is of utmost importance to reap the best benefits. Depending upon the stage of CS, as already described by SCAI, the devices with low complication rates may be chosen in the early stages of CS whereas, more aggressive devices with higher flow rates may be reserved for more severe CS. Presently, we do not know which support can be optimal at what stage. Danish randomized multicenter trial (DanShock; Clinicaltrials.gov: NCT01633502) compares the Impella CP with standard treatment and can answer whether the implanted device on a routine basis improves mortality. A recent trial on the use of VA-ECMO known as the EURO SHOCK trial is underway. This trial's results will indicate whether early initiation of VAECMO after PCI in patients of ACS-CS results in improved mortality and morbidity [40]. Despite all these controversies, current European and American guidelines recommend the use of a percutaneous assist device for circulatory support in refractory CS (IIa recommendation) [41-43].

LV assist devices and heart transplantation

Patients with a non-responsive cardiogenic shock should be evaluated for a cardiac function substitute, either heart transplantation or a durable MCS. Complete psychosocial evaluation and clinical assessment considering risk factors such as age, liver enzymes, RFTs like serial serum urea and creatinine, coagulation disorders, aortic valve regurgitation, right ventricular function, and patient compliance with the medical therapy is necessary. Further research would better guide the healthcare providers towards eligible candidates for such advanced therapies, given the present mortality rates in such a critical patient population. With the updated United Network for Organ Sharing heart allocation protocol prioritizing patients with temporary MCS for expedited heart transplantation, an increasing number of patients with CS have used this pathway [44].

Short review of Management

A short review of management has been depicted beautifully in a (Table 2).

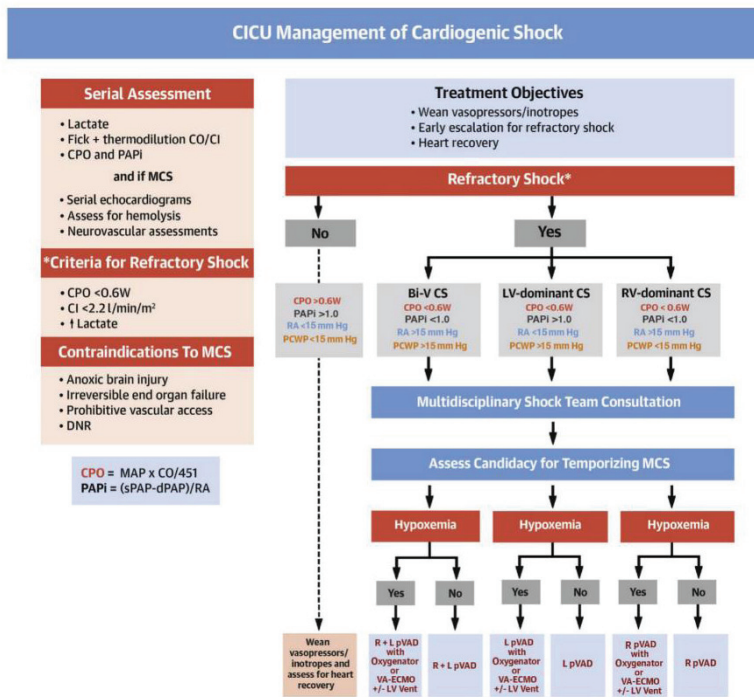


Figure 3: This schematic illustrates the longitudinal and multidisciplinary care pathways for cardiogenic shock (CS) care in a contemporary level 1 cardiac intensive care unit (CICU). CI - cardiac index; CO - cardiac output; CPO - cardiac power output; DNR - Do Not Resuscitate order; dPAP - diastolic pulmonary arterial pressure; L - left; MAP - mean arterial pressure; MCS - mechanical circulatory support; PAPI - pulmonary arterial pulsatility index; PCWP - pulmonary capillary wedge pressure; pVAD - percutaneous ventricular assist device; R - right; sPAP - systolic pulmonary arterial pressure [29].

