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Review

# Current evidence in the diagnosis and management of cardiogenic shock complicating acute coronary syndrome

Rasha Kaddoura[1,*], Salah Elbdri[2]

[1] *Pharmacy Department, Heart Hospital, Hamad Medical Corporation, 3050 Doha, Qatar*

[2] *Cardiology Department, Heart Hospital, Hamad Medical Corporation, 3050 Doha, Qatar*

*Correspondence: rkaddoura@hamad.qa; Rasha.kaddoura@gmail.com (Rasha Kaddoura)

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Cardiogenic shock (CS) is a hemodynamically complex and highly morbid syndrome characterized by circulatory collapse and inadequate end-organ perfusion due to impaired cardiac output. It is usually associated with multiorgan failure and death. Mortality rate is still high despite advancement in treatment. CS has been conceptualised as a vicious cycle of injury and decompensation, both cardiac and systemic. Interrupting the vicious cycle and restoring the hemodynamic stability is a fundamental treatment of CS. Acute coronary syndrome (ACS) is the most frequent cause of CS. Early coronary revascularization is a cornerstone therapy that reduces mortality in patients with ACS complicated by CS. Early diagnosis of CS accompanied with invasive hemodynamics, helps in identification of CS phenotype, classification of CS severity, stratification of risk and prognostication. This can guide a tailored and optimized therapeutic approach. Inotropes and vasopressors are considered the first-line pharmacological option for hemodynamic instability. The current availability of the mechanical circulatory support devices has broadened the therapeutic choices for hemodynamic support. To date there is no pharmacological or nonpharmacological intervention for CS that showed a mortality benefit. The clinical practices in CS management remain inconsistent. Herein, this review discusses the current evidence in the diagnosis and management of CS complicating ACS, and features the changes in CS definition and classification.

*Keywords*

Acute myocardial infarction; Cardiogenic shock; Inotrope; Mechanical circulatory support; Pulmonary artery catheter; Vasopressor

## 1. Introduction

Shock in the general term is a circulatory failure due to impaired oxygen utilization by the body cells, which affects approximately one third of critically ill patients. The most common mechanisms of shock are hypovolemia, cardiac factors, obstruction, and distributive factors. The distributive shock is usually characterized by high cardiac output (CO), reduced systemic vascular resistance (SVR), and altered oxygen extraction. Whereas the three other mechanisms lead to low CO and insufficient oxygen transport (Table 1) [1]. Cardiogenic shock (CS) is a clinical condition that results from ventricular failure due to acute coronary ischemia [1, 2], which eventually leads to inadequate peripheral tissue perfusion, tissue and cellular ischemia, end-organ damage and multiorgan system failure [3, 4]. Up to 40,000 and 80,000 CS patients are annually admitted to hospitals in the United States and Europe, respectively [2].

Acute coronary syndrome (ACS) is the most common cause of CS, accounting for up to 80% of the cases [5]. CS complicates 4–12% of ST-segment elevation myocardial infarction (STEMI) [2, 3, 6–8] and 2–4% of non-STEMI patients [2, 7–10]. Most of acute myocardial infarction (MI) cases develop CS after hospital admission [6, 7, 9, 11, 12] (e.g., 62–89%) [5, 6, 11], and usually within 24 hours of the event [12]. CS may also occur after coronary reperfusion [13]. Non-ACS etiology accounts for one-fifth of the cases [5]. Illnesses or conditions that may cause CS include but not limited to, cardiac tamponade, primary idiopathic pericarditis, myocarditis, acute heart failure, end-stage severe congestive heart failure, severe infections with and without septicaemia, or cor pulmonale due to pulmonary emboli [14]. Figs. 1,2 present the historical perspective of shock, acute MI and their basic aspects of management [14–18].

Mortality rates had varied widely overtime (i.e., from 50% to 90%), probably due to the non-unified definition of CS between studies [15]. However, early mortality due to CS complicating acute MI remains high, in up to 50% of patients [5, 6, 13, 19, 20], even after more than 20 years of the SHOCK trial publication [21]. With recent advancement in STEMI management, the reported rates of early mortality in the recent studies are in the range of 40% [22, 23]. Whereas, the in-hospital mortality is lower (24%) in CS that is not secondary to ACS [23]. Fig. 3A projects the mortality rates over years and Fig. 3B projects rates over short (i.e., 1–4 years) and long (i.e., 10–30 years) periods of time [6, 8, 11, 21, 22, 24–39]. CS and its consequences have a considerable economic impact as well [4]. The objective of this review is to discuss the current evidence in the diagnosis and management of CS complicating ACS, and feature the changes in CS definition and classification.

**Table 1. Types of circulatory shock.**

| Type examples | Percentage | CO or $SvO_2$ | CVP | ECHO |
|---|---|---|---|---|
| Distributive<br>(Vasodilation)<br>Severe sepsis, anaphylaxis | 62%<br>4%[a] | Normal or high | - | - Normal cardiac chambers<br>- Preserved contractility in most of the cases |
| Hypovolemic<br>Internal or external loss of volume (plasma or blood) | 16% | Low | Low | - Small cardiac chambers<br>- Normal or high contractility |
| Cardiogenic<br>(Ventricular failure)<br>Acute MI, end-stage CM, myocarditis | 16% | Low | High | - Large ventricles<br>- Poor contractility |
| Obstructive<br>(Obstruction) Pericardial tamponade, PE, pneumothorax | 2% | Low | High | - Tamponade: pericardial effusion, small ventricles, dilated inferior vena cava |
| All | - Arterial hypotension<br>- Signs of tissue hypoperfusion (altered mental status, mottled and clammy skin, oliguria)<br>- Tachycardia, elevated blood lactate, circulatory shock | | | |

[a]Distributive (non-specific) shock accounts for additional 4%.

