



# HOT TOPICS IN CARDIOLOGIA 2024

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# Review Lancet 2024; 404: 2006–20



## Cardiogenic shock

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Cardiogenic shock is a complex syndrome defined by systemic hypoperfusion and inadequate cardiac output arising from a wide array of underlying causes. Although the understanding of cardiogenic shock epidemiology, specific subphenotypes, haemodynamics, and cardiogenic shock severity staging has evolved, few therapeutic interventions have shown survival benefit. Results from seminal randomised controlled trials support early revascularisation of the culprit vessel in infarct-related cardiogenic shock and provide evidence of improved survival with the use of temporary circulatory support in selected patients. However, numerous questions remain unanswered, including optimal pharmacotherapy regimens, the role of mechanical circulatory support devices, management of secondary organ dysfunction, and best supportive care. This Review summarises current definitions, pathophysiological principles, and management approaches in cardiogenic shock, and highlights key knowledge gaps to advance individualised shock therapy and the evidence-based ethical use of modern technology and resources in cardiogenic shock.

### Introduction

Cardiogenic shock is a complex syndrome characterised by inadequate tissue perfusion due to reduced cardiac output resulting from a wide array of underlying causes.<sup>1</sup> The short-term mortality rate of cardiogenic shock has stagnated at around 40–50%<sup>2,3</sup> despite advances in cardiovascular critical care. Understanding of cardiogenic shock, a complex condition including diverse causes, haemodynamic subtypes, patient-specific variables, and clinical trajectories, has advanced through mechanistic studies and in-depth analyses of large datasets. Most randomised clinical trials evaluating pharmacological or device-based treatment options for the management of cardiogenic shock have not shown clinical benefit, which might partly be due to eligibility criteria that allowed for the inclusion of heterogeneous cardiogenic shock populations.<sup>2,3,4</sup> These insights have tempered expectations of treatment options to improve outcomes when broadly applied in unselected cardiogenic shock populations, and have shifted scientific efforts towards the identification of targeted therapeutic strategies. This Review provides an overview of cardiogenic shock definitions, pathophysiological concepts, current management approaches, and key research questions (panel).

### Definition and classification

Cardiogenic shock is broadly defined as insufficient organ perfusion resulting from cardiac dysfunction.<sup>1,10–20</sup>

#### Search strategy and selection criteria

We searched PubMed for literature published from May 1, 1999, to May 31, 2024, using the search term “cardiogenic shock” in combination with key terms related to pharmacotherapy, revascularisation, mechanical circulatory support, infarct-related mechanical complications, management of organ dysfunction, and supportive care (appendix p 31). We included relevant publications in English with an adult patient population, focusing on randomised controlled trials and large observational studies.

To standardise the definition, the Shock Academic Research Consortium (SHARC) expert panel established specific criteria to enhance consistency across cardiogenic shock clinical trials and registries.<sup>1</sup> Integral elements of the SHARC definition are: a systolic blood pressure below 90 mm Hg for more than 30 min or the need for inotropes, vasopressors, or mechanical circulatory support (MCS) to maintain adequate blood pressure, alongside evidence of systemic hypoperfusion. The SHARC definition also recognises the normotensive cardiogenic shock subtype defined by evidence of hypoperfusion despite systolic blood pressure equal to or greater than 90 mm Hg without the need for vasopressors, inotropes, or MCS, with other potential causes of markers of hypoperfusion excluded. A low cardiac index value of less than or equal to 2.2 L/(min<sup>2</sup>m<sup>2</sup>) and a high systemic vascular resistance index of more than 2200 dynes/(cm<sup>5</sup>sec<sup>2</sup>) have been recognised as thresholds for cardiogenic shock, but objective data from advanced haemodynamic monitoring might not always be available.<sup>1</sup> Cardiogenic shock is often recognised on the basis of readily available signs of organ hypoperfusion, such as elevated arterial lactate, liver and kidney failure, cold or clammy extremities, or altered mental status in a patient with acute cardiac compromise.<sup>10</sup> Signs of volume overload and congestion can be present on physical examination, imaging, and haemodynamic monitoring.

In 2022, the Society for Cardiovascular Angiography and Interventions (SCAI) updated a widely used staging system to categorise cardiogenic shock severity on the basis of haemodynamic status, markers of hypoperfusion, and use of advanced circulatory support, ranging from A (at risk) to E (extremis).<sup>21</sup> Hypoperfusion is absent in lower SCAI stages (A and B) despite the presence of hypotension in stage B, but organ hypoperfusion requiring intervention defines shock in advanced SCAI stages (C to E). Higher SCAI stages have consistently been shown to correlate with higher short-term mortality, despite considerable differences in the populations analysed across validation studies.<sup>14,17</sup> The current SCAI

# Classificazione e cause

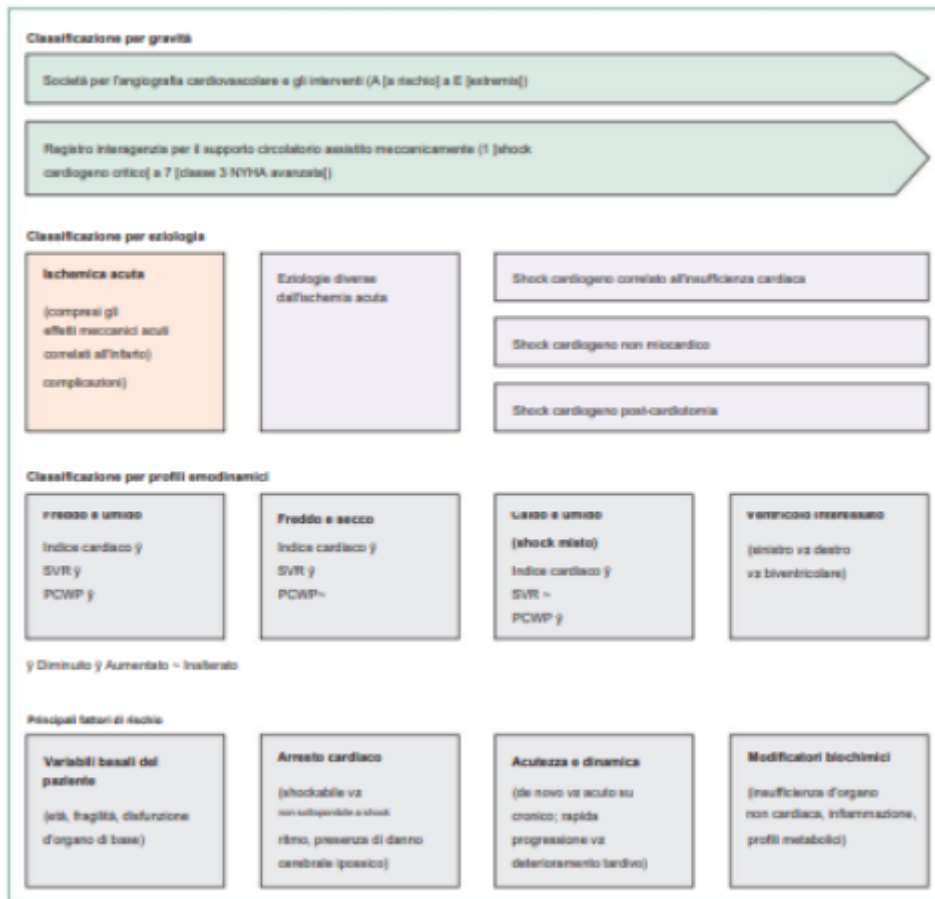


Figura 1: Sistemi di classificazione e fattori di rischio chiave per lo shock cardiogeno  
 NYHA=New York Heart Association. PCWP=pressione di incuneamento capillare polmonare. SVR=resistenza vascolare sistemica.