	Impella RP	TandemHeart RA-PA	VA-ECMO	IABP	Impella (2.5, CP, 5.0, 5.5)	TandemHeart LA-FA
Flow	max 4.0 l/min	max 4.0 l/min	max 7.0 l/min	0.5 l/min	2.5 - 5.5 l/min	max 4.0 l/min
Pump Speed	33000 rpm	max 7500 rpm	max 5000 rpm	NA	max 51,000 rpm	max 7500 rpm
Mechanism	Axial flow continuous pump (RA-to-PA)	Centrifugal flow continuous pump (RA-to-PA)	Centrifugal flow continuous pump (RA-to-AO)	Balloon inflation-deflation (AO)	Axial flow continuous pump (LV-to-AO)	Centrifugal flow continuous pump (LA-to-AO)
Cannula Size	22 F venous	29 F venous	14-19 F arterial 17-21 F venous	7-8 F Arterial	13-21 F arterial	12-19 F arterial 21 F venous
Insertion/Placement	Femoral vein	Internal jugular vein	Femoral vein Femoral artery	Femoral artery Axillary artery	Femoral artery Axillary artery	Femoral artery Femoral vein
LV Unloading	-	-	-	+	++ to +++	++
RV Unloading	+	+	++	-	-	-
Cardiac Power	-	-	↑↑	↑	↑↑	↑↑
Afterload	-	-	↑↑	↓	↑↓	-
Coronary Perfusion	-	-	-	↑	↑	-
Considerations	<ul style="list-style-type: none"> RECOVER RIGHT: 73% survival-to-30 days in RVF post LVAD, AMI or cardiomyopathy May 2019 - FDA post-approval study: 33% survival-to-30 days 	<ul style="list-style-type: none"> IJ access may facilitate early ambulation 	<ul style="list-style-type: none"> Bi-V + oxygenation support for CS following: <ul style="list-style-type: none"> AMI, ADHF or cardiac arrest Cardiotomy Myocarditis Allograft rejection 	<ul style="list-style-type: none"> Requires stable cardiac rhythm and native heart function May consider in select cases of post-AMI mechanical complications 	<ul style="list-style-type: none"> June 2008 - FDA 510(k) approval for HR-PCI April 2016: Expanded indication for CS Contraindicated with mechanical aortic valve, LV thrombus 	<ul style="list-style-type: none"> Requires transeptal access Oxygenator may be added to the circuit

Figure 4: The hemodynamic profiles of the various circulatory support devices available for treatment of cardiogenic shock. ADHF - acute decompensated heart failure; AMI - acute myocardial infarction; AO - aorta; Bi-V - biventricular; CS - cardiogenic shock; FA - femoral artery; FDA - Food and Drug Administration; HR-PCI - high risk percutaneous coronary intervention; IABP - intra-aortic balloon pump; IJ - internal jugular; LA - left atrium; LV - left ventricular; LVAD - left ventricular assist device; PA - pulmonary artery; RA - right atrium; RPM - revolutions per minute; RV - right ventricular; RVF - right ventricular failure; VAECMO - venoarterial extracorporeal membrane oxygenation [29].

Table 1: Abbreviations, in order of appearance: AMI - acute myocardial infarction; CABG - coronary artery bypass grafting; CAD - coronary artery disease; CI - cardiac index; CS - cardiogenic shock; IABP - intra-aortic balloon pump; PCI - percutaneous coronary intervention; PCWP - pulmonary capillary wedge pressure; RCT - randomized controlled trial; SBP - systolic blood pressure.