Abbreviations: MI, myocardial infarction; CM, cardiomyopathy; CO, cardiac output; CVP, central venous pressure; ECHO, echocardiography; LV, left ventricle; PE, pulmonary embolism; RV, right ventricle; $SvO_2$, mixed venous oxygen saturation.

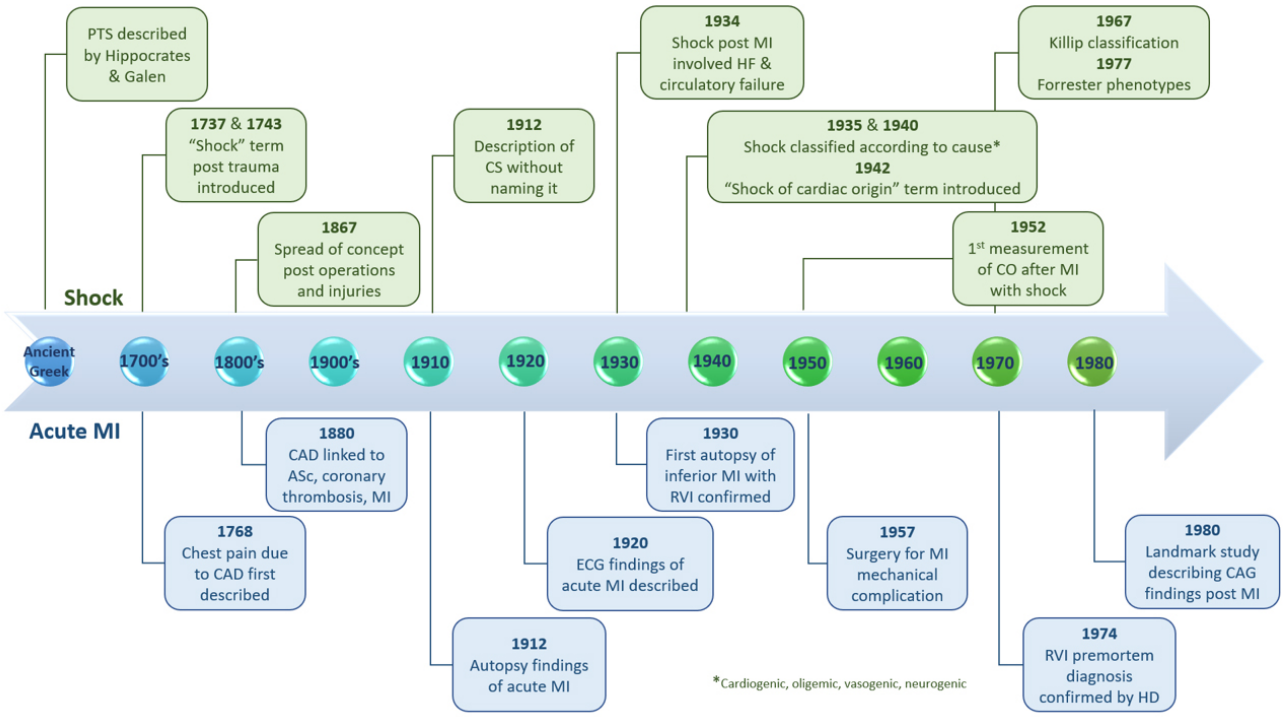


**Fig. 1. Historical perspective of shock and myocardial infarction.** ASc, atherosclerosis; CAD, coronary artery disease; CO, cardiac output; CS, cardiogenic shock; ECG, electrocardiogram; HD, hemodynamics; MI, myocardial infarction; PTS, posttraumatic syndrome; RVI, right ventricular infarction.

## 2. Pathophysiology

The main mechanism of CS is acute MI [1, 2, 5, 40], including its mechanical complications [5, 33, 41, 42], that causes left ventricular (LV) pumping failure [1, 2, 40]. Mechanical complications of an ACS event (e.g., ventricular septal rupture (VSR), free-wall or papillary muscle rupture) account for 12% of CS cases [40] and frequently occur within 24 hours of hospital admission [3]. As an example, VSR has the highest risk of mortality (87%) [40, 42] with a median of 16 hours to occurrence from MI onset. However, other timing data reported in literature varied from three to eight days [42]. The underlying pathology of MI in CS has been studied. Stepwise or progressive myocardial damage and injury may occur. In patients who die due to CS, the extent of damage is greater than in those who die from acute infarction. LV infarction mass was 51% (range 35–68%) in CS non-survivors. Losing half of LV myocardium may explain the clinical and hemodynamic consequences of CS [43]. More-

