Cardiogenic shock

Enzo Lüsebrink, Leonhard Binzenhöfer, Marianna Adamo, Roberto Lorusso, Alexandre Mebazaa, David A Morrow, Susanna Price, Jacob C Jentzer, Daniel Brodie, Alain Combes, Holger Thiele**

Lancet 2024; 404: 2006–20

*Both authors contributed equally

Department of Medicine I, LMU University Hospital, Munich, Germany (E Lüsebrink MD; L Binzenhöfer MD); **Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy** (Prof M Adamo MD); **Department of Cardiology, ASST Spedali Civili, Brescia, Italy** (Prof M Adamo); **Cardio-Thoracic Surgery Department, Maastricht University Medical Centre, Maastricht, Netherlands** (Prof R Lorusso MD); **Cardiovascular Research Institute Maastricht, Maastricht, Netherlands** (Prof R Lorusso); **Université Paris Cité, Unité MASCOT Inserm, APHP Hôpitaux Saint Louis and Lariboisière, Paris, France** (Prof A Mebazaa MD); **Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA, USA** (Prof D A Morrow MD); **Cardiology and Critical Care, Royal Brompton and Harefield Hospitals, Guy's and St Thomas' NHS Foundation Trust, London, UK** (Prof S Price MD); **National Heart and Lung Institute, Imperial College, London, UK** (Prof S Price); **Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA** (Prof J C Jentzer MD); **Department of Medicine, Division of Pulmonary and Critical Care Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, USA** (Prof D Brodie MD); **Institute of Cardiometabolism and Nutrition, Sorbonne Université, Paris, France** (Prof A Combes MD); **Service de Médecine Intensive-Réanimation, Institut de Cardiologie, APHP Sorbonne Université Hôpital Pitié-Salpêtrière, Paris, France** (Prof A Combes); **Leipzig Heart Science, Leipzig, Germany** (Prof H Thiele MD); **Department of Internal Medicine/Cardiology, Heart Center Leipzig at University of Leipzig, Leipzig, Germany** (Prof H Thiele)

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.[1] The short-term mortality rate of cardiogenic shock has stagnated at around 40–50%[2–7] 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.[2,5–9] 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.[1,10–12]

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.[1] 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*m²) and a high systemic vascular resistance index of more than 2200 dynes/(cm*sec^{-5}) have been recognised as thresholds for cardiogenic shock, but objective data from advanced haemodynamic monitoring might not always be available.[1] 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.[11] 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).[13] 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.[13–17] The current SCAI

Correspondence to:
Prof Holger Thiele, Department of Internal Medicine/Cardiology, Heart Center Leipzig at University of Leipzig, Leipzig 04289, Germany
holger.thiele@medizin.uni-leipzig.de

Panel: **Key gaps in evidence**

Definition
- Subtype criteria regarding haemodynamics, aetiology, predominantly affected system (left *vs* right *vs* biventricular failure) and severity of organ dysfunction
- Validity of proposed subphenotypes

Prognostication
- Prospective validation of existing models in large cohorts
- Risk prediction models focused on neurological and quality of life outcomes
- Prediction models for preclinical settings
- Integration of high-frequency data from laboratory and haemodynamic assessments
- Deep phenotyping using machine learning techniques
- Models to predict benefit from existing therapies
- Criteria for futility
- Identification of the need for durable ventricular assist device implantation or heart transplantation
- Multimodal subphenotyping

Pharmacotherapy
- Efficacy and safety of novel substances
- Optimal pharmacotherapeutic strategy for different cardiogenic shock subtypes
- Weaning protocols
- Haemodynamic targets
- Adjunctive therapies in mixed cardiogenic-vasodilatory shock
- Targeted therapies based on biomarker profile

Revascularisation
- Radial versus femoral access
- Efficacy and safety of intravenous platelet inhibition
- Role of coronary artery bypass grafting in emergency situations and in patients with mechanical complications related to myocardial infarction

Mechanical circulatory support
- Optimal patient selection
- Role in cardiogenic shock types other than ST-elevation myocardial infarction
- Timing of initiation, escalation, and weaning
- Combined mechanical circulatory support strategies
- Prevention and management of complications

Management of organ dysfunction and supportive care
- Optimal transfusion thresholds for patients with and without mechanical circulatory support
- Ventilation and sedation strategies
- Optimal renal replacement strategy in different forms of cardiogenic shock
- Early assessment of brain damage

Long-term sequelae and associated costs
- Prevention, early detection, and optimal management of physical and mental sequelae
- Long-term health-related quality of life
- Cost-effectiveness of novel device-based and medical treatment options
- Cost-effectiveness of different staffing models
- Costs associated with long-term follow-up and persisting organ dysfunction in survivors

Clinical trial design
- Evaluation of routine imaging parameters as inclusion criteria
- Consideration of neurological outcomes and quality of life measures as trial endpoints
- Further development of registry-based randomised controlled trials
- Separate investigation of patients after cardiac arrest
- Integration of durable ventricular assist device implantation and transplant into composite outcomes

classification can be further refined with the incorporation of the cause of the cardiogenic shock, affected ventricle (left, right, or biventricular failure), the dynamic state of haemodynamic compromise over time, non-modifiable risk factors, and biochemical profiles. The inclusion of additional variables, such as cardiac arrest with potential anoxic brain injury, the number of pharmacological agents and circulatory support devices (as proposed by the Cardiogenic Shock Working Group[17]), or organ function assessment (as recommended by the 2020 Critical Care Clinical Trialists Workshop[18]) could improve baseline risk estimation and the guidance of interventions.[13,17,18] Furthermore, the Interagency Registry for Mechanically Assisted Circulatory Support classification provides a less refined assessment of cardiogenic shock severity, but can be a useful communication and prognostic tool for patients being evaluated for heart transplantation or durable left ventricular assist device implantation.[19,20]

Criteria for the classification of cardiogenic shock (figure 1) will undoubtedly continue to evolve as machine learning-based clustering algorithms and other advanced statistical techniques, such as latent class analysis, are explored to identify subphenotypes and treatable traits of this condition.[21] The widespread acceptance of a universal definition that includes a standardised severity assessment strategy and incorporates clinically meaningful cardiogenic shock subtypes will be essential to harmonise scientific efforts and advance personalised management.[21–23]

Aetiology

As treatment strategies for acute myocardial infarction (AMI) advance with improved prevention and early revascularisation, the proportion of cardiogenic shock cases attributable to acute coronary syndromes appears to be declining—however, AMI remains a major cause of cardiogenic shock.[24–27] According to current European registry data, 5–15% of patients who have had an AMI also had

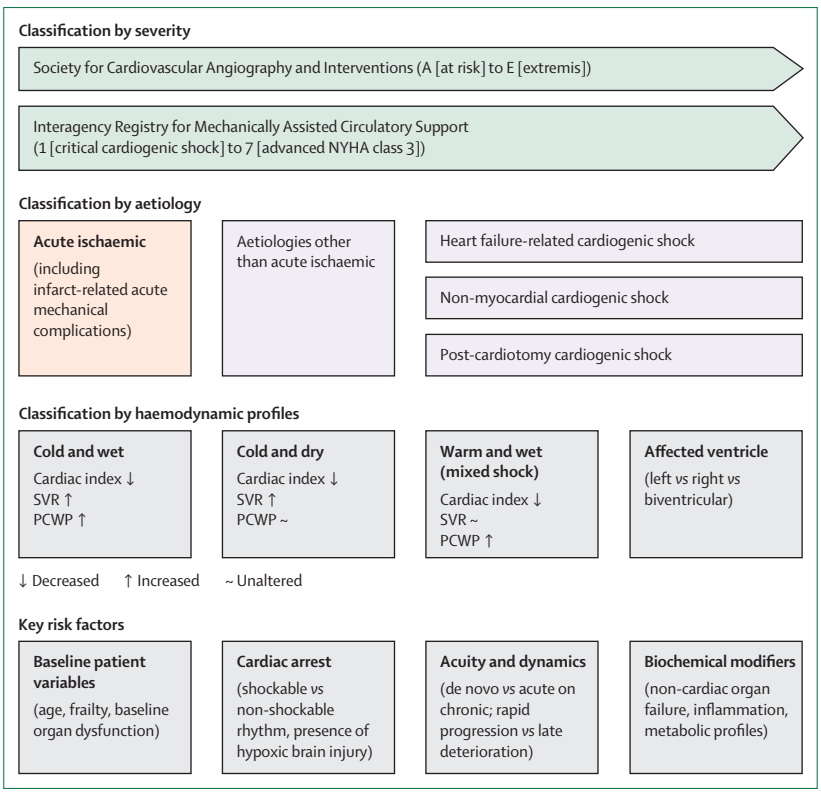

Figure 1: **Classification systems and key risk factors for cardiogenic shock**
NYHA=New York Heart Association. PCWP=pulmonary capillary wedge pressure. SVR=systemic vascular resistance.

See Online for appendix

cardiogenic shock.[26,28] Cardiogenic shock unrelated to AMI has outnumbered AMI-related cardiogenic shock in several studies, highlighting the changing epidemiology of cardiogenic shock to increasingly include de novo or acute on chronic heart failure-related cardiogenic shock, post-cardiotomy cardiogenic shock, and non-myocardial cardiogenic shock causes (appendix p 1).[1,25,29–32] Less common cardiogenic shock causes unrelated to AMI include pericardial diseases, valvular heart diseases, arrhythmias, inflammatory cardiomyopathies, peripartum cardiomyopathy, and cor pulmonale (eg, massive pulmonary embolism). Post-cardiotomy cardiogenic shock represents another distinct subtype, often related to postoperative right ventricular dysfunction, systemic inflammatory response syndrome, and an array of potential short-term complications.[1,12] Rapid identification of the underlying cause is essential for evaluating tailored treatment options and adapting circulatory support to pathophysiological mechanisms, such as severe valvular disease. The current imbalance between the clinical importance of and scarcity of quality evidence in cardiogenic shock unrelated to AMI limits development of cause-specific management algorithms and therapeutic interventions.[32]

Pathophysiology

The fundamental haemodynamic trigger of cardiogenic shock is an inability to maintain an adequate stroke volume despite sufficient preload, leading to reduced cardiac output and tissue hypoperfusion (figure 2). Peripheral vasoconstriction and fluid retention in cardiogenic shock are early and important compensatory mechanisms that attempt to preserve organ perfusion, but ultimately worsen the haemodynamic state by aggravating preload and afterload mismatch, which results in worsening congestion aggravated by diastolic dysfunction. Together, the immediate macrocirculatory changes of decreased cardiac index, elevated pulmonary capillary wedge pressure and central venous pressure, and sympathetic and neurohormonal activation (endogenous catecholamine release, increased systemic vascular resistance, and activation of the renin–angiotensin–aldosterone system) constitute the pathophysiological foundation of the classic so-called cold (referring to peripheral perfusion) and wet (referring to filling pressures) cardiogenic shock phenotype.[11,12] Adrenergic vasoconstriction increases left ventricular afterload and wall stress, further diminishing cardiac output. Hypotension can be aggravated by paradoxical vasodilation and a reduction of systemic vascular resistance due to inflammatory activation, resulting in either a warm and wet or mixed cardiogenic shock phenotype.[1,11] The release of proinflammatory cytokines triggered by hypoxic tissue damage (including systemic ischaemia-reperfusion injury after cardiac arrest) might be compounded by immunological reactions related to intestinal microbial translocation, bacteraemia, blood transfusions, or aspiration.[33,34] Activated nitric oxide synthase, TNF-α, and interleukins are key effectors of peripheral vasodilation and microcirculatory dysfunction.[11,35] In addition to these global processes, pulmonary congestion and oedema might impair gas exchange, aggravate tissue hypoxia, increase work of breathing, increase right ventricular afterload from hypoxic pulmonary vasoconstriction, and exacerbate myocardial ischaemia, which results in deterioration of ventricular function. If therapeutic interventions do not restore cardiac output and organ perfusion in a timely manner, coronary and systemic hypoperfusion and multi-organ failure become progressively worse. Metabolic derangements from acute kidney injury and congestive hepatopathy can dominate the clinical picture, referred to as haemometabolic shock.