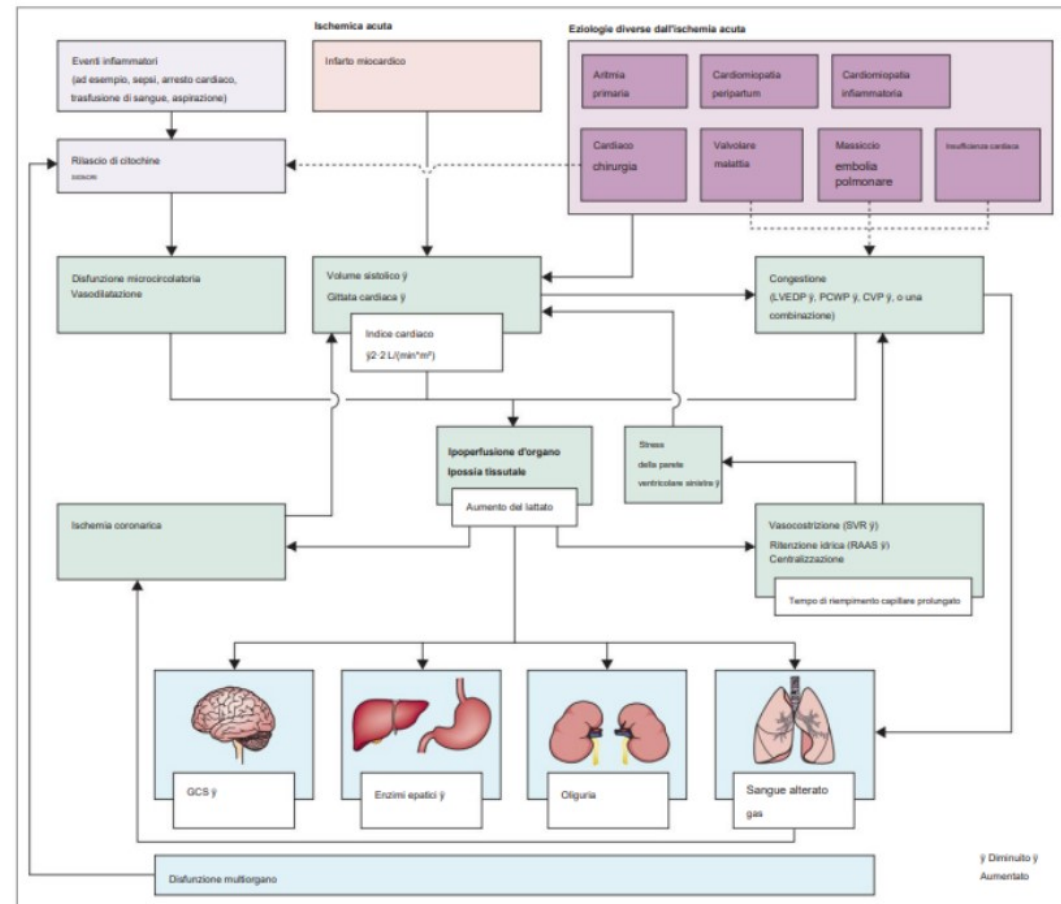


Figura 2: Riepilogo delle principali cause e meccanismi patofisiologici dello shock cardiogeno  
 Le linee tratteggiate indicano potenziali meccanismi secondari che contribuiscono allo shock cardiogeno. CVP=pressione venosa centrale. GCS=Glasgow Coma Scale. LVEDP=pressione telediastolica ventricolare sinistra. PCWP=pressione di incuneamento capillare polmonare. RAAS=sistema renina-angiotensina-aldosterone. SIRS=sindrome da risposta infiammatoria sistemica. SVR=resistenza vascolare sistemica.



# Circulation

## PRIMER

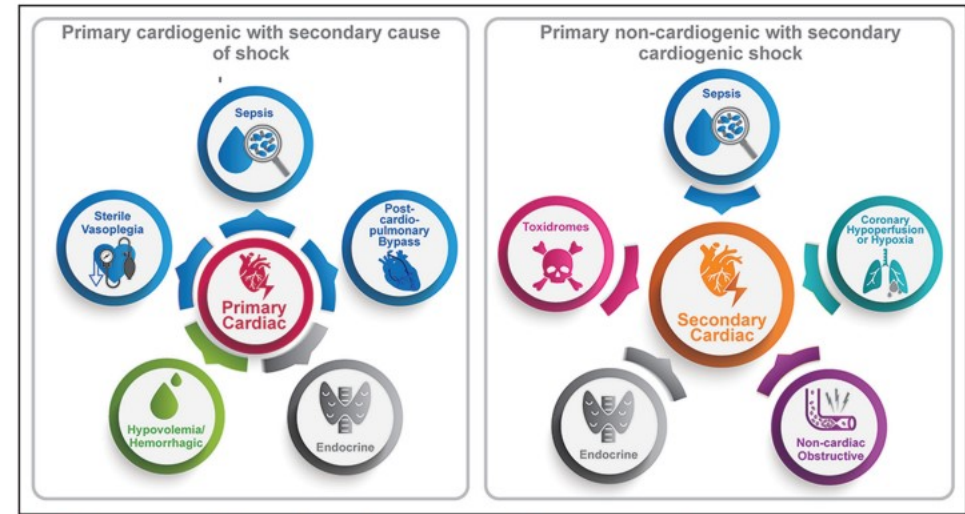
### Mixed Cardiogenic Shock: A Proposal for Standardized Classification, a Hemodynamic Definition, and Framework for Management

Sean van Diepen MD, MSc; Janine Pöss, MD; Janek M. Senaratne, MD, MSc; Ann Gage, MD; David A. Morrow MD, MPH

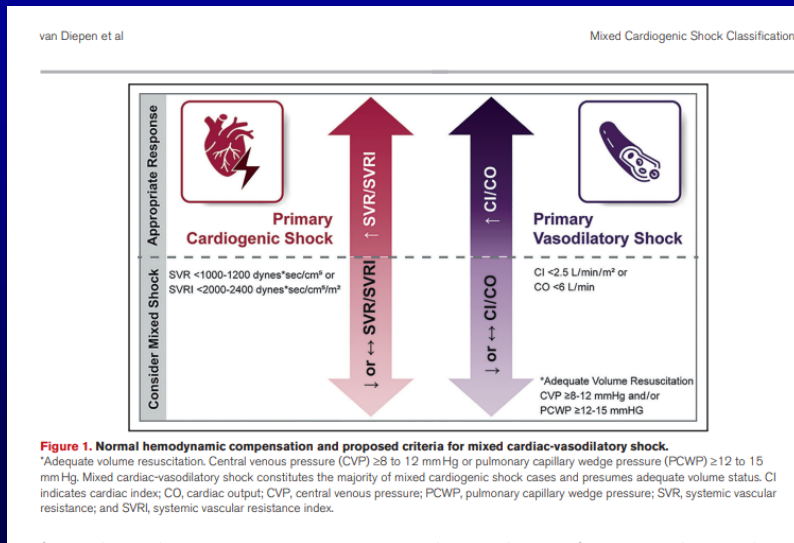
**ABSTRACT:** The classification of cardiogenic shock (CS) has evolved from a singular cold-and wet-hemodynamic profile. Data from registries and clinical trials have contributed to a broader recognition that although all patients with CS have insufficient cardiac output leading to end organ hypoperfusion, there is considerable variability in CS acuity, underlying etiologies, volume status, and systemic vascular resistance. Mixed CS can be broadly categorized as CS with at least 1 additional shock state. Mixed CS states are now the second leading cause of shock in contemporary coronary intensive care units, but there is little high-quality evidence to guide routine care, and there are no standardized classification frameworks or well-established hemodynamic definitions. This primer summarizes the current epidemiology and proposes a classification framework and invasive hemodynamic parameters to guide categorization that could be applied to help better phenotype patients captured in registries and trials, as well as guide management of mixed CS states.

**Key Words:** cardiogenic shock ■ hypovolemic shock ■ mixed shock ■ vasodilatory shock

Check for updates



**Figure 2.** Common causes of mixed cardiogenic shock states in cardiac intensive care units. **Left,** Primary cardiogenic shock with surrounding common secondary causes of noncardiogenic shock. **Right,** Primary noncardiogenic causes of shock in the periphery that may lead to secondary cardiogenic shock.



**Figure 1.** Normal hemodynamic compensation and proposed criteria for mixed cardiac-vasodilatory shock. \*Adequate volume resuscitation. Central venous pressure (CVP) ≥8 to 12 mmHg or pulmonary capillary wedge pressure (PCWP) ≥12 to 15 mmHg. Mixed cardiac-vasodilatory shock constitutes the majority of mixed cardiogenic shock cases and presumes adequate volume status. CI indicates cardiac index; CO, cardiac output; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; SVR, systemic vascular resistance; and SVRI, systemic vascular resistance index.