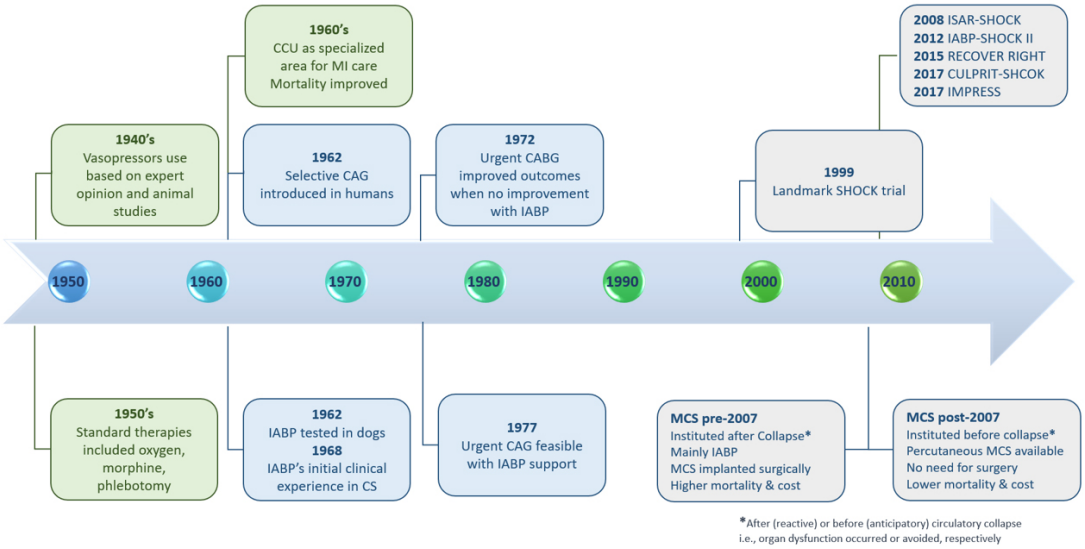


**Fig. 2. Historical perspective of cardiogenic shock management.** CAGB, coronary artery bypass surgery; CAG, coronary angiography; CCU, Coronary Care Unit; CS, cardiogenic shock; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support.

over, the LV infarct size exceeded 40% even after coronary reperfusion [44]. Severe ischemia leads to elevated ventricular filling pressures, reduced CO, hypotension, and systemic tissue hypoperfusion, that eventually affect all body organs [2, 3]. With persistent CS, there are further exacerbation of ischemia, coronary perfusion defect, ongoing cell death, and deterioration of systolic and diastolic functions, resulting in further increments in ventricular filling pressures and worsening of CO [2]. This uninterrupted maladaptive vicious cycle is eventually deadly [2, 4]. Although peripheral vasoconstriction (i.e., early compensatory mechanism) can ameliorate the perfusion, both coronary and peripheral, this is achieved at the expense of an elevated afterload [3]. Circulatory compensatory mechanisms are usually insufficient and may worsen the situation [3, 40]. The acute cardiac event can also provoke a systemic inflammation that leads to pathological vasodilation [2–4], due to the release of inflammatory mediators and nitric oxide (NO) [4, 45]. Inflammatory mediators include tumor necrosis factor and interleukins [46]. High levels of NO produced by NO synthases and the cytotoxic NO-derived species (i.e., peroxynitrite) have many deleterious effects such as inappropriate vasodilation with reduced systemic and coronary perfusion pressures [47]. Fig. 4 summarizes the pathophysiology of infarct-related CS and treatment targets [2, 3, 40, 47].

With regards the consequences of CS on body organs, elevation in the LV filling pressure causes pulmonary edema and congestion, due to rise in pulmonary capillary hydrostatic pressure [2]. Pulmonary vasoconstriction, as a result of hypoxia and inflammation, increases myocardial oxygen consumption and afterload of both ventricles. Renal glomerular filtration rate is reduced, and renin-angiotensin-aldosterone system is activated secondary to renal hypoperfusion. Consequently, tubular sodium reabsorption and fluid overload increase, thus attenuating the response to diuretics. Splanchnic vasoconstriction induced by sympathetic nervous system causes further deterioration of fluid overload, through blood redistribution to the central circulation [2, 4], and precipitation of septic reaction by translocating bacteria or their toxins. Cerebral hypoperfusion is the reason for the altered mental status in CS [2].

## 3. Definitions and classifications

CS is a clinical condition of impaired primary cardiac function with ineffective CO that hinders sufficient blood perfusion to the end-organs (i.e., tissues hypoxia) to meet their metabolic demands [2, 3, 23, 40, 48, 49]. In many cases, the patients are not hypovolemic (i.e., have adequate intravascular volume) [2]. The definition of CS has evolved over years [23] and CS-defining criteria have varied among clinical trials and societal guidelines [4, 49] as summarized in Table 2 (Ref. [2, 3, 6, 7, 16, 21, 24, 26, 27, 32, 35, 36, 38, 39, 48, 50–56]). The widely accepted definition of CS includes clinical signs and symptoms of tissue hypoperfusion (e.g., altered mental status, oliguria, high lactate level) and elevated LV filling pressures (e.g., pulmonary congestion). In addition to hemodynamic parameters (e.g., persistent hypotension with severely reduced cardiac index (CI)) [2, 23, 40].

In 1967, Killip *et al.* [26] proposed a clinical classification of severity for patients presenting with acute MI based on their hemodynamic status. Patients were classified in one of four classes: (I) no clinical signs of cardiac decompensation; (II) heart failure diagnosed by rales, venous hypertension, and S3 gallop; (III) severe heart failure, characterized by