Biventricular failure in cardiogenic shock is common, with right ventricular dysfunction seen in 38% of patients with AMI-related cardiogenic shock in the SHOCK trial,[36] and even higher rates seen in cardiogenic shock unrelated to AMI.[16] The uncommon right ventricular-predominant cardiogenic shock subtype, characterised by normal pulmonary capillary wedge pressure with elevated central venous pressure and decreased right ventricular function (as reflected by reduced pulmonary artery pulsatility index and right ventricular stroke work index), leads to insufficient left ventricular filling.[36] The right ventricle possesses less contractile power and is particularly sensitive to

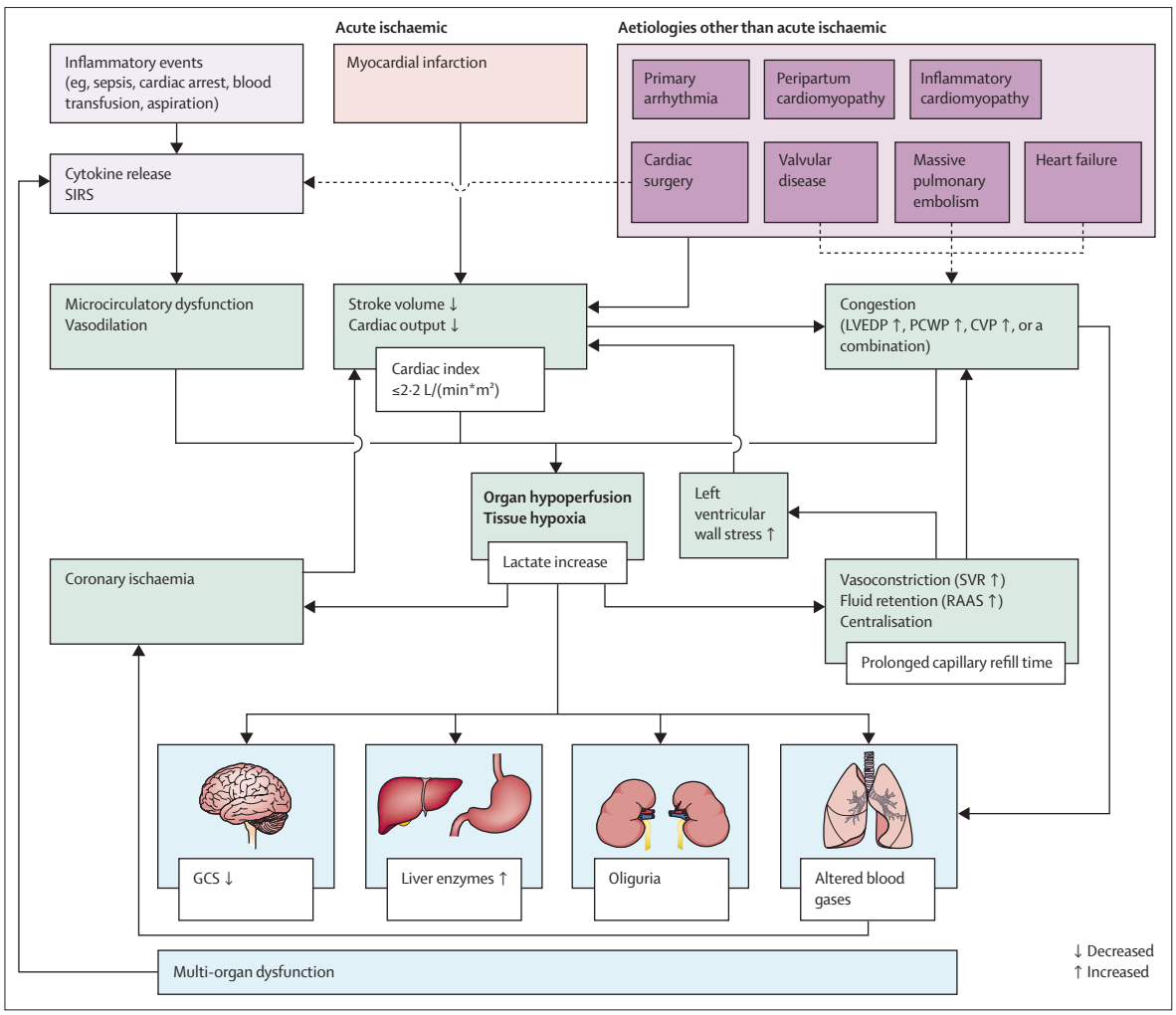

Figure 2: **Summary of main causes and pathophysiological mechanisms of cardiogenic shock**
Dotted lines indicate potential secondary mechanisms contributing to cardiogenic shock. CVP=central venous pressure. GCS=Glasgow Coma Scale. LVEDP=left ventricular end-diastolic pressure. PCWP=pulmonary capillary wedge pressure. RAAS=renin–angiotensin–aldosterone system. SIRS=systemic inflammatory response syndrome. SVR=systemic vascular resistance.

sudden increases in pulmonary vascular resistance and intraventricular pressures, as seen in acute cor pulmonale.[37]

Prognostication

Development of prediction models with high accuracy for progression or death in patients with cardiogenic shock is challenging due to the high baseline risk and the fact that prognostic determinants are difficult to quantify. Such models would ideally enable rapid and reproducible risk assessment in acute settings and account for the dynamic clinical course inherent to cardiogenic shock. However, as of yet, no model has shown value for therapeutic selection. The proposed SCAI three axis model of cardiogenic shock includes shock severity, phenotype and aetiology, and risk factors (modifiable and non-modifiable)—although this framework has not been validated for clinical decision making, an application for temporary MCS selection has been suggested.[13]

Established severity of illness scores from the general intensive care setting have been superseded by scoring systems derived from randomised controlled trial (RCTs; appendix pp 2–3). The CardShock score[24,38] and Cardiogenic Shock Score[39] are externally validated risk predictors for mixed cardiogenic shock populations. The SHOCK trial and registry score,[40] IABP-SHOCK II score,[38,41] and the non-subjective biomarker-based cystatin C, lactate, interleukin-6, and N-terminal pro-B-type natriuretic peptide score[42] have shown usefulness for prognostication in AMI-related cardiogenic shock. Patients at risk of developing overt cardiogenic shock during hospitalisation for acute coronary syndromes could be identified using the Observatoire Régional Breton sur l'Infarctus risk score and circulating dipeptidyl peptidase 3 (DPP3), a novel biomarker reflecting haemodynamic derangement.[43,44] Furthermore, the survival after venoarterial extracorporeal membrane

oxygenation (VA-ECMO) and prediction of cardiogenic shock outcome for AMI patients salvaged by VA-ECMO (ENCOURAGE) scores have shown reasonably good performance in patients treated with VA-ECMO.[45,46] However, no consensus currently exists regarding incorporation of these scores into decision-making algorithms to initiate temporary MCS.[10,11] Generally, factors associated with increased mortality are older age, lower blood pressure, higher requirements for vasoactive medications, higher lactate, poorer kidney function, chronic heart failure, and high risk of or demonstrated hypoxic brain injury.[13,47–50]

The approach to the incorporation of biomarkers is changing rapidly with the advent of current so-called omics approaches, with artificial intelligence potentially leading to improved prediction models as seen by the combination of four circulating proteins with the CardShock score, and circulating DPP3.[44,51–53] Several studies using a multimodal approach detected few phenotypes that could lead to future predictive trials in cardiogenic shock.[23,54,55] A crucial unanswered question is how best to leverage prognostic information provided by these scores to improve patient care, as individuals at high risk might not necessarily respond better to more intensive therapies.

Management of cardiogenic shock

Systems of care

Standardising institutional cardiogenic shock care is a key challenge. Such standardisation involves multidisciplinary shock teams,[56,57] with input from cardiac interventionalists, intensivists, surgeons, and heart failure specialists needed to facilitate early diagnosis, repeated assessment, and rapid decision making. Standardisation also involves regional networks of care that follow a hub and spoke model, where patient needs are adapted to the respective capabilities of member institutions, for example the constant availability of percutaneous coronary intervention, advanced cardiac imaging, specialised cardiac intensive care units, and access to MCS or heart transplantation evaluation. Transfer of patients with acute respiratory failure to a specialist extracorporeal membrane oxygenation (ECMO) centre has been shown to improve survival without severe disability,[58] which could theoretically apply to patients with cardiogenic shock under consideration for advanced circulatory support. Designing regional cardiogenic shock networks is a challenging public health endeavour, but these efforts could contribute to more equitable resource allocation and higher quality of care. An increasing number of centres have put these principles into practice, with data suggesting improved outcomes.[31,57,59–61] Communications between spoke and hub centres should be bilateral, not only during the acute management and transfer of the patients but also in the long term to establish common procedures and optimal continuity and management in the spoke centre, during transport, and at arrival in the hub centre.[62,63] Despite these results, the benefits of cardiogenic shock teams, evidence-based protocols, and interinstitutional operating procedures require confirmation in larger, multicentre, and ideally international studies.