	Pure Cardiogenic	Hypovolemic or Hemorrhagic	Vasodilatory	Obstructive (Selected non-cardiac)
<b>Exam</b>	Assess Volume Status Cardiac Auscultation Assess Limb perfusion	Volume depletion Therapeutic challenge (leg raise) Blood loss	Sepsis: Temperature Anaphylaxis: Medication history, hives, urticaria Neurogenic: Spinal injury Endocrine: Adrenal insufficiency or hypothyroid Vasoplegia: Exclusion of other causes*	Tension Pneumothorax: ↑ JVP, tracheal deviation, absent lung sounds Abdominal Compartment Syndrome: Distended abdomen, Respiratory Distress, Oliguria
<b>Labs</b>	Troponin Lactate Creatinine Liver Function Tests B-type natriuretic peptides	Creatinine, Urea Hemoglobin, Hematocrit	Cultures Cortisol TSH	Creatinine
<b>Imaging</b>	Electrocardiogram Echocardiogram Coronary angiogram Cardiac MRI	Ultrasound (inferior vena cava size) CT scan	Infection specific imaging Spinal imaging	Chest X-ray Point of Care Ultrasound Abdominal Imaging
<b>Invasive Hemodynamics</b>	J <sub>1</sub> -CO, J <sub>1</sub> SVR, J <sub>1</sub> -CVP, J <sub>1</sub> -PCWP	J <sub>1</sub> CO, J <sub>1</sub> CVP, J <sub>1</sub> PCWP, J <sub>1</sub> SVR	J <sub>1</sub> -SVR, J <sub>1</sub> -CO	J <sub>1</sub> CO, J <sub>1</sub> SVR, J <sub>1</sub> -CVP Abdominal Compartment Syndrome: Bladder pressure > 20 mmHG Abdominal perfusion pressure < 60 mmHG


\*Clinical exam guided by history: systemic inflammatory response syndrome, liver dysfunction, extracorporeal circuits, pancreatitis, burns, trauma, drugs and medications. Exclusion of vasodilatory causes.

**Figure 3.** Key elements of a comprehensive approach to evaluation of suspected mixed cardiogenic shock in the cardiac intensive care unit. \*Clinical examination guided by history: systemic inflammatory response syndrome, liver dysfunction, extracorporeal circuits, pancreatitis, burns, trauma, drugs, intravenous vasoactive agents, and preadmission medications. CO indicates cardiac output; CT, computed tomography; CVP, central venous pressure; JVP, jugular venous pressure; MRI, magnetic resonance imaging; PCWP, pulmonary capillary wedge pressure; SVR, systemic vascular resistance; SVV, stroke volume variation; and TSH, thyroid stimulating hormone.

REVIEW

# Management of cardiogenic shock: state-of-the-art



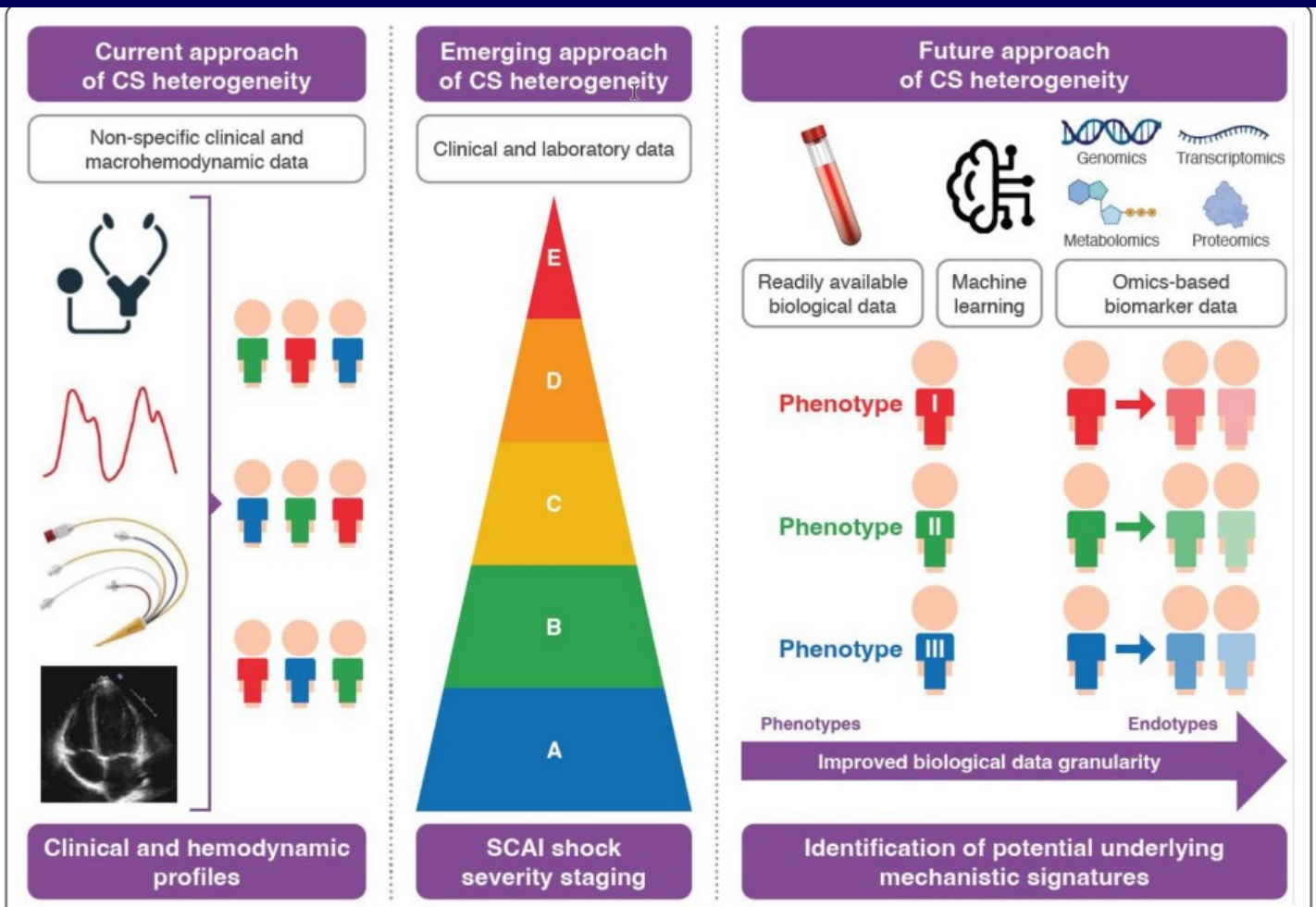
Christian Jung<sup>1,2\*</sup> , Raphael Romano Bruno<sup>1</sup>, Marwan Jumean<sup>3</sup>, Susanna Price<sup>4,5</sup>, Konstantin A. Krychtiuk<sup>6</sup>, Kollengode Ramanathan<sup>7,8</sup>, Josef Dankiewicz<sup>9</sup>, John French<sup>10,11,12</sup>, Clement Delmas<sup>13,14</sup>, Alexandra-Arias Mendoza<sup>15</sup>, Holger Thiele<sup>16</sup> and Sabri Soussi<sup>17,18</sup>