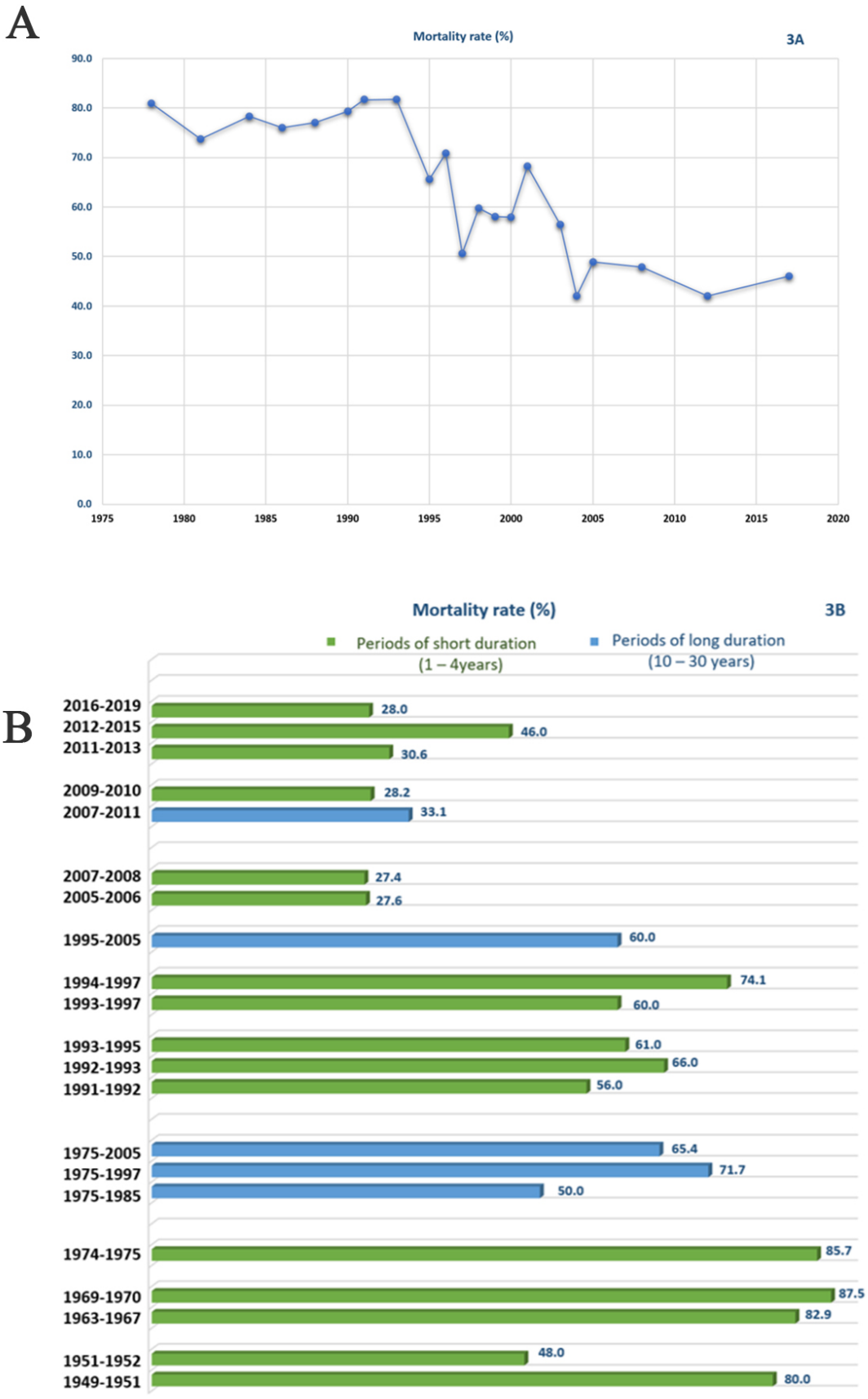


**Fig. 3. (A) Mortality rate over years. (B) Mortality rate over periods of year.** Short period is defined as 1–4 years and long period as 10–30 years.