Pharmacotherapy

First-line interventions to stabilise patients in cardiogenic shock typically include optimisation of volume status and administration of vasoactive and inotropic agents (appendix pp 4–6).[11] However, evidence regarding drug selection for circulatory support, complication rates, standardised assessment of drug failure, and treatment targets in cardiogenic shock is limited and partly extrapolated from studies focusing on other shock entities (appendix pp 7–9).[11,64–67]

Catecholamine titration to the lowest possible dose that maintains adequate organ perfusion is advisable to avoid undesired adrenergic effects.[68] One source of evidence informing current guideline recommendations is the randomised SOAP II trial, which showed a lower risk of tachyarrhythmias with norepinephrine as compared with dopamine in a general shock population, and a nominally lower 28-day mortality in patients in cardiogenic shock, although this subgroup analysis was not powered for mortality.[10,11,69] Similarly, the OPTIMA-CC trial investigating efficacy and safety of epinephrine compared with norepinephrine in AMI-related cardiogenic shock (n=57) was terminated early because of a significantly higher incidence of refractory shock in the epinephrine group (37% *vs* 7%; p=0·008), possibly related to the higher risk of catecholamine-induced myocardial injury.[70] Reflecting the limitations of these trials and observational data, the American Heart Association practice guidelines do not unanimously recommend one specific first-line vasopressor; however, the European Society of Cardiology guidelines do recommend norepinephrine as a first-line vasopressor (Class IIb, level of evidence B).[10,11,71,72]

In current practice, dobutamine is the most frequently used inodilator, despite being associated with dysfunctional remodelling, higher oxygen demand, and risk of arrhythmias.[73–75] The efficacy of milrinone was investigated in the randomised DOREMI trial (94% of participants in SCAI stages C–E), finding no significant difference compared with dobutamine regarding the composite of in-hospital death, resuscitated cardiac arrest, non-fatal myocardial infarction, stroke, transient ischaemic attack, rate of cardiac transplantation or MCS, or renal replacement therapy.[76] A post-hoc analysis of the DOREMI trial suggests that a higher average mean arterial pressure in the initial treatment phase might be associated with better outcomes; however, this result should be interpreted with caution considering potential reverse causation and confounding.[77] The placebo-controlled CAPITAL DOREMI 2 trial is currently investigating in-hospital mortality and haemodynamic deterioration in patients with SCAI C or D stage cardiogenic shock

receiving milrinone or dobutamine versus placebo (NCT05267886). Levosimendan, a calcium-sensitiser and phosphodiesterase III-inhibitor, which is available in Europe but not in the USA, was purported to have a more favourable risk profile compared with dobutamine in cardiogenic shock.[75] However, in 1327 patients randomly assigned to receive either levosimendan or dobutamine in the SURVIVE trial, no significant difference in 1-month and 6-month survival was observed.[8] Because its mechanism of action is independent of adrenergic receptors, levosimendan might theoretically have potential for patients treated with beta-blockers at the time of cardiogenic shock onset, but its long pharmacological half-life presents a challenge.[78] In a network meta-analysis including seven RCTs, levosimendan was associated with lower mortality compared with placebo, although this finding might not be applicable to patients in more advanced shock stages (given that a substantial proportion of included patients were in SCAI A or B stage shock).[79] Results from the upcoming LevoHeartShock trial (NCT04020263), assessing the influence of levosimendan compared with placebo on short-term outcomes (30-day mortality, VA-ECMO, or renal replacement therapy) in patients with cardiogenic shock could provide answers for this gap in evidence.

Novel pharmacological approaches are also emerging. Adrenomedullin regulates vascular tone and showed anti-apoptotic effects on cardiomyocytes in an AMI mouse model.[80] However, the randomised ACCOST-HH trial reported no significant difference in short-term need for cardiovascular organ support and mortality among 77 patients with cardiogenic shock receiving adrecizumab, a non-neutralising antibody that increases circulating adrenomedullin levels.[3] In a randomised crossover trial including 12 patients with cardiogenic shock, an enteral bolus of ketone ester led to significantly improved cardiac power output, left ventricular ejection fraction, and mixed venous saturation, without relevant effects on mean arterial pressure.[81] Given its potential involvement in cardiogenic shock pathophysiology and cardio-depressive properties, inhibition of circulating DPP3 could restore cardiac function, as shown in a murine isoproterenol-induced heart failure model.[82] Exploration of promising novel substances, such as ketone ester, circulating DPP3 inhibitors, or istaroxime, together with additional data from late stage clinical trials, can inform future pharmacological management of cardiogenic shock (appendix p 10).[81–83]

Coronary revascularisation

RCT-based evidence published over the last 25 years has warranted a Class I recommendation (Level of Evidence B [European Society of Cardiology], B-Randomised [American Heart Association]) for early revascularisation of the culprit lesion in patients with AMI-related cardiogenic shock (figure 3; appendix pp 11–13).[4,84–88] Pioneering results from the SHOCK trial showed long-term survival benefit in patients with AMI-related cardiogenic shock (n=302) who were randomly assigned to receive emergency interventional or surgical revascularisation within 12 h after cardiogenic shock onset versus initial medical therapy, irrespective of age, sex, or diabetes status.[86,87,89] Furthermore, multivessel coronary artery disease is prevalent in approximately 75% of patients with AMI-related cardiogenic shock and is associated with increased mortality.[5,6,90] Results from the randomised CULPRIT-SHOCK trial indicate that percutaneous coronary intervention of the infarct-related artery and delayed staged complete revascularisation, as opposed to immediate multivessel percutaneous coronary intervention, significantly reduces 30-day all-cause mortality and the need for renal replacement therapy (relative risk [RR] 0·83 [95% CI 0·71–0·96]).[4] Optimal strategies for combined anti-thrombotic therapy after percutaneous coronary intervention in patients with AMI-related cardiogenic shock is a matter of ongoing research.[11] Considering potential alterations in oral bioavailability of $P2Y_{12}$ inhibitors related to opioids, gastrointestinal hypoperfusion, and other factors, the efficacy of intravenous cangrelor in this context is currently being investigated in the randomised DAPT-SHOCK-AMI trial (NCT03551964; appendix p 14).

Despite observational data suggesting lower mortality in primary coronary artery bypass grafting compared with the current standard primary percutaneous coronary intervention strategies, the overall percentage of early coronary artery bypass grafting performed has decreased from 24·5% in the SHOCK trial to less than 5% in more recent trials and registries.[5,6,86,91–93] In the absence of additional data, surgical revascularisation remains an essential option in case of unsuccessful or infeasible percutaneous coronary intervention, mechanical complications, and staged hybrid coronary artery bypass grafting approaches after initial culprit lesion percutaneous coronary intervention.[84,94]

Since the publication of the SHOCK trial, revascularisation rates among patients with AMI-related cardiogenic shock have improved.[6,26,92,95,96] However, despite the association with long-term survival, a 2023 population-based study in Canada showed that percutaneous coronary intervention or coronary artery bypass grafting is performed in only 65% of cases.[96] Factors such as cardiogenic shock before admission, longer time interval between symptom onset and revascularisation, and resuscitation following cardiac arrest are associated with worse outcomes, highlighting the importance of regionalised systems of care and cardiogenic shock protocols to streamline decision making regarding reperfusion therapy for ST-elevation myocardial infarction and selection of suitable advanced management facilities.[49,97–99] On the basis of data from the National Inpatient Sample and other registries, current guidelines endorse the role of high-volume cardiogenic shock centres in coordinating patient logistics and

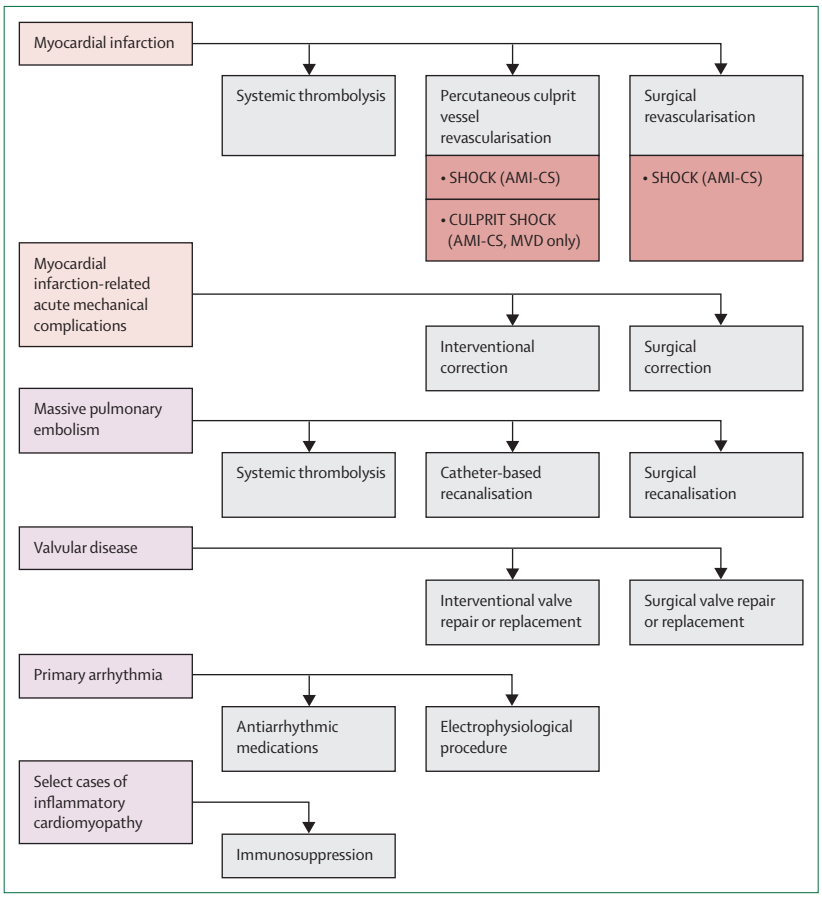

Figure 3: **Emergent treatment of specific underlying causes of cardiogenic shock**
Key medical treatment strategies are summarised in the first column, interventional strategies in the second column, and surgical strategies in the third column. Boxes underneath management options indicate mortality-powered 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.

establishing optimal revascularisation strategies within multidisciplinary heart teams.[11,12,100,101]

Mechanical circulatory support

Optimal pharmacotherapy and treatment of the underlying cardiogenic shock cause might not stabilise patients in advanced shock stages. Since the early 1960s, several temporary MCS devices—providing different degrees of haemodynamic and respiratory support—have been developed for patients with cardiogenic shock.[102,103] However, scarce clinical trial evidence exists to support MCS deployment as a bridge to recovery, bridge to decision, durable assist device implantation, or heart transplantation (figure 4; appendix pp 4–5, 15–16).[10,71,102,103]

Despite being the most used temporary MCS device in many centres, scant data show either a clinical or haemodynamic benefit of the intra-aortic balloon pump (IABP) in cardiogenic shock. In the randomised IABP-SHOCK II trial, IABP implantation in patients with infarct-related cardiogenic shock (n=600) did not result in early or long-term survival benefit, recurrence of myocardial infarction, or rehospitalisation for cardiac cause.[5,104] On the basis of this data, routine IABP use in AMI-related cardiogenic shock is not recommended and overall use has substantially decreased.[10,84] In non-ischaemic cardiogenic shock, mechanical complications after myocardial infarction, or in cases of unsuccessful percutaneous coronary intervention, placement of an IABP might be considered, despite the low level of supporting evidence.[10,84,105,106] Some observational evidence supports the concept that, in selected patients with chronic heart failure-related cardiogenic shock, use of an IABP is associated with a higher probability of clinical stabilisation and successful bridging to destination therapies, prompting an ongoing trial of IABP versus pharmacological support only in heart failure-related cardiogenic shock (NCT04369573).[107]

VA-ECMO is the most potent and versatile MCS device and is rapidly deployable in various clinical scenarios.[103] Despite being capable of partly or fully replacing cardiopulmonary function temporarily, a patient data meta-analysis (n=567) including data from four RCTs did not indicate a survival benefit following unselected use of VA-ECMO in patients experiencing AMI-related cardiogenic shock.[6,7,108–110] Beyond that, prespecified subgroup analyses found no significant difference in 30-day all-cause mortality in any subgroup with versus without VA-ECMO.[6,108] However, an increased risk of bleeding and vascular complications, as well as a large proportion of patients randomly assigned after resuscitation for cardiac arrest with high risk of acute hypoxic-ischaemic brain injury could have obscured any clinical benefit.