	SHOCK Trial (1999)	IABP-SHOCK II Trial (2012)	IMPRESS Trial (2017)	CULPRIT-SHOCK Trial (2017)	ESC heart failure guidelines
Study design	RCT	RCT	RCT	RCT	
Clinical criteria	<ul style="list-style-type: none"> SBP less than 90 mm of Hg for 30 mins or more OR need of vasopressors to maintain SBP more than or equal to 90 mm of Hg AND End-organ hypoperfusion (urine output less than 30 ml/hr) 	<ul style="list-style-type: none"> SBP less than 90 mm of Hg for 30 minutes or more or vasopressors to maintain SBP more than 90 mm of Hg AND Clinical pulmonary congestion AND Impaired tissue perfusion with at least 1 of the following criteria: <ul style="list-style-type: none"> Cold/clammy skin and Extremities Altered mental status Urine output of less than 30 ml/hr. Serum Lactate of more than 2.0 mmol/l 	<ul style="list-style-type: none"> SBP less than 90 mm Hg for 30 min or more OR need for inotropes to maintain SBP more than 90 mm Hg. 	<ul style="list-style-type: none"> SBP less than 90 mm Hg for more than 30 min or need for inotropes to maintain SBP more than 90 mm Hg Clinical signs of pulmonary edema Impaired end-organ perfusion With at least one of the following criteria: <ul style="list-style-type: none"> Cold/clammy skin and Extremities AMS Lactate >2.0 Urine output <30 ml/h 	SBP less than 90 mmHg with adequate volume and clinical or laboratory signs of hypoperfusion. <ul style="list-style-type: none"> Signs of Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, and narrow pulse pressure. Signs of Laboratory hypoperfusion: Metabolic acidosis Elevated lactate Elevated creatinine
Hemodynamic criteria	CI #2.2 l/min/m ² and Pulmonary capillary wedge pressure >15 mm Hg	-	-	-	

Abbreviations, in order of appearance: AMI - acute myocardial infarction, CABG - coronary artery bypass grafting, CAD - coronary artery disease; CI - cardiac index; CS - cardiogenic shock; IABP - intra-aortic balloon pump; PCI - percutaneous coronary intervention; PCWP - pulmonary capillary wedge pressure; RCT - randomized controlled trial; SBP - systolic blood pressure.

Table 2: This table represents the take home points that we have derived from the entire review article [45].

1	Cardiogenic shock is a complex state of low cardiac output and hemodynamic instability that translates to hypoperfusion of various body tissues leading to multi-organ dysfunction and, eventually, death.
2	As RCTs in such a critically ill population are not practical, no single best set of guidelines have been established towards managing such patients, and the mortality rates still exceed 40%.
3	Norepinephrine is hailed as the first-line vasopressor agent, but other agents are also useful retrospectively.
4	Pulmonary Artery Catheter (PAC) use may lead to earlier identification of CS so that medical and device-based therapies may be started based on this.
5	Early and timely revascularization is the mainstay of treatment.
6	AMI-CS leading to cardiac arrest accompanies various time-dependent complications. Hence, a holistic approach, keeping in mind the overall prognosis, should be followed.
7	Consulting a team of an interventional cardiologist, cardiothoracic surgeon, cardiac intensivist, and advanced heart failure specialist is recommended for acute severe or refractory CS to put the patient on mechanical circulatory support (MCS).
8	In select patients with left ventricular (LV)-dominant CS and normotensive hypoperfusion, pure vasodilators may be effective.
9	Evaluation of the existing and emerging modalities of CS management via various RCTs is the need of the hour.

This table represents the take home points that we have derived from the entire review article.⁴⁵

Conclusion

With advancements in the management of STEMI like cardiac ICUs, catheterization labs, and newer anti-thrombotic drugs, such cases' prognosis has improved. Despite efforts to improve outcomes further, the prognosis has not improved in recent decades. Controversies remain about the choice of optimal pharmacological therapies, revascularization strategies, the role of MCS. Due to the current informed consent protocol for clinical trials, the patients with CS are too sick to give their consent so testing treatments in CS patients is a challenge. Fortunately, several trials are underway for the various MCS options [47, 48]. Recently, the results from the National Cardiogenic Shock Initiative, German Impella Registry and Japan VAD Council (IMPELLA Committee) are showing favorable outcomes and increased survival rates of up to 70% [49, 50]. Hence, the early use of MCS in AMI-CS has a potential to alter the prognosis in these patients. Only the RCTs in future will address this issue.

Author Contributions

The lead author of the case report is Dr Rohit Mody. Dr Debabrata Dash, Dr Bhavya Mody, Dr Aditya Saholi, Dr Shubham Sachdeva had equal and substantial contributions in the formation of this case report. They were involved in conceptualization, data curation, formal analysis, resources, software, validation, visualization, writing – original draft, writing – review & editing.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was not required since it is an accepted procedure.

Consent for Publication

Written consent has been obtained to publish the case report from the guardian. The consent copy is available with the authors and ready to be submitted if required.

Competing Interests

The authors declare that they have no competing interests.

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