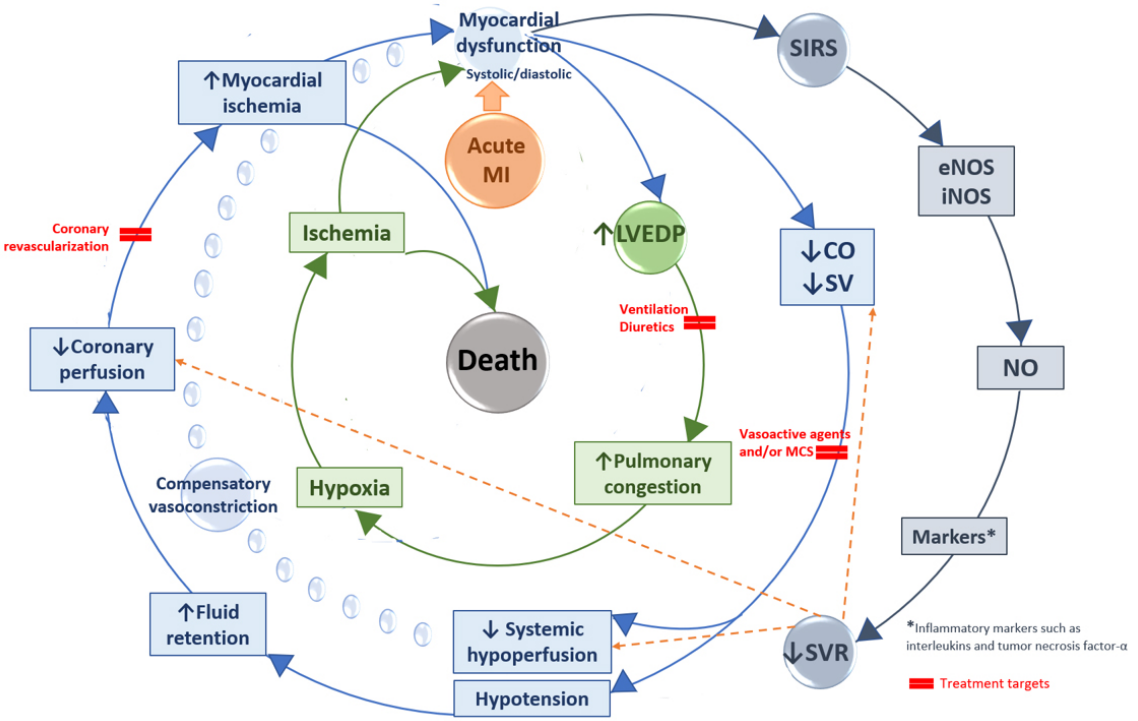


**Fig. 4. Pathophysiology of cardiogenic shock and treatment targets.** CO, cardiac output; eNOS, endothelial NO synthase; iNOS, inducible NO synthase; LVEDP, left ventricular end-diastolic pressure; MCS, mechanical circulatory support; MI, myocardial infarction; NO, nitric oxide; SIRS, systemic inflammatory response syndrome; SV, stroke volume; SVR, systemic vascular resistance.

frank pulmonary edema; and (IV) CS, characterized by hypotension (i.e., systolic blood pressure (BP) $\leq$90 mmHg), peripheral vasoconstriction evident by oliguria, cyanosis, and diaphoresis. Heart failure with pulmonary edema is usually present [26]. Forrester *et al.* [57], in 1977, classified patients with acute MI into four clinical subsets which were correlated with hemodynamic parameters (i.e., CI (cut-off of 2.2 L/min/m$^2$) and pulmonary capillary pressure (PCP) (cut-off of 18 mmHg)). The subsets of Diamond-Forrester classification are: (I) no pulmonary congestion or peripheral hypoperfusion (CI 2.7 $\pm$ 0.5 L/min/m$^2$; PCP 12 $\pm$ 7 mmHg); (II) isolated pulmonary congestion (CI 2.3 $\pm$ 0.4 L/min/m$^2$; PCP 23 $\pm$ 5 mmHg); (III) isolated peripheral hypoperfusion (CI 1.9 $\pm$ 0.4 L/min/m$^2$; PCP 12 $\pm$ 5 mmHg); and (IV) both pulmonary congestion and hypoperfusion (CI 1.6 $\pm$ 0.6 L/min/m$^2$; PCP 27 $\pm$ 8 mmHg) [57]. Acute MI event complicated by CS is commonly presented with severe LV function impairment [7, 40], which is usually associated with anterior wall MI [58]. CS due to severe right ventricular (RV) dysfunction, occurs in 5% of patients [3, 40] especially those presenting with inferior wall MI [40]. The severity of shock due to RV impairment is dependent on the degree of ischemia in both ventricles [3]. Those patients do not usually develop pulmonary congestion unless there is concurrent involvement of the LV [55]. In MI complicated with CS, especially in the first event, mechanical complications should be highly suspected [40]. With regard other hemodynamic phenotypes of CS, patients with decompensated heart failure, are generally classified into four phenotypes based on cardiac output (i.e., insufficient [cold] versus sufficient [warm]) and volume status (i.e., overloaded [wet] versus euvolemic [dry]) which reflect tissue perfusion and congestion, respectively [48, 59–61].

Given that CS presentation encompasses a wide range of clinical and hemodynamic parameters, the definition of CS should consider a continuum of stages rather than a binary diagnosis such as the classic construct of "cold and wet" phenotype [23]. The classification systems by Killip and Forrester also assess congestion and perfusion through physical exam findings and hemodynamic parameters. However, such classifications do not gauge CS severity, allow better hemodynamic-guided management of CS, or address the timely use of mechanical circulatory support (MCS) devices [62]. Thus, other terminologies have been proposed to address the broad range of CS presentation and describe progression that can assist in escalating management from the use of vasoactive agents to MCS devices. One proposal suggested that stages such as pre-, mild, profound, and refractory shock can be more appropriate [23]. In response to such unfulfilled demands and in search of a new lexicon and uniform system to define CS severity, the Society for Cardiovascular Angiography and Interventions (SCAI) has published a five-stage classification system based on expert opinion. This consensus document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS). The purpose of the SCAI