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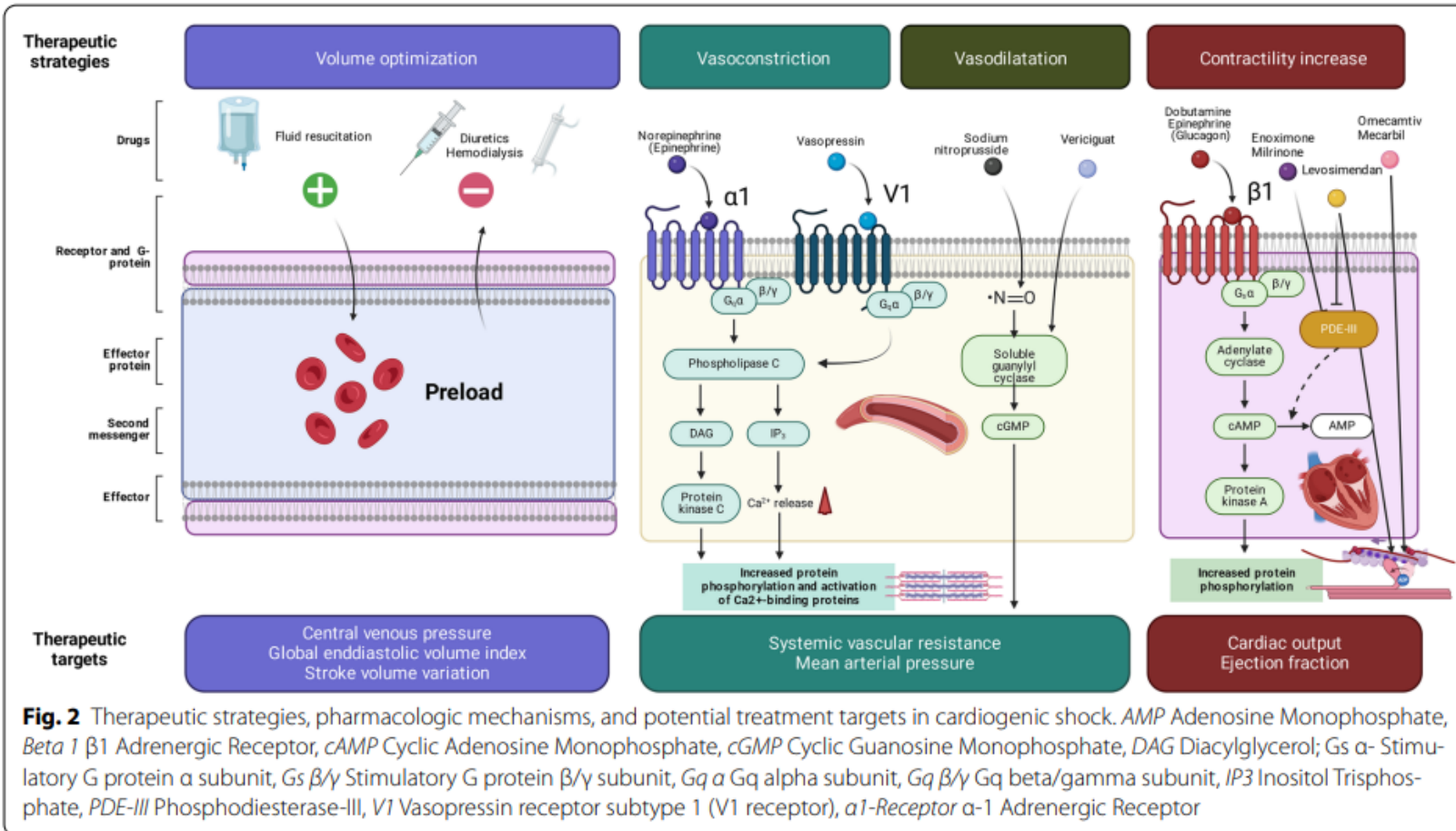
## Abstract

The management of cardiogenic shock is an ongoing challenge. Despite all efforts and tremendous use of resources, mortality remains high. Whilst reversing the underlying cause, restoring/maintaining organ perfusion and function are cornerstones of management. The presence of comorbidities and preexisting organ dysfunction increases management complexity, aiming to integrate the needs of vital organs in each individual patient. This review provides a comprehensive overview of contemporary literature regarding the definition and classification of cardiogenic shock, its pathophysiology, diagnosis, laboratory evaluation, and monitoring. Further, we distill the latest evidence in pharmacologic therapy and the use of mechanical circulatory support including recently published randomized-controlled trials as well as future directions of research, integrating this within an international group of authors to provide a global perspective. Finally, we explore the need for individualization, especially in the face of neutral randomized trials which may be related to a dilution of a potential benefit of an intervention (i.e., average effect) in this heterogeneous clinical syndrome, including the use of novel biomarkers, artificial intelligence, and machine learning approaches to identify specific endotypes of cardiogenic shock (i.e., subclasses with distinct underlying biological/molecular mechanisms) to support a more personalized medicine beyond the syndromic approach of cardiogenic shock.

**Keywords:** Cardiogenic shock, Intensive care, Myocardial infarction, Heart failure, Assist device, Outcome



**Fig. 1** Summary of the traditional (clinical), current/emerging (SCAI shock stages), and future approaches (biomarker-driven phenotypes) to unravel CS heterogeneity. CS cardiogenic shock, SCAI Society for Cardiovascular Angiography and Interventions





Review > Eur Cardiol. 2024 Nov 12:19:e21. doi: 10.15420/ecr.2024.16. eCollection 2024.

## Levosimendan, a Promising Pharmacotherapy in Cardiogenic Shock: A Comprehensive Review

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Mochamad Yusuf Alsagaff <sup>1 2</sup>, Henry Sutanto <sup>6</sup>, Chaq El Chaq Zamzam Multazam <sup>7</sup>

Affiliations + expand

PMID: 39588250 PMID: PMC11588109 DOI: 10.15420/ecr.2024.16

### Abstract

Cardiogenic shock (CS) is a critical condition with high mortality rate, as the current management of CS presents significant challenges. Exploration of more effective therapies is necessitated. This review article comprehensively examines the efficacy and safety of levosimendan in the management of CS. By synthesising evidence from numerous studies, a comparison of levosimendan over traditional inotropic agents, such as enoximone, dobutamine, dopamine and norepinephrine, is highlighted. The unique mechanism of action of levosimendan enhances myocardial contractility without increasing oxygen demand, offering a promising alternative for patients with CS. This review also delves into comparative studies that demonstrate the superiority of levosimendan in improving survival rates, haemodynamic parameters, and reducing the incidence of CS complications. Safety profiles and adverse effects are critically assessed to provide a balanced view of the therapeutic window provided by levosimendan. The review concludes that levosimendan is a valuable addition to the therapeutic strategy against CS, with the potential to improve patient outcomes.

**Keywords:** Levosimendan; adenosine triphosphate-dependent potassium channel opener; calcium sensitiser; cardiogenic shock; cardiovascular disease.

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# Dipende dalla causa

Review > [Cardiol Clin.](#) 2025 Feb;43(1):151-167. doi: 10.1016/j.ccl.2024.07.001. Epub 2024 Aug 30.

## Cardiac Complications of Immune Checkpoint Inhibitors and Chimeric Antigen Receptor T Cell Therapy

Bhargav Makwana <sup>1</sup>, Aishwarya Malode <sup>1</sup>, Sumanth Khadke <sup>1</sup>, Vahin Patel <sup>1</sup>, Rushin Shah <sup>1</sup>, Manav Patel <sup>1</sup>, Aneri Parikh <sup>1</sup>, Sourbha S Dani <sup>1</sup>, Sarju Ganatra <sup>2</sup>

Affiliations + expand

PMID: 39551556 DOI: [10.1016/j.ccl.2024.07.001](#)

### Abstract

Immune checkpoint inhibitors and chimeric antigen receptor T-cell therapy have revolutionized cancer treatment but can cause life-threatening cardiovascular toxicities through immune-related adverse events. Myocarditis is the most common and potentially fatal toxicity with immune checkpoint inhibitors. T-cell therapies can potentially lead to cytokine release syndrome. Diagnosis of ICI-myocarditis requires a multimodal approach, including biomarkers, imaging, and endomyocardial biopsy, while CRS is characterized by a clinical syndrome resembling distributive shock. Management involves discontinuing the offending therapy, immunosuppression with corticosteroids for ICI-myocarditis, and interleukin-6 antagonists for CRS. Collaboration between oncologists and cardiologists is crucial for early recognition and prompt treatment.

**Keywords:** CAR T-cell therapy; Cardiotoxicity; Cytokine release syndrome (CRS); Immune checkpoint inhibitors; Myocarditis; Pericarditis.

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Review > [Heart Fail Rev.](#) 2024 Nov 6. doi: 10.1007/s10741-024-10458-y. Online ahead of print.

## Adrenal crisis-induced cardiogenic shock (ACCS): a comprehensive review

Maryam Heidarpour <sup>1</sup>, Davood Shafie <sup>2</sup>, Reza Eshraghi <sup>3</sup>, Seyed Reza Mirjalili <sup>4</sup>, Ashkan Bahrami <sup>3</sup>, Mohammad Reza Movahed <sup>5 6</sup>

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PMID: 39503801 DOI: [10.1007/s10741-024-10458-y](#)

### Abstract

Adrenal insufficiency (AI) is a disorder in which inadequate glucocorticoid and mineralocorticoid hormone production leads to a variety of symptoms, including fatigue, weight loss, and nausea. In some patients with unknown AI, adrenal crisis-induced cardiogenic shock (ACCS) can be the first presentation, resulting in a fatal situation. The ACCS may exhibit unresponsiveness to inotropes and fluid therapy; thus, glucocorticoid administration is the primary vital intervention, making early detection of AI essential. Hence, in this study, we review the case reports demonstrating acute cardiomyopathies in the context of AI. The review addresses the suggested underlying mechanisms, including the diminished protective effects of glucocorticoids against catecholamines in AI. We also highlighted some clues to aid physicians in considering AI as a differential diagnosis in critically ill patients presenting cardiogenic shock.

**Keywords:** Adrenal crisis; Adrenal insufficiency; Cardiogenic shock; Hormone deficiency; Shock.

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Review > US Cardiol. 2024 Aug 13;18:e11. doi: 10.15420/usc.2024.16. eCollection 2024.