No adequately powered RCTs informing the efficacy of VA-ECMO in cardiogenic shock of non-ischaemic origin have been published. In a propensity score-weighted retrospective multicentre analysis including 212 patients with sepsis-induced cardiogenic shock, 60% of patients receiving VA-ECMO survived to 90 days, compared with 25% in the control group (RR 0·54 [95%CI 0·40–0·70]).[111] On the basis of the available evidence from retrospective studies, whether temporary circulatory support with VA-ECMO can improve survival in patients suffering fulminant myocarditis, acute decompensated chronic heart failure, post-cardiotomy cardiogenic shock, or massive pulmonary embolism remains unclear.[103] For these patients, VA-ECMO might be most useful as a bridging strategy to either myocardial recovery, transplantation, or implantation of a durable ventricular assist device.

In addition to neurological, bleeding, and ischaemic complications related to VA-ECMO, this device can even harm the heart itself owing to generation of retrograde blood flow towards the aortic valve, potentially leading to progressive left ventricular distension, impairment of function, and pulmonary congestion.[6,103,108,112] Early active unloading with Impella microaxial flow pumps (Abiomed, Danvers, MA, USA) or IABP aims to mitigate these adverse effects and has been associated with better

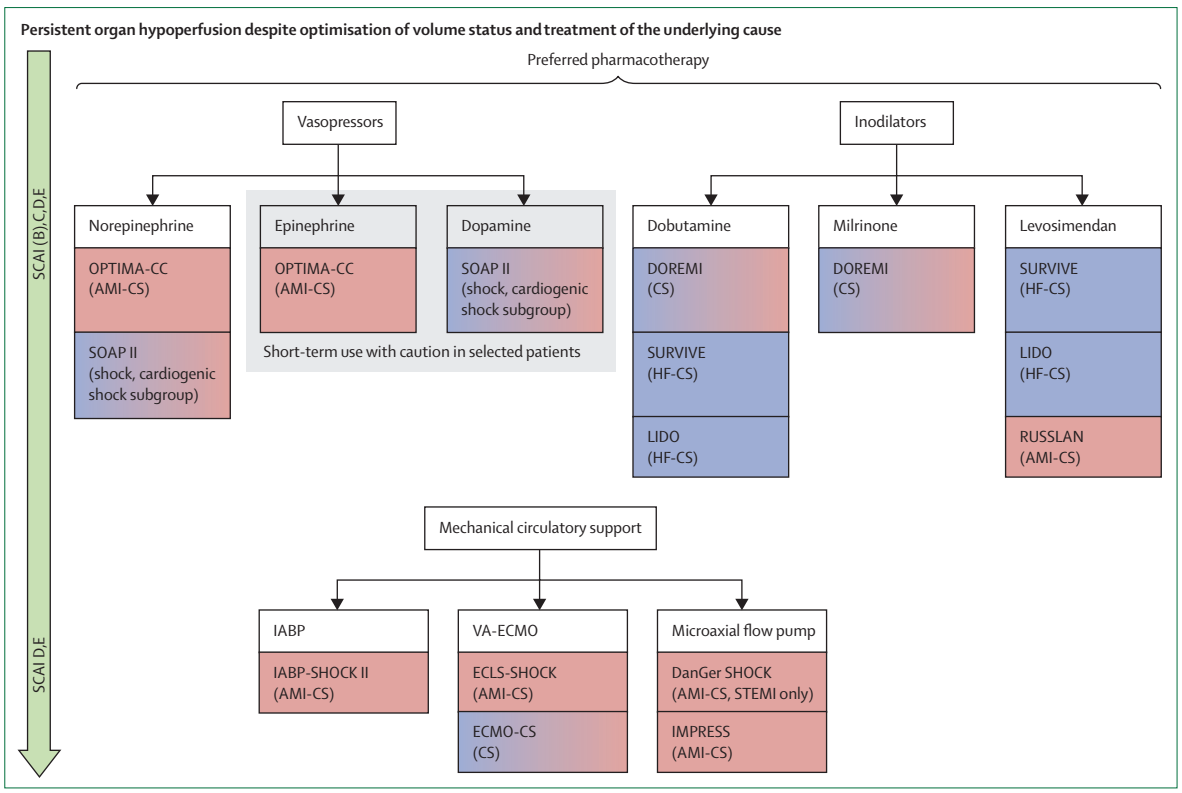

Figure 4: **Circulatory support**
Boxes underneath management options indicate selected randomised controlled trials investigating circulatory support options in specific cardiogenic shock scenarios (trial patient population in brackets). Colour change from purple to red indicates general cardiogenic shock trial population including both ischaemic and non-ischaemic cardiogenic shock causes. AMI-CS=acute myocardial infarction-related cardiogenic shock. CS=cardiogenic shock. HF-CS=heart failure-related cardiogenic shock. IABP=intra-aortic balloon pump. SCAI=Society for Cardiovascular Angiography and Interventions. STEMI=ST-elevation myocardial infarction. VA-ECMO=venoarterial extracorporeal membrane oxygenation.

outcomes in observational studies,[113–115] with investigation of combined temporary MCS approaches in the randomised UNLOAD ECMO (NCT05577195) and ANCHOR (NCT04184635) trials underway (appendix p 17). Routine transseptal left atrial cannulation—another form of active left ventricular unloading—did not result in higher VA-ECMO weaning (EVOLVE-ECMO) or 30-day survival rate (EARLY-UNLOAD) in randomised trials.[116,117]

Impella (Abiomed, Danvers, MA, USA) devices are peripherally inserted temporary ventricular assist devices providing up to 5·5 L/min of antegrade flow without capability of respiratory support.[102] Results from the randomised DanGer Shock trial showed a significantly lower 180-day mortality among patients with ST-elevation myocardial infarction-related cardiogenic shock without anoxic brain injury randomly assigned in selected experienced centres to receive an Impella CP compared with standard therapy alone (45·8% *vs* 58·5%; hazard ratio [HR] 0·74 [95% CI 0·55–0·99]).[118] Potential device-related complications, such as moderate or severe bleeding (RR 2·06 [1·15–3·66]) and limb ischaemia (5·15 [1·11–23·84]), occurred more frequently in the Impella group. Despite the lower risk of adverse events, the mortality rate in the control group was remarkably high, considering that the number of patients randomised after cardiac arrest and median arterial lactate level at admission were lower than in the CULPRIT-SHOCK and ECLS-SHOCK trials.[4,6,118] The divergence of Kaplan–Meier curves beyond 30 days, explanation for higher renal replacement therapy requirement in the Impella group (RR 1·98 [1·27–3·09]), and differences between groups in short-term haemodynamic changes will have to be deciphered to identify treatment effects attributable to the Impella device from potential confounding variables or biases.[119] In addition, whether the benefit versus risk achieved in DanGer Shock is applicable to centres less experienced with microaxial flow pumps is uncertain.[120] Nonetheless, the DanGer Shock trial represents a milestone that reflects successful application of a temporary MCS device in a selected subgroup of patients with ST-elevation myocardial infarction-related cardiogenic shock.

Future trials should consider substantial differences in cardiogenic shock cause, phenotype, dynamics, and patient-specific prognostic factors. Furthermore, comparing the timing of MCS initiation before or after percutaneous coronary intervention should be considered when establishing eligibility criteria for future trials. Complications of all MCS remain high and can lead to

severe disability for survivors; they must be meticulously registered, and marked reductions of MCS complications should become a main objective of future trials and research. Lastly, evidence on the risks and benefits of combined MCS strategies, practices surrounding escalation and de-escalation, complication management, costs, and the role of novel therapeutic targets is still insufficient.[121]

Management considerations for patients experiencing cardiac arrest

Initiation of VA-ECMO for haemodynamic stabilisation during refractory cardiac arrest is also known as extracorporeal cardiopulmonary resuscitation (ECPR). ECPR can improve outcomes in out-of-hospital cardiac arrest within carefully structured health-care networks (appendix p 18).[103,122–124] However, the multicentre pragmatic INCEPTION trial did not find a significant survival benefit with favourable neurological status in patients randomised to ECPR or conventional cardiopulmonary resuscitation after out-of-hospital cardiac arrest.[9] This result was supported by a recent meta-analysis suggesting no significant difference in in-hospital mortality among out-of-hospital cardiac arrest patients undergoing ECPR.[125] In patients suffering in-hospital cardiac arrest, retrospective analyses have shown more consistent clinical benefit with ECPR, underscoring structural and organisational requirements for successful implementation in such complex clinical environments.[103,125–127]

After return of spontaneous circulation, myocardial dysfunction is a common occurrence resulting from ischaemia-reperfusion injury, catecholamine-induced myocardial injury, and various other factors.[128,129] RCTs informing management of post-resuscitation cardiogenic shock are absent and post-hoc analyses suggesting a lack of efficacy of IABP or VA-ECMO after cardiac arrest are subject to potential interaction effects and confounders.[5,6,108] Reliable early neurological prognostication after cardiac arrest, including anoxic brain injury reversibility for patients in coma, is challenging yet essential for individualised management according to the goals and preferences of the patient. Considering differences in acuity, extent and mechanism of organ damage, and the role of neuroprotective treatment strategies in survivors of cardiac arrest and patients with cardiogenic shock who were not resuscitated, separate investigation of these subgroups is key to refine post-resuscitation care.[130,131]

Management of infarct-related acute mechanical complications

Rates of acute mechanical complications, such as papillary muscle rupture with subsequent mitral regurgitation or ventricular septal and free wall defects, have decreased to less than 1% in patients with AMI.[132] These events are commonly associated with haemodynamic compromise and require correction (appendix pp 19–20).[132–135] Surgical repair is the therapeutic gold standard; however, even in operable patients, 1-year mortality rates of up to 46% have been reported.[136] Especially in patients with prohibitive surgical risk and haemodynamic instability, catheter-based treatment options have emerged as an alternative approach.[137–140] Evidence on optimal timing, efficacy of temporary MCS as a bridge to treatment, and the role of concomitant coronary artery bypass grafting is scarce, and management of these patients relies on expert consensus within local heart teams.

Management of organ dysfunction

Elevated left ventricular end-diastolic pressure and subsequent pulmonary oedema are important hallmarks of cardiogenic shock due to left ventricular failure. The rationale behind positive-pressure ventilation in the context of cardiogenic shock is to reduce work of breathing, decrease pulmonary vascular congestion, and improve alveolar recruitment. In patients with isolated left ventricular failure, positive-pressure ventilation could reduce both left ventricular preload and afterload, which can result in an increase in cardiac output. However, positive-pressure ventilation might have the opposite effect on the right ventricle and could reduce cardiac output in settings of left ventricular preload dependence or concomitant right ventricular failure.[141] Although sound evidence supporting optimal ventilation strategies in cardiogenic shock is scarce (appendix pp 21–22), endotracheal intubation and invasive mechanical ventilation is often necessary in the presence of severe compromise in gas exchange, despite the potential harmful haemodynamic effects (including those attributable to concomitant sedative medications). Invasive mechanical ventilation, which has been associated with worse outcomes after adjustment for potential confounders, was required by more than 70% of patients in the DanGer Shock trial[118] and more than 85% of patients in the ECLS-SHOCK trial.[6,142] One prospective analysis of data from 219 patients with cardiogenic shock found that non-invasive ventilation was used more often than invasive mechanical ventilation in less severe shock stages, although no association with worse outcomes after propensity matching was observed.[143] Clinical decision making regarding respiratory support options in cardiogenic shock is also limited by the absence of evidence for specific tidal volume, airway pressure, gas exchange and pH targets. In patients undergoing VA-ECMO, pulmonary congestion resulting from device-related increase in left ventricular afterload might necessitate left ventricular unloading.[112] An ongoing randomised trial comparing ultraprotective (tidal volume of 4 mL/kg of predicted body weight) versus protective (6 mL/kg) ventilation settings could shed light on optimal respiratory support during VA-ECMO (ChiCTR2200067118).