**Table 2. Definitions of cardiogenic shock.**

| **Prior to SHOCK trial** | | | | |
|---|---|---|---|---|
| Griffith 1954 [24] | Binder 1955 [50] | Malach 1960 [16]<br>Killip 1967 [26] | Goldberg 1991 [27]<br>(1975 to 1988) | Hochman 1995 [32]<br>Holmes 1995 [6]<br>Holmes 1999 [7] |
| - Marked hypotension for $\geq$1 hr with signs of peripheral circulatory collapse | - SBP ≤80 mmHg | - SBP <70 mmHg or total decline of SBP of $\geq$70 mmHg in presence of circulatory collapse signs [16] | - SBP <80 mmHg in absence of hypovolemia; associated with cold extremities, cyanosis, changes in mental status, persistent oliguria, or congestive HF | - SBP <90 mmHg for >1 hr despite fluid challenge and signs of hypoperfusion or a CI of <2.2 L/min/m$^2$, [6, 7, 32] and evidence of elevated filling pressures [32] |
| - In normotensive patients: SBP $\leq$80 mmHg | - Pulse rate $\geq$110 (unless AV block present) | - Hypotension (SBP $\leq$90 mmHg) and evidence of peripheral vasoconstriction such as oliguria, cyanosis and diaphoresis [26] | | - SBP increased to >90 mmHg within 1 hr after inotrope administration [6, 32] |
| - In hypertensive patients: SBP $\leq$100 mmHg | - Clinical signs of peripheral circulatory collapse | | | |
| | - No improvement for 30 min after pain relief and $O_2$ administration | | | |
| **SHOCK trial and beyond** | | | | |
| Hochman 1999 [21, 51] (SHOCK) | Burkhoff 2006 [52] | Thiele 2012 [38, 53] (IABP-SHOCK II) | Thiele 2017 [39, 54] (CULPRIT-SHOCK) | Ouweneel 2017 [36] (IMPRESS) |
| - SBP <90 mmHg for $\geq$30 min or need for supportive measures to maintain SBP $\geq$90 mmHg, and end-organ hypoperfusion | - CI $\leq$2.2 L/min/m$^2$, MAP $\leq$70 mmHg, PCWP $\geq$15 mmHg | - SBP <90 mmHg for >30 min or need for catecholamines to maintain SBP >90 mmHg | - SBP <90 mmHg for >30 min or catecholamine use to maintain SBP >90 mmHg | - SBP <90 mmHg for >30 min or the need for inotropes or vasopressors to maintain SBP >90 mmHg |
| - CI $\leq$2.2 L/min/m$^2$ and a PCWP $\geq$15 mmHg | - End-organ hypoperfusion or need for high-dose pressor and/or inotropic support | - Clinical signs of pulmonary congestion, and impaired end-organ perfusion | - Clinical signs of pulmonary congestion, and signs of impaired organ perfusion | |
| **Registries and guidelines** | | | | |
| Menon 2000 [55]<br>(SHOCK trial registry) | Wayangankar 2016 [35] (CathPCI Registry) | 2016 ESC HF [48]<br>2017 ESC STEMI [56] | 2017 AHA [3]<br>Scientific Statement | 2020 ACCA Position [2]<br>Statement |
| - SBP <90 mmHg for >30 min | - SBP <90 mmHg for > 30 min and/or CI <2.2 L/min/m$^2$, and/or need for inotropic or vasopressor agents or mechanical support to maintain SBP and CI above those specified levels | - SBP <90 mmHg despite adequate filling with signs of hypoperfusion, [48, 56] or if inotropes and/or mechanical support to maintain SBP >90mmHg [56] | - Persistent hypotension unresponsive to volume replacement with clinical features of end-organ hypoperfusion requiring pharmacological or mechanical support | - SBP <90 mmHg for >30 min, or need for catecholamines to maintain BP |
| - Evidence of tissue hypoperfusion with adequate or elevated LV filling pressures | | | - Hemodynamic parameters are not mandatory but help confirm diagnosis | - Pulmonary congestion and signs of end organ failure |

Abbreviations: ACCA, Acute Cardiovascular Care Association; AHA, American Heart Association; AV, atrioventricular; CI, cardiac index; CS, cardiogenic shock; ESC, European Society of Cardiology; HF, heart failure; hr, hour; IMPRESS, IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; LV, left ventricle or ventricular; MAP, mean arterial pressure; min, minute(s); $O_2$, oxygen; PCWP, Pulmonary capillary wedge pressure; SBP, systolic blood pressure; SHOCK-IABP II, Intraaortic Balloon Pump in Cardiogenic Shock II.

classification was to offer a simplified scheme in order to facilitate a clear and easy communication about patients' status and a better differentiation between patients' subsets in clinical trials. Other aims were, to assist in rapid patient assessment, reassessment and re-classification, to be applicable to multiple clinical settings and retrospectively to prior clinical trials, and to have a prognostication potential of different CS subsets [13].

The SCAI classification, inspired by the ACC/AHA classification of heart failure [63] and the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) classification [64], is the first standardized set of definitions for CS. The SCAI scheme stratifies CS into five stages: at-risk (stage A), beginning (stage B), classic (stage C), deteriorating (stage D), and extremis (stage E). Each stage has been described in three domains: physical exam or bedside finings, biochemical markers, and hemodynamic parameters (Fig. 5). Furthermore, the cardiac arrest as an important prognosis modifier (i.e., the ($_A$) modifier), can be applied to any CS stage to describe patients who suffer a cardiac arrest [13]. Subsequently, the prognostic ability of the scheme has been retrospectively validated in unselected cardiac intensive care unit patients (n = 10,004) at Mayo Clinic. Stages from "A" to "E" accounted for 46.0%, 30.0%, 15.7%, 7.3%, and 1.0% of patients, respectively. With each higher stage at admission, there was a robust association with increased hospital mortality [65]. The SCAI classification has predicted the post-discharge mortality as well by analyzing the hospital survivors (n = 9096) from the aforementioned study [66]. When the SCAI classification was retrospectively applied to patients presenting with acute MI and CS (n = 300) in the National Cardiogenic Shock Initiative, the analysis demonstrated that such classification was reproducible and provided prognostic guidance among this subset of patients when applied on admission and at 24 hours after admission. The proportions of patients presented in stages "C" through "E" were 61.0%, 8.0%, and 31.0%, respectively [67]. The first prospective study (n = 166) to validate the SCAI classification showed that initial SCAI stage was a robust predictor of survival in critically ill patients. Age and initial stage, but not the mode of MCS, were the strongest predictors. When reassessing SCAI stage at 24 hours, improved stage was associated with better survival unlike the deteriorating or unchanged stage. This finding highlighted the importance of reassessment of the shock stage [68]. Several other studies have retrospectively validated the SCAI scheme. Analysis of a registry data (n = 1414) found that SCAI stages predicted in-hospital mortality [69]. In a large study of unselected CS patients (n = 1004), SCAI classification system was independently associated with the 30-day survival as well [70]. The classification was also validated in the setting of out-of-hospital cardiac arrest [71].