## Management of Post-cardiotomy Shock

Eric J Hall <sup>1</sup>, Alexander I Papolos <sup>2</sup>, P Elliott Miller <sup>3</sup>, Christopher F Barnett <sup>4</sup>, Benjamin B Kenigsberg <sup>2</sup>

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PMID: 39494414 PMCID: PMC11526484 DOI: 10.15420/usc.2024.16

### Abstract

Patients undergoing cardiac surgery experience significant physiologic derangements that place them at risk for multiple shock phenotypes. Any combination of cardiogenic, obstructive, hemorrhagic, or vasoplegic shock occurs commonly in post-cardiotomy patients. The approach to the diagnosis and management of these shock states has many facets that are distinct compared to non-surgical cardiac intensive care unit patients. Additionally, the approach to and associated outcomes of cardiac arrest in the post-cardiotomy population are uniquely characterized by emergent bedside re sternotomy if the circulation is not immediately restored. This review focuses on the unique aspects of the diagnosis and management of post-cardiotomy shock.

**Keywords:** Shock; cardiac surgery; cardiogenic shock; cardiotomy; mechanical circulatory support; post-cardiotomy shock.

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Review > Clin Transplant. 2024 Nov;38(11):e15482. doi: 10.1111/ctr.15482.

## Lessons Learned From Extracorporeal Life Support Practice and Outcomes During the COVID-19 Pandemic

George Gill <sup>1</sup>, Michael O'Connor <sup>2</sup>, Mark E Nunnally <sup>3</sup>, Alain Combes <sup>4</sup>, Michael Harper <sup>5</sup>, David Baran <sup>6</sup>, Mary Avila <sup>7</sup>, Barbara Pisani <sup>8</sup>, Hannah Copeland <sup>9</sup>, Michael Nurok <sup>1</sup>

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PMID: 39469754 DOI: 10.1111/ctr.15482

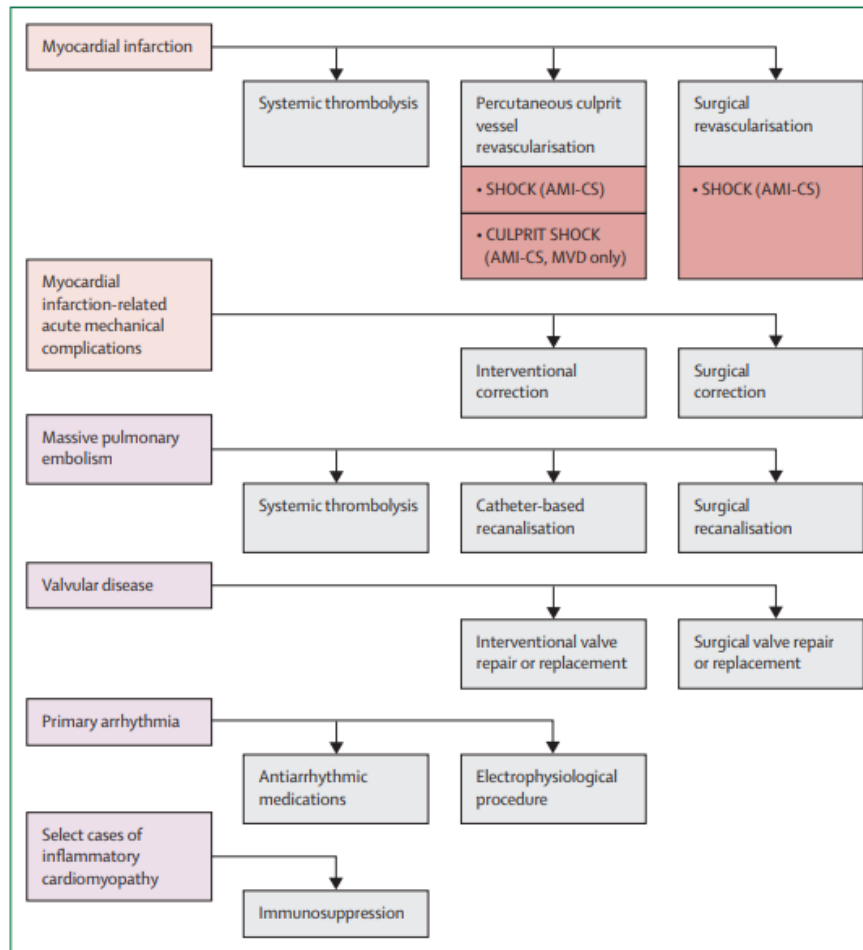
### Abstract

Extracorporeal membrane oxygenation is increasingly being used to support patients with hypoxemic respiratory failure and cardiogenic shock. During the COVID-19 pandemic, consensus guidance recommended extracorporeal life support for patients with COVID-19-related cardiopulmonary disease refractory to optimal conventional therapy, prompting a substantial expansion in the use of this support modality. Extracorporeal membrane oxygenation was particularly integral to the bridging of COVID-19 patients to heart or lung transplantation. Limited human and physical resources precluded widespread utilization of mechanical support during the COVID-19 pandemic, necessitating careful patient selection and optimal management by expert healthcare teams for judicious extracorporeal membrane oxygenation use. This review outlines the evidence supporting the use of extracorporeal life support in COVID-19, describes the practice and outcomes of extracorporeal membrane oxygenation for COVID-19-related respiratory failure and cardiogenic shock, and proposes lessons learned for the implementation of extracorporeal membrane oxygenation as a bridge to transplantation in future public health emergencies.

**Keywords:** extracorporeal membrane oxygenation (ECMO); heart disease: infectious; lung disease: infectious.

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**Figure 3: Emergent treatment of specific underlying causes of cardiogenic shock**

Key medical treatment strategies are summarised in the first column, interventional strategies in the second column, and surgical strategies in the third column. Boxes underneath management options indicate mortality-powered randomised controlled trials investigating specific treatment approaches (trial patient population is included in brackets). AMI-CS=acute myocardial infarction-related cardiogenic shock. MVD=multivessel disease.



STATE OF THE ART

## Hemodynamic management of cardiogenic shock in the intensive care unit

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Benedikt Schrage, MD PhD,<sup>j</sup> and Thomas C. Hanff, MD MSCE<sup>k</sup>

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### KEYWORDS:

cardiogenic shock;  
mechanical circulatory  
support;  
hemodynamics;  
inotropes;  
heart transplantation;  
left ventricular assist  
devices

Hemodynamic derangements are defining features of cardiogenic shock. Randomized clinical trials have examined the efficacy of various therapeutic interventions, from percutaneous coronary intervention to inotropes and mechanical circulatory support (MCS). However, hemodynamic management in cardiogenic shock has not been well-studied. This State-of-the-Art review will provide a framework for hemodynamic management in cardiogenic shock, including a description of the 4 therapeutic phases from initial 'Rescue' to 'Optimization', 'Stabilization' and 'de-Escalation or Exit therapy' (R-O-S-E), phenotyping and phenotype-guided tailoring of pharmacological and MCS support, to achieve hemodynamic and therapeutic goals. Finally, the premises that form the basis for clinical management and the hypotheses for randomized controlled trials will be discussed, with a view to the future direction of cardiogenic shock.

J Heart Lung Transplant 2024;43:1059–1073

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The prevalence of cardiogenic shock (CS) has been variably reported, typically accounting for about 15% of intensive care unit admissions, with a increasing trend of CS unrelated to acute myocardial infarction (AMI).<sup>1</sup> Short-term mortality is high at 50–60%, with most deaths within 30 days related to cardiac causes.<sup>2</sup> The assessment,

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### Editor's Comment

## The Management and Treatment of Cardiogenic Shock: Is Sex Still a Factor?

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Durham, North Carolina

Cardiogenic shock is associated with significant morbidity and mortality. However, to date, no consensus has been made on how sex-based differences may affect these outcomes. Several challenges are present that make this a complex topic of study. One important barrier is that women tend to represent only a minority of the cases, with most studies reporting women accounting for less than one-third of patients admitted for cardiogenic shock.<sup>1,4</sup> Women also tend to be older with a higher burden of comorbidities on presentation, making it difficult to appropriately compare against their younger and more numerous male counterparts.<sup>1</sup> Additionally, several studies have noted that women are treated subsequently with fewer guideline-directed interventions and support devices, such as percutaneous left ventricular assist devices, mechanical circulatory support, coronary angiography, and percutaneous coronary interventions (PCIs).