Acute kidney injury has been shown to complicate up to 35% of all AMI-related cardiogenic shock admissions (appendix p 23).[144] The classically accepted mechanism of acute kidney injury occurring in cardiogenic shock is prerenal via a low cardiac output state progressing to acute

tubular necrosis. Further mechanisms, including renal venous congestion in right ventricular failure, inflammation, and intrinsic acute kidney injury have additionally been proposed as factors aggravating renal dysfunction in cardiogenic shock.[145–147] Renal replacement therapy is commonly required and this need has been associated with increased mortality.[147,148] Although randomised studies have assessed the role of renal replacement therapy in the setting of acute decompensated heart failure, patients meeting cardiogenic shock criteria have often been excluded from analysis.[149] Thus, the indication for renal replacement therapy proposed by the 2017 American Heart Association scientific statement might not be optimal for all forms of cardiogenic shock and should be investigated further.[11,147]–Hypoxic hepatitis has been reported in 18% of patients with AMI-related cardiogenic shock, with increases in aminotransferase of over 20 times the upper limit of normal within 24 h after admission being associated with higher mortality.[150] To date, the effect of different volume and central venous pressure targets as well as strategies for nutrition on outcomes remains unclear.

Although targeted temperature management with active fever prevention is recommended for neuroprotection in patients in coma after cardiac arrest,[151] optimal target temperature in patients with cardiogenic shock remains unknown. Given potential adverse haemodynamic effects and the uncertainty regarding the neurological and survival benefits of hypothermia, fevers should be avoided but lowering body temperature in patients with cardiogenic shock in coma following cardiac arrest might not be necessary. Targeted mild hypothermia (compared with targeted normothermia) did not provide a mortality benefit in an unselected cohort of patients treated with VA-ECMO and did not result in improvement in cardiac power index in patients with AMI-related cardiogenic shock who were not resuscitated following percutaneous coronary intervention.[30,152] Nonetheless, patients receiving VA-ECMO for cardiogenic shock after resuscitation following cardiac arrest could benefit from moderate hypothermia, as suggested by a post-hoc analysis of the randomised HYPO-ECMO trial.[153]

Bleeding and thromboembolic events occur frequently in patients with cardiogenic shock, especially in those requiring MCS and those receiving aggressive antithrombotic therapy for AMI.[102,103] Early detection of platelet dysfunction and coagulopathies, such as acquired von Willebrand syndrome or heparin-induced thrombocytopenia, can help to prevent life-threatening complications.[154,155]

Intensive supportive care

Invasive measurement of central venous pressure, pulmonary capillary wedge pressure, pulmonary arterial pressures, pulmonary artery pulsatility index, cardiac output, and oxygen saturation obtained from pulmonary artery catheterisation (in conjunction with information obtained by non-invasive measures, such as serial echocardiographic assessment), allows for differentiation of left ventricular-predominant, right ventricular-predominant, or biventricular forms of cardiogenic shock. Identification can permit early detection of haemodynamic changes and responses to treatment algorithms and help to guide targeted shock therapy. Given the absence of data from randomised trials, routine placement of a pulmonary artery catheter at shock onset is currently not recommended. However, placement of a pulmonary artery catheter could potentially be useful in cases of diagnostic uncertainty, mixed shock and right ventricular involvement, unresponsiveness to treatment, weaning from temporary MCS, and candidacy assessment for durable MCS or heart transplantation (appendix pp 24–25).[11] However, the restrictive use of pulmonary artery catheterisation has been challenged by retrospective evidence suggesting that pulmonary artery catheter-based haemodynamic profiling within the first hours of admission might be beneficial.[29,156–158] This hypothesis is under investigation in the randomised PACCS trial assessing early pulmonary artery catheter use in 400 patients with acute decompensated heart failure-related cardiogenic shock (NCT05485376; appendix p 26).

Evidence-based recommendations regarding fluid management in cardiogenic shock are not available and estimation of preload responsiveness can be challenging. In the few patients with cardiogenic shock who do not have volume overload, a small, controlled fluid bolus can be attempted with close monitoring. More often, diuresis is indicated to relieve congestion, and this can improve pulmonary, cardiac, and in some cases renal function. In a single-centre retrospective analysis, positive fluid balance 96 h after admission was independently associated with increased 30-day mortality in patients with AMI-related cardiogenic shock.[159] Invasive haemodynamic monitoring might offer guidance for fluid management in selected cases.[160] Lastly, optimal red blood cell transfusion thresholds and indication for other blood products in cardiogenic shock are unknown. Retrospective data suggested lower in-hospital mortality in patients with a haemoglobin transfusion threshold of less than 8 g/dL and no added benefit at a higher threshold of less than 10 g/dL.[161]

Sedatives can potentially have adverse haemodynamic effects in cardiogenic shock, including decrease of cardiac output, systemic vascular resistance, and mean arterial pressure related to reduction of sympathetic tone. These effects can be aggravated by direct vasodilatory or myocardial depressant effects, yet uncertainty exists regarding the clinical relevance and influence on outcomes in cardiogenic shock. A retrospective comparison of propofol with midazolam as a sedative in patients with cardiogenic shock was associated with a higher 30-day survival and lower catecholamine dose with the use of propofol.[162]

Few clinical trials inform cardiogenic shock management in individuals over the age of 75 years, although the incidence of cardiogenic shock in this age group is

expected to increase.[163] Cognitive status before shock onset, frailty, multimorbidity, and advanced directives must be considered in patient-centred clinical decision making.[163–165] Development of prediction scores for futility and routine integration of palliative care into clinical practice is warranted.[166]

Long-term sequelae and associated costs

Although long-term outcomes and quality of life after cardiogenic shock compared with those after other acute life-threatening diseases are still being investigated, survivors of cardiogenic shock are frequently affected by physical and mental health sequelae. A multicentre analysis found that the incidence of a composite endpoint of anxiety and other psychiatric disorders in survivors of AMI-related cardiogenic shock was 110 per 1000 person-years.[167] Diagnosis and treatment for such comorbidities and health-related quality of life has not been well researched, but must be addressed as part of a comprehensive long-term cardiogenic shock care bundle. The risk of rehospitalisation and subsequent death can be high even among survivors of cardiogenic shock, requiring a diligent approach to medical optimisation and follow-up care that is ideally coordinated by specialised multidisciplinary clinics.

A European single-centre analysis reported a cardiogenic shock hospital stay-related expenditure of €9632 per life-year gained.[168] Larger-scale estimation of the economic burden associated with cardiogenic shock requires further analyses of reimbursement and staffing models, readmission rates, and relative cost efficacy of novel (device-based) treatment options.[169,170]

Conclusion and future directions

Many notable preclinical and clinical studies examining cardiogenic shock subtypes, prognostication, and different facets of care have prepared the foundations towards evidence-based precision medicine for patients with cardiogenic shock, although important evidence gaps remain. Novel analytical methods are likely to shape the ongoing endeavour of deciphering the complexity of cardiogenic shock through deep phenotyping, development of prognostic models, and identification of promising treatment targets. With the public health burden of cardiogenic shock expected to increase over time, further development of emergency and intensive care algorithms combined with the exploration of long-term management options is crucial to improve survival and quality of life after cardiogenic shock.

Contributors

EL, AC, and HT were responsible for conceptualisation, methodology, project administration, resources, software, supervision, validation, visualisation, and writing and revision of the original draft. LB, MA, RL, AM, DAM, SP, JCJ, and DB contributed to data validation and to the revision of the manuscript.

Declaration of interests

MA reports speaker honoraria from Abbott Vascular and Edwards Lifesciences, unrelated to the submitted work. RL reports research grants from Medtronic and LivaNova paid to their institution; consulting fees from Medtronic and LivaNova paid to their institution; speaker honoraria from Abiomed; travel support from Medtronic and LivaNova; lab supplies from Medtronic, unrelated to the submitted work; and is an advisory board member for Eurosets and Xenios (fees paid to institution). AM reports research grants from Roche, 4TEEN4, Sphyngotec, Abbott Diagnostics, and Windtree; consulting fees from Roche, Adrenomed, Corteria, and Fire1; speaker honoraria from Merck, Novartis, Roche, and Bayer; and lab supplies by Sphyngotec, unrelated to the submitted work; and is an advisory board member for Secret-HF, S-Form Pharma, and Implicity. DAM reports research grants from Abbott Laboratories, Abiomed, Amgen, Anthos Therapeutics, Arca Biopharma, AstraZeneca, Daiichi Sankyo, Intarcia, Janssen, Merck & Co, Novartis, Pfizer, Poxel, Regeneron, Roche Diagnostics, Siemens, Softcell Medical, and Zora Biosciences (paid to the institution); consulting fees from Abbott Laboratories, Arca Biopharma, Merck & Co, Novartis, Regeneron, and Roche Diagnostics unrelated to the submitted work; and is an advisory board member for InCarda Therapeutics. DB reports a research grant from LivaNova paid to their institution; consulting fees from LivaNova, Xenios, Medtronic, Inspira, Cellenkos, and HBOX Therapies; and payment from UpToDate, unrelated to the submitted work. AC reports speaker honoraria from Getinge, Baxter, and Xenios unrelated to the submitted work. All other authors declare no competing interests.

References

1 Waksman R, Pahuja M, van Diepen S, et al. Standardized definitions for cardiogenic shock research and mechanical circulatory support devices: scientific expert panel from the shock academic research consortium (SHARC). *Circulation* 2023; **148:** 1113–26.

2 Alexander JH, Reynolds HR, Stebbins AL, et al. Effect of tilarginine acetate in patients with acute myocardial infarction and cardiogenic shock: the TRIUMPH randomized controlled trial. *JAMA* 2007; **297:** 1657–66.

3 Karakas M, Akin I, Burdelski C, et al. Single-dose of adrecizumab versus placebo in acute cardiogenic shock (ACCOST-HH): an investigator-initiated, randomised, double-blinded, placebo-controlled, multicentre trial. *Lancet Respir Med* 2022; **10:** 247–54.

4 Thiele H, Akin I, Sandri M, et al. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl J Med* 2017; **377:** 2419–32.

5 Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012; **367:** 1287–96.

6 Thiele H, Zeymer U, Akin I, et al. Extracorporeal life support in infarct-related cardiogenic shock. *N Engl J Med* 2023; **389:** 1286–97.

7 Ostadal P, Rokyta R, Karasek J, et al. Extracorporeal membrane oxygenation in the therapy of cardiogenic shock: results of the ECMO-CS randomized clinical trial. *Circulation* 2023; **147:** 454–64.

8 Mebazaa A, Nieminen MS, Packer M, et al. Levosimendan vs dobutamine for patients with acute decompensated heart failure: the SURVIVE randomized trial. *JAMA* 2007; **297:** 1883–91.