## 4. Clinical presentation and diagnosis

The diagnosis of CS is usually differentiated from other types of shock (i.e., distributive, hypovolemic, non-obstructive) based on history, physical examination, laboratory data, and electrocardiogram characteristics. As any condition leading to profound LV or RV impairment can result in CS [40], various causes should be identified such as acute MI, acute decompensated heart failure, post-cardiotomy shock, atrial or ventricular arrhythmias, or valvular diseases [2, 59]. CS diagnosis should also distinguish between CS and mixed shock type due to other contributing factors [2], such as infection, bowel ischemia, or hemorrhage in the setting of MI. Interestingly, CS may develop as an iatrogenic illness. Medication classes that are used to treat acute MI can be associated with the development of shock such as beta-blockers and angiotensin-converting enzymes inhibitors [40]. Regardless of its type, shock is diagnosed based on clinical, hemodynamic, and biochemical components [1]. The clinical signs of cutaneous, renal and brain tissue hypoperfusion are featured as cold and clammy skin, cyanosis due to vasoconstriction, oliguria (i.e., urine output $<$0.5 mL/kg/hour), and altered mental status (e.g., confusion, disorientation) [1, 40]. Hemodynamically, and associated with tachycardia, hypotension (i.e., systolic BP $<$90 mmHg or mean arterial pressure (MAP) $<$70 mmHg) is generally present. However, patients with history of chronic hypertension may experience a milder degree of hypotension. Elevated lactate level in blood ($>$1.5 mmol/L) is considered a biochemical marker for a distorted oxygen metabolism in the body cells [1]. Hemodynamic derangement can range from unremarkable tissue hypoperfusion to severe shock state. The severity of shock can directly correlate with short-term outcomes [40].

The differentiation between the hemodynamic phenotypes of CS needs invasive hemodynamic monitoring using pulmonary artery (i.e., Swan-Ganz) catheter (PAC) [3, 13, 40]. Hemodynamic monitoring can confirm CS diagnosis when uncertain or when there is no response to therapy. In addition, it can direct therapy and evaluate the need for MCS [2, 40, 72–75]. Among all CS phenotypes, the common hemodynamic characteristic is low CI, while other parameters (e.g., volume, SVR, pulmonary capillary wedge pressure (PCWP)) may vary. Although the widely accepted CI cut-off in CS is $<$1.8 to 2.2 L/min/m$^2$, proposing absolute CI values may not be broadly applicable given that higher CI values have been reported with end-organ tissue hypoperfusion. The classic CS phenotype (i.e., cold and wet) accounts for almost two third of MI cases complicated with CS [3], and is characterized by low CI with elevated PCWP and SVR [3, 13]. Fig. 6 presents the characteristics of CS phenotypes [13, 48, 59].

Historically since 1970, PAC was the first device used in critically ill patients to classify the hemodynamic parameters. In patients presented with acute MI, the use of PAC consistently and significantly increased from 7.2% to 19.9% in 1975 throughout 1984, respectively [76]. Despite its widespread use for diagnosis and decision-making in management, PAC use has progressively decreased thereafter [74]. A multicentre longitudinal study (n = 15,006) found a decrease in PAC