Questions remain as to why there are still different treatments for the same disease processes between sexes. Several post hoc analyses of randomized trials evaluated sex-based differences in cardiogenic shock outcomes when examining differences with early revascularization, single vs multivessel revascularization with PCI, and inotrope selection. These analyses found no difference in mortality between the sexes.<sup>3–5</sup> However, other observational analyses using the National Inpatient Sample database found an increased risk for mortality in women with cardiogenic shock.<sup>6,7</sup> The advantage of large cohorts from observational registries is the ability to capture not only data from tertiary care centers, but data from all hospitals, including rural and small facilities. Using these comprehensive samples, it has been found that cardiogenic shock may be more prevalent in Hispanic and Black women, as well as in women from lower socioeconomic statuses.<sup>8,7</sup> It may be possible that the lack of mortality

differences seen in randomized controlled trials is due to patient selection that often exists in patients participating in clinical trials.

In the current paper by Darlington et al,<sup>8</sup> the authors further examine sex-based disparities in the treatment and outcomes of women with cardiogenic shock. The authors evaluated a retrospective cohort of 1495 consecutive, unique adult cardiovascular intensive care unit admissions from 2007 to 2018. Data were extracted from the electronic health record, and validated algorithms were calculated. The authors found that overall 37.1% of their population were women. These women were older (71.7 years vs 67.8 years) compared with men, but were found to have similar comorbidities. Women presented at similar rates as men with acute myocardial infarction and there were no differences in the use of coronary angiography and PCI. However, they noted that women received temporary mechanical circulatory support less frequently than men. Additionally, women who underwent PCI had a lower risk of 1-year mortality compared with women who underwent coronary angiography without PCI. Ultimately, they found no differences in in-hospital or 1-year mortality between the sexes, despite age and resource use differences.

Several limitations of this study included that the data were derived from an observational retrospective cohort from a single tertiary center with a predominantly White population. Additionally, they were unable to determine from record review why certain therapies were provided; thus, they lacked perspective into the providers' choices. Nonetheless, the authors highlighted several key issues, including lower female representation and decreased resource use, without evidence of sex-based differences in in-hospital or 1-year mortality rates, which contributes to the body of literature with further evidence from a large sample of patients from a tertiary care center.

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Expert Review

## Cardiogenic Shock Update: New Trials, Evolving Management Paradigms, and Artificial Intelligence



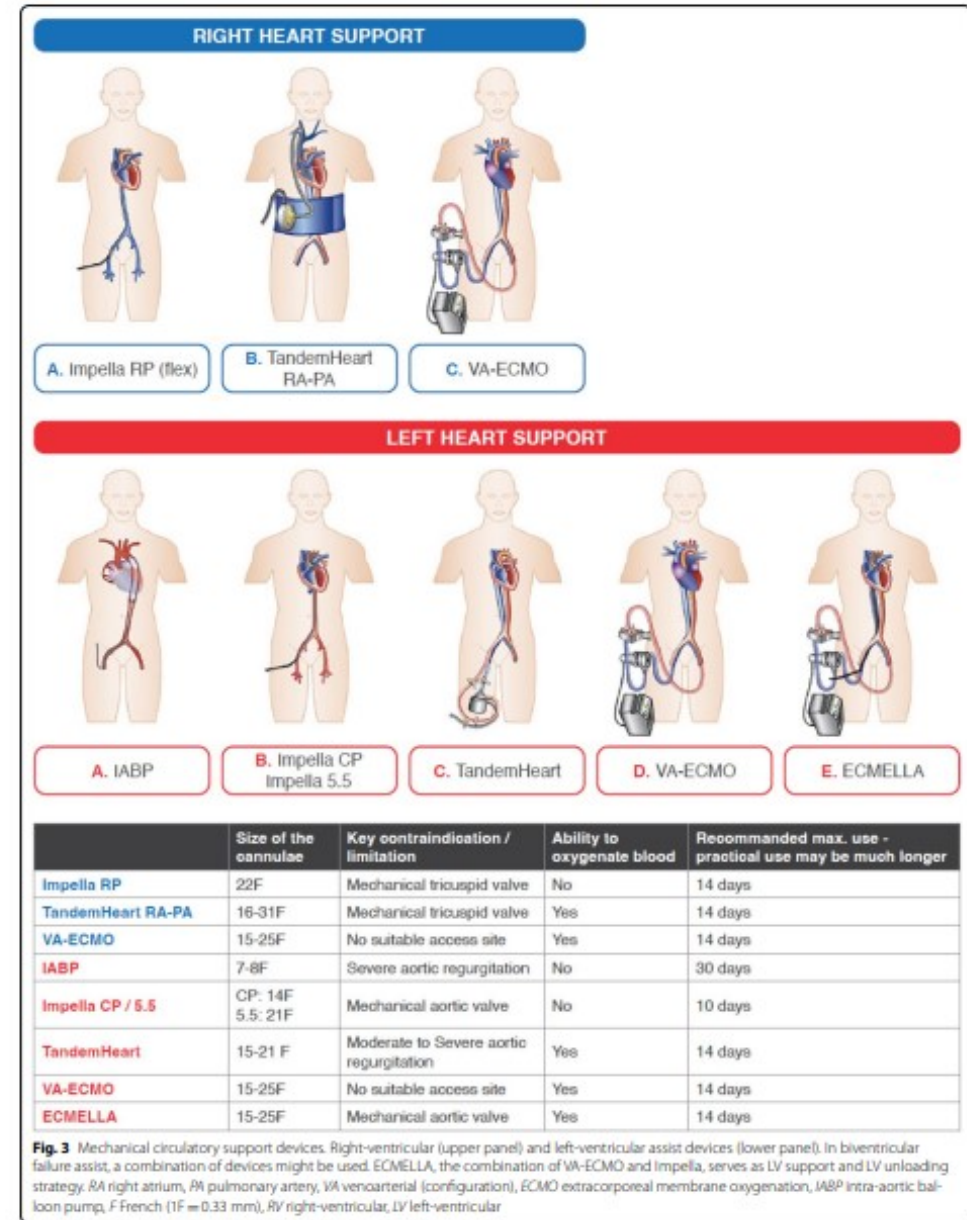
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# Sistemi di assistenza



# Aumento mortalità

Research

JAMA Cardiology | Original Investigation

## Comparative Effectiveness of Percutaneous Microaxial Left Ventricular Assist Device vs Intra-Aortic Balloon Pump or No Mechanical Circulatory Support in Patients With Cardiogenic Shock

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**IMPORTANCE** Recent studies have produced inconsistent findings regarding the outcomes of the percutaneous microaxial left ventricular assist device (LVAD) during acute myocardial infarction with cardiogenic shock (AMICS).

**OBJECTIVE** To compare the percutaneous microaxial LVAD vs alternative treatments among patients presenting with AMICS using observational analyses of administrative data.

**DESIGN, SETTING, AND PARTICIPANTS** This comparative effectiveness research study used Medicare fee-for-service claims of patients admitted with AMICS undergoing percutaneous coronary intervention from October 1, 2015, through December 31, 2019. Treatment strategies were compared using (1) inverse probability of treatment weighting to estimate the effect of different baseline treatments in the overall population; (2) instrumental variable analysis to determine the effectiveness of the percutaneous microaxial LVAD among patients whose treatment was influenced by cross-sectional institutional practice patterns; (3) an instrumented difference-in-differences analysis to determine the effectiveness of treatment among patients whose treatment was influenced by longitudinal changes in institutional practice patterns; and (4) a grace period approach to determine the effectiveness of initiating the percutaneous microaxial LVAD within 2 days of percutaneous coronary intervention. Analysis took place between March 2021 and December 2022.

**INTERVENTIONS** Percutaneous microaxial LVAD vs alternative treatments (including medical therapy and intra-aortic balloon pump).

**MAIN OUTCOMES AND MEASURES** Thirty-day all-cause mortality and readmissions.

**RESULTS** Of 23 478 patients, 14 264 (60.8%) were male and the mean (SD) age was 73.9 (9.8) years. In the inverse probability of treatment weighting analysis and grace period approaches, treatment with percutaneous microaxial LVAD was associated with a higher risk-adjusted 30-day mortality (risk difference, 14.9%; 95% CI, 12.9%-17.0%). However, patients receiving the percutaneous microaxial LVAD had a higher frequency of factors associated with severe illness, suggesting possible confounding by measures of illness severity not available in the data. In the instrumental variable analysis, 30-day mortality was also higher with percutaneous microaxial LVAD, but patient and hospital characteristics differed across levels of the instrumental variable, suggesting possible confounding by unmeasured variables (risk difference, 13.5%; 95% CI, 3.9%-23.2%). In the instrumented difference-in-differences analysis, the association between the percutaneous microaxial LVAD and mortality was imprecise, and differences in trends in characteristics between hospitals with different percutaneous microaxial LVAD use suggested potential assumption violations.