9 Suverein MM, Delnoij TSR, Lorusso R, et al. Early Extracorporeal CPR for refractory out-of-hospital cardiac arrest. *N Engl J Med* 2023; **388:** 299–309.

10 McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021; **42:** 4901.

11 van Diepen S, Katz JN, Albert NM, et al. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation* 2017; **136:** e232–68.

12 Chioncel O, Parissis J, Mebazaa A, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2021; **23:** 345.

13 Naidu SS, Baran DA, Jentzer JC, et al. SCAI SHOCK stage classification expert consensus update: a review and incorporation of validation studies: this statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. *J Soc Cardiovasc Angiogr Interv* 2022; **1:** 100008.

14 Jentzer JC, van Diepen S, Barsness GW, et al. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. *J Am Coll Cardiol* 2019; **74:** 2117–28.

15 Schrage B, Dabboura S, Yan I, et al. Application of the SCAI classification in a cohort of patients with cardiogenic shock. *Catheter Cardiovasc Interv* 2020; **96:** E213–19.

16 Thayer KL, Zweck E, Ayouty M, et al. Invasive hemodynamic assessment and classification of in-hospital mortality risk among patients with cardiogenic shock. *Circ Heart Fail* 2020; **13:** e007099.

17 Kapur NK, Kanwar M, Sinha SS, et al. Criteria for defining stages of cardiogenic shock severity. *J Am Coll Cardiol* 2022; **80:** 185–98.

18 Arrigo M, Price S, Baran DA, et al. Optimising clinical trials in acute myocardial infarction complicated by cardiogenic shock: a statement from the 2020 Critical Care Clinical Trialists Workshop. *Lancet Respir Med* 2021; **9:** 1192–202.

19 Stevenson LW, Pagani FD, Young JB, et al. INTERMACS profiles of advanced heart failure: the current picture. *J Heart Lung Transplant* 2009; **28:** 535–41.

20 Barge-Caballero E, Segovia-Cubero J, Almenar-Bonet L, et al. Preoperative INTERMACS profiles determine postoperative outcomes in critically ill patients undergoing emergency heart transplantation: analysis of the Spanish National Heart Transplant Registry. *Circ Heart Fail* 2013; **6:** 763–72.

21 Jentzer JC, Rayfield C, Soussi S, et al. Machine learning approaches for phenotyping in cardiogenic shock and critical illness: part 2 of 2. *JACC Adv* 2022; **1:** 100126.

22 Zweck E, Thayer KL, Helgestad OKL, et al. Phenotyping cardiogenic shock. *J Am Heart Assoc* 2021; **10:** e020085.

23 Zweck E, Kanwar M, Li S, et al. Clinical course of patients in cardiogenic shock stratified by phenotype. *JACC Heart Fail* 2023; **11:** 1304–15.

24 Harjola VP, Lassus J, Sionis A, et al. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail* 2015; **17:** 984.

25 Berg DD, Bohula EA, van Diepen S, et al. Epidemiology of shock in contemporary cardiac intensive care units. *Circ Cardiovasc Qual Outcomes* 2019; **12:** e005618.

26 Hunziker L, Radovanovic D, Jeger R, et al. Twenty-year trends in the incidence and outcome of cardiogenic shock in AMIS Plus registry. *Circ Cardiovasc Interv* 2019; **12:** e007293.

27 Schrage B, Becher PM, Goßling A, et al. Temporal trends in incidence, causes, use of mechanical circulatory support and mortality in cardiogenic shock. *ESC Heart Fail* 2021; **8:** 1295–303.

28 Rathod KS, Koganti S, Iqbal MB, et al. Contemporary trends in cardiogenic shock: incidence, intra-aortic balloon pump utilisation and outcomes from the London Heart Attack Group. *Eur Heart J Acute Cardiovasc Care* 2018; **7:** 16–27.

29 Garan AR, Kanwar M, Thayer KL, et al. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. *JACC Heart Fail* 2020; **8:** 903–13.

30 Levy B, Girerd N, Amour J, et al. Effect of moderate hypothermia vs normothermia on 30-day mortality in patients with cardiogenic shock receiving venoarterial extracorporeal membrane oxygenation: a randomized clinical trial. *JAMA* 2023; **329:** 1226.

31 Tehrani BN, Sherwood MW, Rosner C, et al. A standardized and regionalized network of care for cardiogenic shock. *JACC Heart Fail* 2022; **10:** 768–81.

32 Kanwar MK, Billia F, Randhawa V, et al. Heart failure related cardiogenic shock: an ISHLT consensus conference content summary. *J Heart Lung Transplant* 2024; **43:** 189–203.

33 Cuinet J, Garbagnati A, Rusca M, et al. Cardiogenic shock elicits acute inflammation, delayed eosinophilia, and depletion of immune cells in most severe cases. *Sci Rep* 2020; **10:** 7639.

34 Kohsaka S, Menon V, Lowe AM, et al. Systemic inflammatory response syndrome after acute myocardial infarction complicated by cardiogenic shock. *Arch Intern Med* 2005; **165:** 1643–50.

35 Debrunner M, Schuiki E, Minder E, et al. Proinflammatory cytokines in acute myocardial infarction with and without cardiogenic shock. *Clin Res Cardiol* 2008; **97:** 298–305.

36 Lala A, Guo Y, Xu J, et al. Right ventricular dysfunction in acute myocardial infarction complicated by cardiogenic shock: a hemodynamic analysis of the should we emergently revascularize occluded coronaries for cardiogenic shock (SHOCK) trial and registry. *J Card Fail* 2018; **24:** 148–56.

37 Kanwar MK, Everett KD, Gulati G, Brener MI, Kapur NK. Epidemiology and management of right ventricular-predominant heart failure and shock in the cardiac intensive care unit. *Eur Heart J Acute Cardiovasc Care* 2022; **11:** 584–94.

38 Rivas-Lasarte M, Sans-Roselló J, Collado-Lledó E, et al. External validation and comparison of the CardShock and IABP-SHOCK II risk scores in real-world cardiogenic shock patients. *Eur Heart J Acute Cardiovasc Care* 2021; **10:** 16–24.

39 Beer BN, Jentzer JC, Weimann J, et al. Early risk stratification in patients with cardiogenic shock irrespective of the underlying cause—the Cardiogenic Shock Score. *Eur J Heart Fail* 2022; **24:** 657–67.

40 Sleeper LA, Reynolds HR, White HD, Webb JG, Dzavík V, Hochman JS. A severity scoring system for risk assessment of patients with cardiogenic shock: a report from the SHOCK trial and registry. *Am Heart J* 2010; **160:** 443–50.

41 Pöss J, Köster J, Fuernau G, et al. Risk stratification for patients in cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol* 2017; **69:** 1913–20.

42 Ceglarek U, Schellong P, Rosolowski M, et al. The novel cystatin C, lactate, interleukin-6, and N-terminal pro-B-type natriuretic peptide (CLIP)-based mortality risk score in cardiogenic shock after acute myocardial infarction. *Eur Heart J* 2021; **42:** 2344–52.

43 Auffret V, Cottin Y, Leurent G, et al. Predicting the development of in-hospital cardiogenic shock in patients with ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention: the ORBI risk score. *Eur Heart J* 2018; **39:** 2090–102.

44 Wenzl FA, Bruno F, Kraler S, et al. Dipeptidyl peptidase 3 plasma levels predict cardiogenic shock and mortality in acute coronary syndromes. *Eur Heart J* 2023; **44:** 3859–71.

45 Muller G, Flecher E, Lebreton G, et al. The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock. *Intensive Care Med* 2016; **42:** 370–78.

46 Schmidt M, Burrell A, Roberts L, et al. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J* 2015; **36:** 2246–56.

47 Kalra S, Ranard LS, Memon S, et al. Risk prediction in cardiogenic shock: current state of knowledge, challenges and opportunities. *J Card Fail* 2021; **27:** 1099–110.

48 Zeymer U, Alushi B, Noc M, et al. Influence of culprit lesion intervention on outcomes in infarct-related cardiogenic shock with cardiac arrest. *J Am Coll Cardiol* 2023; **81:** 1165–76.

49 Jentzer JC, Henry TD, Barsness GW, Menon V, Baran DA, Van Diepen S. Influence of cardiac arrest and SCAI shock stage on cardiac intensive care unit mortality. *Catheter Cardiovasc Interv* 2020; **96:** 1350–59.

50 Patel SM, Berg DD, Bohula EA, et al. Early serial assessment of aggregate vasoactive support and mortality in cardiogenic shock: insights from the critical care cardiology trials network registry. *Circ Heart Fail* 2024; **17:** e011736.

51 Rueda F, Borràs E, García-García C, et al. Protein-based cardiogenic shock patient classifier. *Eur Heart J* 2019; **40:** 2684–94.

52 Takagi K, Blet A, Levy B, et al. Circulating dipeptidyl peptidase 3 and alteration in haemodynamics in cardiogenic shock: results from the OptimaCC trial. *Eur J Heart Fail* 2020; **22:** 279–86.

53 Iborra-Egea O, Rueda F, García-García C, Borràs E, Sabidó E, Bayes-Genis A. Molecular signature of cardiogenic shock. *Eur Heart J* 2020; **41:** 3839–48.

54 Soussi S, Ahmadiankalati M, Jentzer JC, et al. Clinical phenotypes of cardiogenic shock survivors: insights into late host responses and long-term outcomes. *ESC Heart Fail* 2024; **11:** 1242–48.

55 Mebazaa A, Soussi S. Precision Medicine in cardiogenic shock: we are almost there! *JACC Heart Fail* 2023; **11:** 1316–19.

56 Senman B, Jentzer JC, Barnett CF, et al. Need for a cardiogenic shock team collaborative-promoting a team-based model of care to improve outcomes and identify best practices. *J Am Heart Assoc* 2024; **13:** e031979.

57 Papolos AI, Kenigsberg BB, Berg DD, et al. Management and outcomes of cardiogenic shock in cardiac ICUs with versus without shock teams. *J Am Coll Cardiol* 2021; **78:** 1309–17.

58 Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009; **374:** 1330.

59 Tehrani BN, Truesdell AG, Sherwood MW, et al. Standardized team-based care for cardiogenic shock. *J Am Coll Cardiol* 2019; **74:** 481.

60 Taleb I, Koliopoulou AG, Tandar A, et al. Shock team approach in refractory cardiogenic shock requiring short-term mechanical circulatory support: a proof of concept. *Circulation* 2019; **140:** 98–100.

61 Lee F, Hutson JH, Boodhwani M, et al. Multidisciplinary code shock team in cardiogenic shock: a Canadian centre experience. *CJC Open* 2020; **2:** 249–57.

62 Garan AR, Kataria R, Li B, et al. Outcomes of patients transferred to tertiary care centers for treatment of cardiogenic shock: a cardiogenic shock working group analysis. *J Card Fail* 2024; **30:** 564–75.

63 Alviar CL, Hall S, Mebazaa A. Outcomes of patients with cardiogenic shock in hub and spoke centers: the importance of protocol standardization at a network level. *J Card Fail* 2024; **30:** 576–79.

64 van Diepen S, Reynolds HR, Stebbins A, et al. Incidence and outcomes associated with early heart failure pharmacotherapy in patients with ongoing cardiogenic shock. *Crit Care Med* 2014; **42:** 281–88.

65 Mathew R, Fernando SM, Hu K, et al. Optimal perfusion targets in cardiogenic shock. *JACC Adv* 2022; **1:** 100034.

66 Asfar P, Meziani F, Hamel JF, et al. High versus low blood-pressure target in patients with septic shock. *N Engl J Med* 2014; **370:** 1583–93.

67 Burstein B, Tabi M, Barsness GW, Bell MR, Kashani K, Jentzer JC. Association between mean arterial pressure during the first 24 hours and hospital mortality in patients with cardiogenic shock. *Crit Care* 2020; **24:** 513.

68 Basir MB, Lemor A, Gorgis S, et al. Vasopressors independently associated with mortality in acute myocardial infarction and cardiogenic shock. *Catheter Cardiovasc Interv* 2022; **99:** 650–57.

69 De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med* 2010; **362:** 779–89.

70 Levy B, Clere-Jehl R, Legras A, et al. Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol* 2018; **72:** 173–82.

71 Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2023; **147:** e674.

72 Henry TD, Tomey MI, Tamis-Holland JE, et al. Invasive management of acute myocardial infarction complicated by cardiogenic shock: a scientific statement from the American Heart Association. *Circulation* 2021; **143:** e815–29.

73 Tarvasmäki T, Lassus J, Varpula M, et al. Current real-life use of vasopressors and inotropes in cardiogenic shock—adrenaline use is associated with excess organ injury and mortality. *Crit Care* 2016; **20:** 208.

74 Mebazaa A, Motiejunaite J, Gayat E, et al. Long-term safety of intravenous cardiovascular agents in acute heart failure: results from the European Society of Cardiology heart failure long-term registry. *Eur J Heart Fail* 2018; **20:** 332–41.

75 Maack C, Eschenhagen T, Hamdani N, et al. Treatments targeting inotropy. *Eur Heart J* 2019; **40:** 3626–44.

76 Mathew R, Di Santo P, Jung RG, et al. Milrinone as compared with dobutamine in the treatment of cardiogenic shock. *N Engl J Med* 2021; **385:** 516–25.

77 Parlow S, Di Santo P, Mathew R, et al. The association between mean arterial pressure and outcomes in patients with cardiogenic shock: insights from the DOREMI trial. *Eur Heart J Acute Cardiovasc Care* 2021; **10:** 712–20.

78 Mebazaa A, Nieminen MS, Filippatos GS, et al. Levosimendan vs. dobutamine: outcomes for acute heart failure patients on beta-blockers in SURVIVE. *Eur J Heart Fail* 2009; **11:** 304–11.

79 Fernando SM, Mathew R, Sadeghirad B, et al. Inotropes, vasopressors, and mechanical circulatory support for treatment of cardiogenic shock complicating myocardial infarction: a systematic review and network meta-analysis. *Can J Anaesth* 2022; **69:** 1537–53.

80 Hinrichs S, Scherschel K, Krüger S, et al. Precursor proadrenomedullin influences cardiomyocyte survival and local inflammation related to myocardial infarction. *Proc Natl Acad Sci USA* 2018; **115:** E8727–36.

81 Berg-Hansen K, Christensen KH, Gopalasingam N, et al. Beneficial effects of ketone ester in patients with cardiogenic shock: a randomized, controlled, double-blind trial. *JACC Heart Fail* 2023; **11:** 1337–47.

82 Deniau B, Rehfeld L, Santos K, et al. Circulating dipeptidyl peptidase 3 is a myocardial depressant factor: dipeptidyl peptidase 3 inhibition rapidly and sustainably improves haemodynamics. *Eur J Heart Fail* 2020; **22:** 290–99.

83 Metra M, Chioncel O, Cotter G, et al. Safety and efficacy of istaroxime in patients with acute heart failure-related pre-cardiogenic shock—a multicentre, randomized, double-blind, placebo-controlled, parallel group study (SEISMiC). *Eur J Heart Fail* 2022; **24:** 1967–77.

84 Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2024; **45:** 1145.

85 Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2022; **145:** e772.

86 Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK investigators. Should we emergently revascularize occluded coronaries for cardiogenic shock. *N Engl J Med* 1999; **341:** 625–34.

87 Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA* 2006; **295:** 2511–15.

88 Thiele H, Akin I, Sandri M, et al. One-year outcomes after PCI strategies in cardiogenic shock. *N Engl J Med* 2018; **379:** 1699–710.

89 Dzavik V, Sleeper LA, Cocke TP, et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK Trial Registry. *Eur Heart J* 2003; **24:** 828–37.

90 Sanborn TA, Sleeper LA, Webb JG, et al. Correlates of one-year survival inpatients with cardiogenic shock complicating acute myocardial infarction: angiographic findings from the SHOCK trial. *J Am Coll Cardiol* 2003; **42:** 1373–79.

91 Kolte D, Khera S, Aronow WS, et al. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc* 2014; **3:** e000590.

92 Smilowitz NR, Alviar CL, Katz SD, Hochman JS. Coronary artery bypass grafting versus percutaneous coronary intervention for myocardial infarction complicated by cardiogenic shock. *Am Heart J* 2020; **226:** 255–63.

93 White HD, Assmann SF, Sanborn TA, et al. Comparison of percutaneous coronary intervention and coronary artery bypass grafting after acute myocardial infarction complicated by cardiogenic shock: results from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. *Circulation* 2005; **112:** 1992–2001.

94 Smilowitz NR, Galloway AC, Ohman EM, et al. Coronary revascularization and circulatory support strategies in patients with myocardial infarction, multi-vessel coronary artery disease, and cardiogenic shock: Insights from an international survey. *Am Heart J* 2020; **225:** 55–59.

95 Damluji AA, Bandeen-Roche K, Berkower C, et al. Percutaneous coronary intervention in older patients with ST-segment elevation myocardial infarction and cardiogenic shock. *J Am Coll Cardiol* 2019; **73:** 1890–900.

96 Sterling LH, Fernando SM, Talarico R, et al. Long-term outcomes of cardiogenic shock complicating myocardial infarction. *J Am Coll Cardiol* 2023; **82:** 985–95.

97 Zeymer U, Vogt A, Zahn R, et al. Predictors of in-hospital mortality in 1333 patients with acute myocardial infarction complicated by cardiogenic shock treated with primary percutaneous coronary intervention (PCI); results of the primary PCI registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK). *Eur Heart J* 2004; **25:** 322–28.

98 Jeger RV, Harkness SM, Ramanathan K, et al. Emergency revascularization in patients with cardiogenic shock on admission: a report from the SHOCK trial and registry. *Eur Heart J* 2006; **27:** 664–70.

99 Omer MA, Tyler JM, Henry TD, et al. Clinical characteristics and outcomes of STEMI patients with cardiogenic shock and cardiac arrest. *JACC Cardiovasc Interv* 2020; **13:** 1211–19.

100 Lu DY, Adelsheimer A, Chan K, et al. Impact of hospital transfer to hubs on outcomes of cardiogenic shock in the real world. *Eur J Heart Fail* 2021; **23:** 1927–37.

101 Shaefi S, O'Gara B, Kociol RD, et al. Effect of cardiogenic shock hospital volume on mortality in patients with cardiogenic shock. *J Am Heart Assoc* 2015; **4:** e001462.

102 Lüsebrink E, Kellnar A, Krieg K, et al. Percutaneous transvalvular microaxial flow pump support in cardiology. *Circulation* 2022; **145:** 1254–84.

103 Lüsebrink E, Binzenhöfer L, Hering D, et al. Scrutinizing the role of venoarterial extracorporeal membrane oxygenation: has clinical practice outpaced the evidence? *Circulation* 2024; **149:** 1033–52.

104 Thiele H, Zeymer U, Thelemann N, et al. Intraaortic balloon pump in cardiogenic shock complicating acute myocardial infarction: long-term 6-year outcome of the randomized IABP-SHOCK II trial. *Circulation* 2019; **139:** 395–403.

105 Hawranek M, Gierlotka M, Pres D, Zembala M, Gąsior M. Nonroutine use of intra-aortic balloon pump in cardiogenic shock complicating myocardial infarction with successful and unsuccessful primary percutaneous coronary intervention. *JACC Cardiovasc Interv* 2018; **11:** 1885–93.

106 Kettner J, Sramko M, Holek M, Pirk J, Kautzner J. Utility of intra-aortic balloon pump support for ventricular septal rupture and acute mitral regurgitation complicating acute myocardial infarction. *Am J Cardiol* 2013; **112:** 1709–13.

107 Morici N, Marini C, Sacco A, et al. Early intra-aortic balloon pump in acute decompensated heart failure complicated by cardiogenic shock: rationale and design of the randomized Altshock-2 trial. *Am Heart J* 2021; **233:** 39–47.

108 Zeymer U, Freund A, Hochadel M, et al. Venoarterial extracorporeal membrane oxygenation in patients with infarct-related cardiogenic shock: an individual patient data meta-analysis of randomised trials. *Lancet* 2023; **402:** 1338–46.

109 Brunner S, Guenther SPW, Lackermair K, et al. Extracorporeal life support in cardiogenic shock complicating acute myocardial infarction. *J Am Coll Cardiol* 2019; **73:** 2355–57.

110 Banning AS, Sabaté M, Orban M, et al. Venoarterial extracorporeal membrane oxygenation or standard care in patients with cardiogenic shock complicating acute myocardial infarction: the multicentre, randomised EURO SHOCK trial. *EuroIntervention* 2023; **19:** 482–92.

111 Bréchot N, Hajage D, Kimmoun A, et al. Venoarterial extracorporeal membrane oxygenation to rescue sepsis-induced cardiogenic shock: a retrospective, multicentre, international cohort study. *Lancet* 2020; **396:** 545–52.

112 Lüsebrink E, Orban M, Kupka D, et al. Prevention and treatment of pulmonary congestion in patients undergoing venoarterial extracorporeal membrane oxygenation for cardiogenic shock. *Eur Heart J* 2020; **41:** 3753–61.

113 Lüsebrink E, Binzenhöfer L, Kellnar A, et al. Venting during venoarterial extracorporeal membrane oxygenation. *Clin Res Cardiol* 2023; **112:** 464–505.

114 Schrage B, Becher PM, Bernhardt A, et al. Left ventricular unloading is associated with lower mortality in patients with cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation: results from an international, multicenter cohort study. *Circulation* 2020; **142:** 2095–106.

115 Schrage B, Sundermeyer J, Blankenberg S, et al. Timing of active left ventricular unloading in patients on venoarterial extracorporeal membrane oxygenation therapy. *JACC Heart Fail* 2023; **11:** 321–30.

116 Kim MC, Lim Y, Lee SH, et al. Early left ventricular unloading or conventional approach after venoarterial extracorporeal membrane oxygenation: the EARLY-UNLOAD randomized clinical trial. *Circulation* 2023; **148:** 1570–81.

117 Park H, Yang JH, Ahn JM, et al. Early left atrial venting versus conventional treatment for left ventricular decompression during venoarterial extracorporeal membrane oxygenation support: the EVOLVE-ECMO randomized clinical trial. *Eur J Heart Fail* 2023; **25:** 2037–46.

118 Møller JE, Engstrøm T, Jensen LO, et al. Microaxial flow pump or standard care in infarct-related cardiogenic shock. *N Engl J Med* 2024; **390:** 1382–93.