**CONCLUSIONS** In observational analyses comparing the percutaneous microaxial LVAD to alternative treatments among patients with AMICS, the percutaneous microaxial LVAD was associated with worse outcomes in some analyses, while in other analyses, the association was too imprecise to draw meaningful conclusions. However, the distribution of patient and institutional characteristics between treatment groups or groups defined by institutional differences in treatment use, including changes in use over time, combined with clinical knowledge of illness severity factors not captured in the data, suggested violations of key assumptions that are needed for valid causal inference with different observational analyses. Randomized clinical trials of mechanical support devices will allow valid comparisons across candidate treatment strategies and help resolve ongoing controversies.

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# Extracorporeal life support (ECLS)

The NEW ENGLAND JOURNAL of MEDICINE

## ORIGINAL ARTICLE

### Extracorporeal Life Support in Infarct-Related Cardiogenic Shock

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#### ABSTRACT

##### BACKGROUND

Extracorporeal life support (ECLS) is increasingly used in the treatment of infarct-related cardiogenic shock despite a lack of evidence regarding its effect on mortality.

##### METHODS

In this multicenter trial, patients with acute myocardial infarction complicated by cardiogenic shock for whom early revascularization was planned were randomly assigned to receive early ECLS plus usual medical treatment (ECLS group) or usual medical treatment alone (control group). The primary outcome was death from any cause at 30 days. Safety outcomes included bleeding, stroke, and peripheral vascular complications warranting interventional or surgical therapy.

##### RESULTS

A total of 420 patients underwent randomization, and 417 patients were included in final analyses. At 30 days, death from any cause had occurred in 100 of 209 patients (47.8%) in the ECLS group and in 102 of 208 patients (49.0%) in the control group (relative risk, 0.98; 95% confidence interval [CI], 0.80 to 1.19;  $P=0.81$ ). The median duration of mechanical ventilation was 7 days (interquartile range, 4 to 12) in the ECLS group and 5 days (interquartile range, 3 to 9) in the control group (median difference, 1 day; 95% CI, 0 to 2). The safety outcome consisting of moderate or severe bleeding occurred in 23.4% of the patients in the ECLS group and in 9.6% of those in the control group (relative risk, 2.44; 95% CI, 1.50 to 3.95); peripheral vascular complications warranting intervention occurred in 11.0% and 3.8%, respectively (relative risk, 2.86; 95% CI, 1.31 to 6.25).

##### CONCLUSIONS

In patients with acute myocardial infarction complicated by cardiogenic shock with planned early revascularization, the risk of death from any cause at the 30-day follow-up was not lower among the patients who received ECLS therapy than among those who received medical therapy alone. (Funded by the Else Kröner Fresenius Foundation and others; ECLS-SHOCK ClinicalTrials.gov number, NCT03637205.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Thiele can be contacted at holger.thiele@medizin.uni-leipzig.de or at Heart Center Leipzig, Department of Internal Medicine and Cardiology, University of Leipzig, Strümpellstr. 39, 04289 Leipzig, Germany.

\*Investigators in the ECLS-SHOCK trial are listed in the Supplementary Appendix, available at NEJM.org.

Drs. Thiele and Zeymer and Drs. Desch and Freund contributed equally to this article.

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# ECLS shock

Rischio di morte a 30 gg sovrapponibile  
> sanguinamento

# Impella and venoarterial extracorporeal membrane oxygenation in cardiogenic shock complicating acute myocardial infarction

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## Aims

This study aimed to give contemporary insight into the use of Impella and venoarterial extracorporeal membrane oxygenation (VA-ECMO) in acute myocardial infarction-related cardiogenic shock (AMICS) and into associated outcomes, adverse events, and resource demands.

## Methods and results

This nationwide observational cohort study describes all AMICS patients treated with Impella (ABIOMED, Danvers, MA, USA) and/or VA-ECMO in 2020–2021. Impella and/or VA-ECMO were used in 20% of all AMICS cases ( $n = 4088$ ). Impella patients were older (34% vs. 13% >75 years,  $p < 0.001$ ) and less frequently presented after an out-of-hospital cardiac arrest (18% vs. 40%,  $p < 0.001$ ). In-hospital mortality was lower in the Impella versus VA-ECMO cohort (61% vs. 67%,  $p = 0.001$ ). Adverse events occurred less frequently in Impella-supported patients: acute haemorrhagic anaemia (36% vs. 68%,  $p < 0.001$ ), cerebrovascular accidents (4% vs. 11%,  $p < 0.001$ ), thromboembolisms of the extremities (5% vs. 8%,  $p < 0.001$ ), systemic inflammatory response syndrome (21% vs. 25%,  $p = 0.004$ ), acute kidney injury (44% vs. 53%,  $p < 0.001$ ), and acute liver failure (7% vs. 12%,  $p < 0.001$ ). Impella patients were discharged home directly more often (20% vs. 11%,  $p < 0.001$ ) whereas VA-ECMO patients were more often discharged to another care facility (22% vs. 19%,  $p = 0.031$ ). Impella patients had shorter hospital stays and lower hospital costs.

## Conclusion

This is the largest, most recent European cohort study describing outcomes, adverse events, and resource demands based on claims data in patients with Impella and/or VA-ECMO. Overall, adverse event rates and resource consumption were high. Given the current lack of beneficial evidence, our study reinforces the need for prospectively established, high-quality evidence to guide clinical decision-making.

ORIGINAL ARTICLE

## Microaxial Flow Pump or Standard Care in Infarct-Related Cardiogenic Shock

J.E. Møller, T. Engstrøm, L.O. Jensen, H. Eiskjær, N. Mangner, A. Polzin, P.C. Schulze, C. Skurk, P. Nordbeck, P. Clemmensen, V. Panoulas, S. Zimmer, A. Schäfer, N. Werner, M. Frydland, L. Holmvang, J. Kjærgaard, R. Sørensen, J. Lønborg, M.G. Lindholm, N.L.J. Udesen, A. Junker, H. Schmidt, C.J. Terkelsen, S. Christensen, E.H. Christiansen, A. Linke, F.J. Woitek, R. Westenfeld, S. Möbius-Winkler, K. Wachtell, H.B. Ravn, J.F. Lassen, S. Boesgaard, O. Gerke, and C. Hassager, for the DanGer Shock Investigators\*

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at NEJM.org.

**DOI: 10.1056/NEJMoa2312572**

# DanGer Shock

- Pz acuti con ST up
- Ipoperfusione documentata (lattati  $\geq 2.5$  mmol/L; mg/dl dividi per 0.111),
- Disfunzione VS ( FE $<45\%$ ), senza disfunzione VD
- Non in coma (Glasgow Coma Scale score  $\geq 8$  in caso di arresto cardiaco precedente)



# Risultati

- 360 pazienti
- Morte per tutte le cause 180 gg45.8% (microaxial-flow-pump group ) Impella
- Controllo 58.5%)  
(hazard ratio, 0.74; 95% confidence interval [CI], 0.55 to 0.99; **P = 0.04**).

# Complicanze

- End point composito di **sicurezza** 43 patients (24.0%)  
Impella
- 11 (6.2%) controllo
- **Dialisi** 75 pazienti (41.9%) Impella
- 47 patients (26.7%) controllo

# Anticoagulation Medications, Monitoring, and Outcomes in Patients with Cardiogenic Shock Requiring Temporary Mechanical Circulatory Support

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PMID: 39389745 DOI: 10.1016/j.cardfail.2024.07.013

## Abstract

Cardiogenic shock (CS) is a syndrome of low cardiac output resulting in critical end-organ hypoperfusion and hypoxia. The mainstay of management involves optimizing preload, afterload and contractility. In medically refractory cases, temporary percutaneous mechanical support (MCS) is used as a bridge to recovery, surgical ventricular assist device, or transplant. Anticoagulation is recommended to prevent device-related thromboembolism. However, MCS can be fraught with hemorrhagic complications, compounded by incident multisystem organ failure often complicating CS. Currently, there are limited data on optimal anticoagulation strategies that balance the risk of bleeding and thrombosis, with most centers adopting local antithrombotic stewardship practices. In this review, we detail anticoagulation protocols, including anticoagulation agents, therapeutic monitoring, and complication mitigation in CS requiring MCS. This review is intended to provide an evidence-based framework in this population at high risk for in-hospital bleeding and mortality.