119 Lüsebrink E, Binzenhöfer L, Thiele H. The DanGer Shock trial: a new dawn but much to uncover. *Eur Heart J* 2024; ehae516.

120 Tavazzi G, Morrow DA. Efficacy and safety of mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: DanGer trial in perspective. *Eur Heart J Acute Cardiovasc Care* 2024; **13:** 365–67.

121 Swain L, Bhave S, Qiao X, et al. Novel role for cardiolipin as a target of therapy to mitigate myocardial injury caused by venoarterial extracorporeal membrane oxygenation. *Circulation* 2024; **149:** 1341–53.

122 Yannopoulos D, Bartos J, Raveendran G, et al. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. *Lancet* 2020; **396:** 1807–16.

123 Rob D, Smalcova J, Smid O, et al. Extracorporeal versus conventional cardiopulmonary resuscitation for refractory out-of-hospital cardiac arrest: a secondary analysis of the Prague OHCA trial. *Crit Care* 2022; **26:** 330.

124 Belohlavek J, Smalcova J, Rob D, et al. Effect of intra-arrest transport, extracorporeal cardiopulmonary resuscitation, and immediate invasive assessment and treatment on functional neurologic outcome in refractory out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA* 2022; **327:** 737–47.

125 Low CJW, Ramanathan K, Ling RR, et al. Extracorporeal cardiopulmonary resuscitation versus conventional cardiopulmonary resuscitation in adults with cardiac arrest: a comparative meta-analysis and trial sequential analysis. *Lancet Respir Med* 2023; **11:** 883–93.

126 Chen YS, Lin JW, Yu HY, et al. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. *Lancet* 2008; **372:** 554–61.

127 Abrams D, Garan AR, Abdelbary A, et al. Position paper for the organization of ECMO programs for cardiac failure in adults. *Intensive Care Med* 2018; **44:** 717–29.

128 Jozwiak M, Bougouin W, Geri G, Grimaldi D, Cariou A. Post-resuscitation shock: recent advances in pathophysiology and treatment. *Ann Intensive Care* 2020; **10:** 170.

129 Jentzer JC, Chonde MD, Dezfulian C. Myocardial dysfunction and shock after cardiac arrest. *BioMed Res Int* 2015; **2015:** 314796.

130 Rajajee V, Muehlschlegel S, Wartenberg KE, et al. Guidelines for neuroprognostication in comatose adult survivors of cardiac arrest. *Neurocrit Care* 2023; **38:** 533–63.

131 Jentzer JC, van Diepen S, Henry TD. Understanding how cardiac arrest complicates the analysis of clinical trials of cardiogenic shock. *Circ Cardiovasc Qual Outcomes* 2020; **13:** e006692.

132 Elbadawi A, Elgendy IY, Mahmoud K, et al. Temporal trends and outcomes of mechanical complications in patients with acute myocardial infarction. *JACC Cardiovasc Interv* 2019; **12:** 1825–36.

133 Damluji AA, van Diepen S, Katz JN, et al. Mechanical complications of acute myocardial infarction: a scientific statement from the American Heart Association. *Circulation* 2021; **144:** e16–35.

134 Sanmartín-Fernández M, Raposeiras-Roubin S, Anguita-Sánchez M, et al. In-hospital outcomes of mechanical complications in acute myocardial infarction: analysis from a nationwide Spanish database. *Cardiol J* 2021; **28:** 589–97.

135 Kwok CS, Qureshi AI, Will M, Schwarz K, Lip GYH, Borovac JA. Structural complications following st-elevation myocardial infarction: an analysis of the national inpatient sample 2016 to 2020. *J Cardiovasc Dev Dis* 2024; **11:** 59.

136 Matteucci M, Ronco D, Kowalewski M, et al. Long-term survival after surgical treatment for post-infarction mechanical complications: results from the Caution study. *Eur Heart J Qual Care Clin Outcomes* 2024; published online Feb 7. https://doi.org/10.1093/ehjqcco/qcae010.

137 Adamo M, Curello S, Chiari E, et al. Percutaneous edge-to-edge mitral valve repair for the treatment of acute mitral regurgitation complicating myocardial infarction: a single centre experience. *Int J Cardiol* 2017; **234:** 53–57.

138 Calvert PA, Cockburn J, Wynne D, et al. Percutaneous closure of postinfarction ventricular septal defect: in-hospital outcomes and long-term follow-up of UK experience. *Circulation* 2014; **129:** 2395–402.

139 Thiele H, Kaulfersch C, Daehnert I, et al. Immediate primary transcatheter closure of postinfarction ventricular septal defects. *Eur Heart J* 2009; **30:** 81–88.

140 Valle JA, Miyasaka RL, Carroll JD. Acute mitral regurgitation secondary to papillary muscle tear: is transcatheter edge-to-edge mitral valve repair a new paradigm? *Circ Cardiovasc Interv* 2017; **10:** e005050.

141 Alviar CL, Miller PE, McAreavey D, et al. Positive pressure ventilation in the cardiac intensive care unit. *J Am Coll Cardiol* 2018; **72:** 1532–53.

142 Rubini Giménez M, Miller PE, Alviar CL, et al. Outcomes associated with respiratory failure for patients with cardiogenic shock and acute myocardial infarction: a substudy of the CULPRIT-SHOCK trial. *J Clin Med* 2020; **9:** 860.

143 Hongisto M, Lassus J, Tarvasmaki T, et al. Use of noninvasive and invasive mechanical ventilation in cardiogenic shock: a prospective multicenter study. *Int J Cardiol* 2017; **230:** 191–97.

144 Vallabhajosyula S, Dunlay SM, Barsness GW, et al. Temporal trends, predictors, and outcomes of acute kidney injury and hemodialysis use in acute myocardial infarction-related cardiogenic shock. *PLoS One* 2019; **14:** e0222894.

145 Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. *J Am Coll Cardiol* 2008; **52:** 1527–39.

146 Van Avondt K, Nur E, Zeerleder S. Mechanisms of haemolysis-induced kidney injury. *Nat Rev Nephrol* 2019; **15:** 671–92.

147 Jentzer JC, Bihorac A, Brusca SB, et al. Contemporary management of severe acute kidney injury and refractory cardiorenal syndrome: JACC council perspectives. *J Am Coll Cardiol* 2021; **77:** 107–09.

148 Lauridsen MD, Gammelager H, Schmidt M, et al. Acute kidney injury treated with renal replacement therapy and 5-year mortality after myocardial infarction-related cardiogenic shock: a nationwide population-based cohort study. *Crit Care* 2015; **19:** 452.

149 Bart BA, Goldsmith SR, Lee KL, et al. Ultrafiltration in decompensated heart failure with cardiorenal syndrome. *N Engl J Med* 2012; **367:** 2296–304.

150 Jung C, Fuernau G, Eitel I, et al. Incidence, laboratory detection and prognostic relevance of hypoxic hepatitis in cardiogenic shock. *Clin Res Cardiol* 2017; **106:** 341–49.

151 Perman SM, Elmer J, Maciel CB, et al. 2023 American Heart Association focused update on adult advanced cardiovascular life support: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2024; **149:** e254–73.

152 Fuernau G, Beck J, Desch S, et al. Mild hypothermia in cardiogenic shock complicating myocardial infarction. *Circulation* 2019; **139:** 448–57.

153 Levy B, Girerd N, Duarte K, et al. Hypothermia in patients with cardiac arrest prior to ECMO-VA: insight from the HYPO-ECMO trial. *Resuscitation* 2024; **200:** 110235.

154 Lüsebrink E, Scherer C, Binzenhöfer L, et al. Heparin-induced thrombocytopenia in patients undergoing venoarterial extracorporeal membrane oxygenation. *J Clin Med* 2023; **12:** 362.

155 Flierl U, Tongers J, Berliner D, et al. Acquired von Willebrand syndrome in cardiogenic shock patients on mechanical circulatory microaxial pump support. *PLoS One* 2017; **12:** e0183193.

156 Kanwar MK, Blumer V, Zhang Y, et al. Pulmonary artery catheter use and risk of in-hospital death in heart failure cardiogenic shock. *J Card Fail* 2023; **29:** 1234–44.

157 Kadosh BS, Berg DD, Bohula EA, et al. Pulmonary artery catheter use and mortality in the cardiac intensive care unit. *JACC Heart Fail* 2023; **11:** 903–14.

158 Osman M, Syed M, Patel B, et al. Invasive hemodynamic monitoring in cardiogenic shock is associated with lower in-hospital mortality. *J Am Heart Assoc* 2021; **10:** e021808.

159 Arbel Y, Mass R, Ziv-Baran T, et al. Prognostic implications of fluid balance in ST elevation myocardial infarction complicated by cardiogenic shock. *Eur Heart J Acute Cardiovasc Care* 2017; **6:** 462–67.

160 Adler C, Reuter H, Seck C, Hellmich M, Zobel C. Fluid therapy and acute kidney injury in cardiogenic shock after cardiac arrest. *Resuscitation* 2013; **84:** 194–99.

161 Jentzer JC, Lawler PR, Katz JN, et al. Red blood cell transfusion threshold and mortality in cardiac intensive care unit patients. *Am Heart J* 2021; **235:** 24–35.

162 Scherer C, Kleeberger J, Kellnar A, et al. Propofol versus midazolam sedation in patients with cardiogenic shock—an observational propensity-matched study. *J Crit Care* 2022; **71:** 154051.

163 Blumer V, Kanwar MK, Barnett CF, et al. Cardiogenic shock in older adults: a focus on age-associated risks and approach to management: a scientific statement from the American Heart Association. *Circulation* 2024; **149:** e1051–65.

164 Damluji AA, Forman DE, van Diepen S, et al. Older adults in the cardiac intensive care unit: factoring geriatric syndromes in the management, prognosis, and process of care: a scientific statement from the American Heart Association. *Circulation* 2020; **141:** e6–32.

165 Damluji AA, Forman DE, Wang TY, et al. Management of acute coronary syndrome in the older adult population: a scientific statement from the American Heart Association. *Circulation* 2023; **147:** e32–62.

166 Vallabhajosyula S, Prasad A, Dunlay SM, et al. Utilization of palliative care for cardiogenic shock complicating acute myocardial infarction: a 15-year national perspective on trends, disparities, predictors, and outcomes. *J Am Heart Assoc* 2019; **8:** e011954.

167 Fernando SM, Qureshi D, Talarico R, et al. Mental health sequelae in survivors of cardiogenic shock complicating myocardial infarction. A population-based cohort study. *Intensive Care Med* 2024; **50:** 901–12.

168 Collado E, Luiso D, Ariza-Solé A, et al. Hospitalization-related economic impact of patients with cardiogenic shock in a high-complexity reference centre. *Eur Heart J Acute Cardiovasc Care* 2021; **10:** 50–53.

169 Choi KH, Kang D, Lee J, et al. Association between intensive care unit nursing grade and mortality in patients with cardiogenic shock and its cost-effectiveness. *Crit Care* 2024; **28:** 99.

170 Schuster A, Faulkner M, Zeymer U, et al. Economic implications of intra-aortic balloon support for myocardial infarction with cardiogenic shock: an analysis from the IABP-SHOCK II-trial. *Clin Res Cardiol* 2015; **104:** 566–73.