**Keywords:** Critical care cardiology; anticoagulation; intra-aortic balloon pump; percutaneous left ventricular assist device; veno-arterial extracorporeal membrane oxygenation.

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JAMA Cardiology | Original Investigation

## Microaxial Flow Pump Hemodynamic and Metabolic Effects in Infarct-Related Cardiogenic Shock

### A Substudy of the DanGer Shock Randomized Clinical Trial

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**IMPORTANCE** Mechanical circulatory support with a microaxial flow pump (MAFP) has been shown to improve survival in ST-elevation myocardial infarction-induced cardiogenic shock (STEMI-CS). Understanding the impact on hemodynamic stability over time is crucial for optimizing patient treatment.

**OBJECTIVE** To determine if an MAFP reduces the need for pharmacological circulatory support without compromising hemodynamics compared with standard care in STEMI-CS.

**DESIGN, SETTING, AND PARTICIPANTS** This was a substudy of the Danish-German (DanGer) Shock trial, an international, multicenter, open-label randomized clinical trial. Patients from 14 heart centers across Denmark, Germany, and the UK were enrolled. Inclusion criteria for the trial were STEMI and systolic blood pressure less than 100 mm Hg or ongoing vasopressor treatment, left ventricular ejection fraction less than 45%, and arterial lactate level greater than 2.5 mmol/L. Of the enrolled patients, after exclusions from death in the catheterization laboratory or immediately on intensive care unit (ICU) admission, the remaining patients had serial recordings of hemodynamics, arterial lactate, and use of vasoactive drugs. Patients who were in comas after cardiac arrest and patients with mechanical complications or right ventricular failure were excluded. Data were analyzed from May to September 2024.

**INTERVENTIONS** MAFP and standard of care or standard of care alone.

**MAIN OUTCOMES AND MEASURES** Hemodynamic status in terms of heart rate and blood pressure, metabolic status in terms of arterial lactate concentration, and vasoactive-inotropic score (VIS). The clinical events during the first 72 hours were as follows: death from all causes, escalation of mechanical circulatory support, and discharge alive from the ICU.

**RESULTS** From 355 enrolled patients, 324 (mean [IQR] age, 68 [58-75] years; 259 male [80%]) underwent ICU treatment (169 [52%] in the MAFP group, 155 [48%] in the standard-care group). Baseline characteristics were balanced. There was no difference in heart rate between groups, and mean arterial pressure was above the treatment target of 65 mm Hg in both groups but was achieved with a lower VIS in the MAFP group. No difference in arterial lactate level was found between groups at randomization, but on arrival to the ICU, the MAFP group had significantly lower arterial lactate levels compared with the standard-care group (mean difference, 1.3 mmol/L; 95% CI, 0.7-1.9 mmol/L), a difference that persisted throughout the first 24 hours of observation. The MAFP group achieved lactate normalization (<2 mmol/L) 12 hours (95% CI, 5-18 hours) before the standard-care group.

**CONCLUSIONS AND RELEVANCE** Use of a MAFP reduces the use of vasopressors and inotropic medication while maintaining hemodynamic stability and achieving faster normalization of lactate level in patients with STEMI-CS.

**TRIAL REGISTRATION** ClinicalTrials.gov Identifier: NCT01633502

 Editorial

 Supplemental content

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Group Information:** The DanGer Shock Investigators appear in Supplement 2.

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Impella riduce l'uso di inotropi e vasopressori mantenendo stabilità emodinamica

# Drug therapy and catheter ablation for management of arrhythmias in continuous flow left ventricular assist device's patients: a Clinical Consensus Statement of the European Heart Rhythm Association and the Heart Failure Association of the ESC

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PMID: 39478667 PMCID: [PMC11580222](#) DOI: [10.1093/europace/euae272](#)

## Abstract

Left ventricular assist devices (LVADs) are an increasingly used strategy for the management of patients with advanced heart failure. Although these devices effectively improve survival, atrial and ventricular arrhythmias are common with a prevalence of 20-50% at one year after LVAD implantation. Arrhythmias predispose these patients to additional risk and are associated with considerable morbidity from recurrent implantable cardioverter-defibrillator shocks, progressive failure of the unsupported right ventricle, and herald an increased risk of mortality. Management of patients with arrhythmias and LVAD differs in many aspects from the general population heart failure patients. These include ruling out the reversible causes of arrhythmias that in LVAD patients may include mechanical irritation from the inflow cannula and suction events. For patients with symptomatic arrhythmias refractory to medical treatment, catheter ablation might be relevant. There are specific technical and procedural challenges perceived to be unique to LVAD-related ventricular tachycardia (VT) ablation such as vascular and LV access, signal filtering, catheter manoeuvrability within decompressed chambers, and electroanatomic mapping system interference. In some patients, the arrhythmogenic substrate might not be readily accessible by catheter ablation after LVAD implantation. In this regard, the peri-implantation period offers a unique opportunity to surgically address arrhythmogenic substrate and suppress future VT recurrences. This document aims to address specific aspects of the management of arrhythmias in LVAD patients focusing on anti-arrhythmic drug therapy and ablations.

**Keywords:** Atrial fibrillation; Catheter ablation; Heart failure; Left ventricular assist device; Ventricular arrhythmia.



# Purtroppo interrotto

Early Impella Support in Patients With ST-Segment Elevation  
Myocardial Infarction Complicated by Cardiogenic Shock  
(RECOVER IV) ( nord america)

## E nel Futuro?

- Cateterismo destro e fenotipo emodinamico CS per selezionare potenziali candidati MCS e guidare la selezione del device, l'ottimizzazione e l'escalation-descalation
- Diversificare l'arruolamento nei trials futuri (donne)
- Quando mettere device ( prima o dopo rivascularizzazione).
- Pazienti con non-STEMI AMI-CS
- Device alternativi MCS potrebbero avere simili benefici con selezioni accurate

# Trials

Trial name	Inclusion criteria	No. of participants	Intervention	Control	Institution	Primary outcome	Key secondary outcomes	Estimated study completion
EARLY-UNLOAD (NCT04775472)	Cardiogenic shock	116	VA-ECMO + atrial septostomy within 12 hours	VA-ECMO alone	Chonnam National University Hospital, Korea	All-cause mortality at 30 days	Rate of atrial septostomy in control group Incidence of cardiac death	October 2023
REVERSE (NCT03431467)	Cardiogenic shock	96	VA-ECMO + Impella CP	VA-ECMO alone	Multicenter, United States	Recovery from cardiogenic shock at 30 days (survival; free from MCS, transplant, or inotropic support)	Survival to hospital discharge	January 2025
ECLS-SHOCK (NCT03637205)	Cardiogenic shock secondary to acute myocardial infarction	420	VA-ECMO +/- LV unloading	Standard care (escalation to other MCS [eg, IABP or pLVAD] allowed)	Multicenter, Germany	All-cause mortality at 30 days	Time to death at 6- and 12-month follow-up; duration of catecholamine therapy	November 2023
ANCHOR (NCT04184635)	Cardiogenic shock secondary to acute myocardial infarction	400	VA-ECMO + IABP	Standard care (no MCS device allowed)	Multicenter, France	Treatment failure at 30 days (death in ECMO group or rescue ECMO in the control group)	Mortality at 30 days; MACE at 30 days	November 2024
HERACLES (ISRCTN82431978)	Cardiogenic shock being treated with VA-ECMO	36	VA-ECMO + Impella CP	VA-ECMO + IABP	Multicenter, United Kingdom	Change in device coronary flow reserve	Change in LVEDP; time to VA-ECMO decannulation	February 2025

ANCHOR indicates Assessment of ECMO in Acute Myocardial Infarction Cardiogenic Shock; EARLY-UNLOAD, Early Left Atrial Septostomy Versus Conventional Approach After Venoarterial Extracorporeal Membrane Oxygenation; ECLS-SHOCK, Extracorporeal Life Support in Cardiogenic Shock; ECMO, extracorporeal membrane oxygenation; HERACLES, Hemodynamic Effects of Reducing Left Ventricular Afterload With Impella or Intraaortic Balloon Counterpulsation During Venoarterial Extracorporeal Membrane Oxygenation in Cardiogenic Shock; IABP, intra-aortic balloon pump; LV, left ventricle; MCS, mechanical circulatory support; pLVAD, percutaneous left ventricular assist device; REVERSE, Impella CP with VA-ECMO for Cardiogenic Shock; and VA-ECMO, venoarterial extra corporeal membrane oxygenation.

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**INNOVATION**

LIVE CASES

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