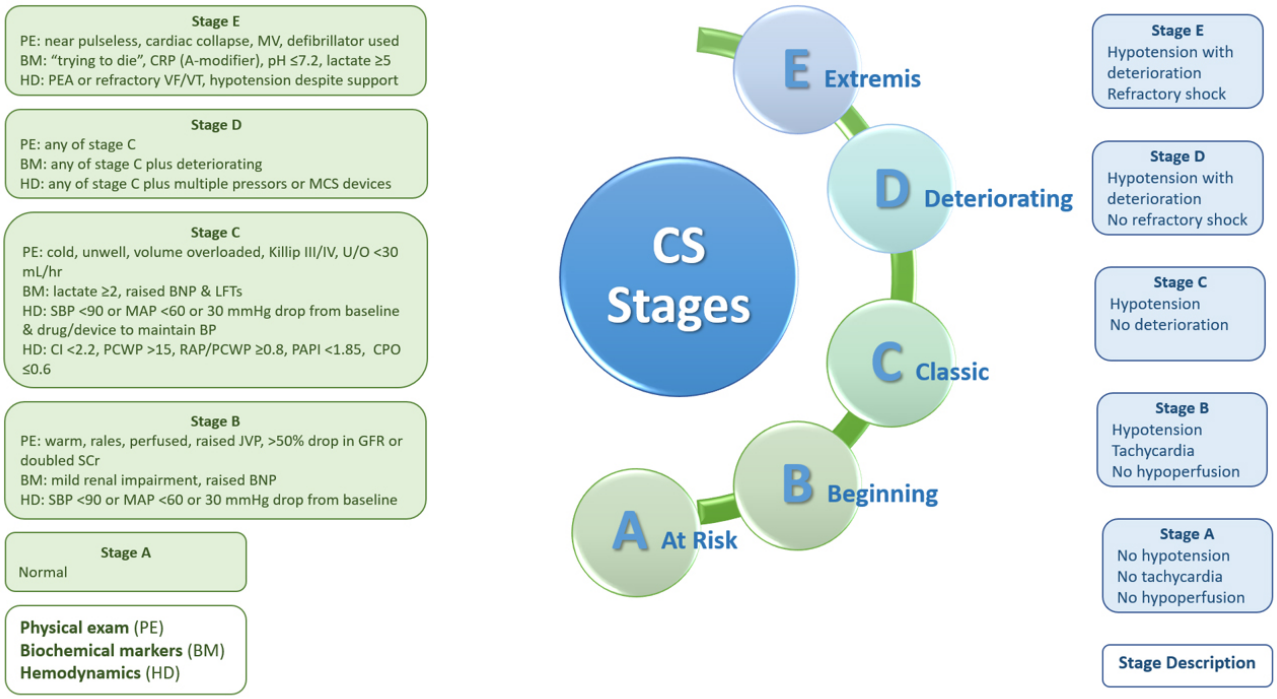


**Fig. 5. SCAI classification of cardiogenic shock.** BNP, brain natriuretic peptide; BP, blood pressure; CI, cardiac index; CPO, cardiac power output; CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; GFR, glomerular filtration rate; JVP, jugular venous pressure; LFTs, liver function tests; MAP, mean arterial BP; MCS, mechanical circulatory support; MV, mechanical ventilation; PAPI, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; PEA, pulseless electrical activity; RAP, right atrial pressure; SBP, systolic BP; SCr, serum creatinine; U/O, urine output; VF/VT, ventricular fibrillation/tachycardia.

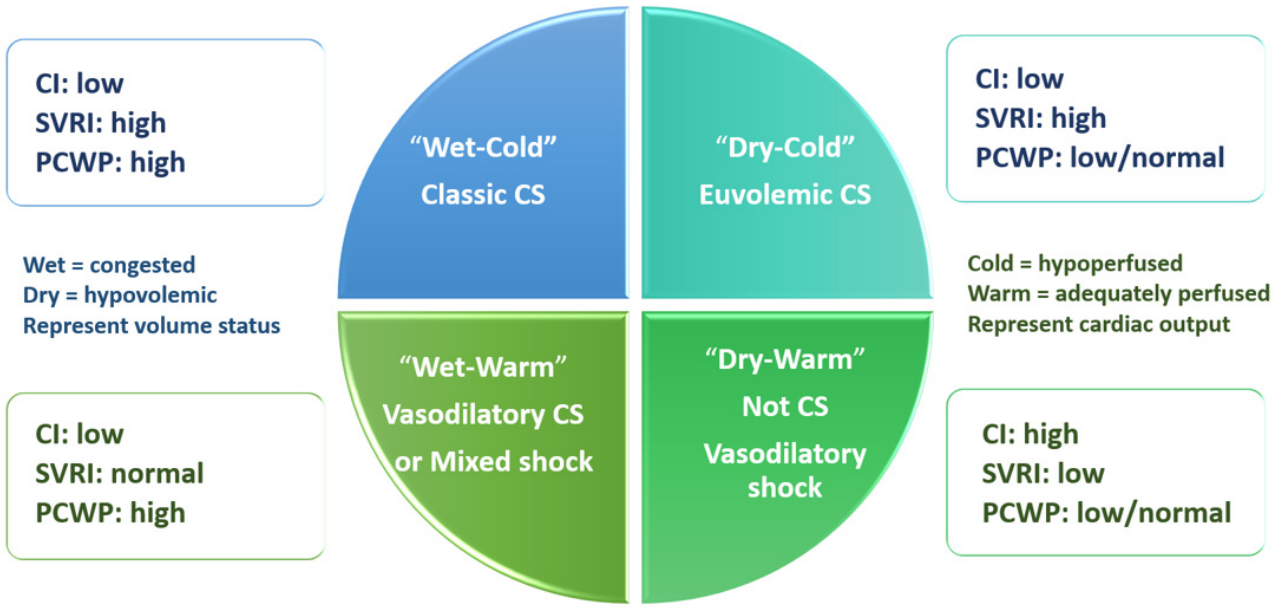


**Fig. 6. Phenotypes of cardiogenic shock.** CI, cardiac index; CS, cardiogenic shock; ECG, electrocardiogram; PCWP, pulmonary capillary wedge pressure; SVRI, systemic vascular resistance index.

use from 16.4% in 2002 to 6.5% in 2006 (i.e., decrease by >50%). CS was among the determinants of PAC use without any change over time [77]. Another recent retrospective study (n = 364,001) from the United States reported a PAC use in 8.1% of patients with a 75% decrease in use between 2000 and 2014 [78]. The decline in PAC use was related to

its association with poor clinical outcomes as suggested by observational studies [40, 74]. Subsequently, evidence from randomized control trials (RCTs) did not show any benefit [74, 79]. However, previous studies did not specifically investigate CS patients [74]. Studies in general included small number of patients with CS, for example, 1.8% [80], 4.7% [81] and 20.8% [82] of cases. Evidence on PAC use in CS complicating acute MI is limited [78] and inconclusive. The reported rate of PAC use in CS patients from the CardShock study (n = 219) was 37.4%. The analysis showed that PAC use was associated with increased use of mechanical ventilation, vasoactive agents, MCS devices, and renal replacement therapy, but not with 30-day mortality [83]. In a recent retrospective study, PAC use was associated with increased in-hospital mortality rates, longer hospital-stay, and higher hospitalization cost [78]. In the first prospective study (n = 129) that enrolled patients presenting with CS of any cause, PAC was used in 64% of patients and was associated with lower adjusted mortality rates, both short- and long-term. Nevertheless, a subgroup analysis found that the significant association was in the patients without ACS (e.g., cardiomyopathy, valvular abnormalities, pericardial diseases) [74]. ACS Patients enrolled in the GUSTO IIb [84] and GUSTO III [85] trials (n = 26,437) who presented with Killip class III/IV accounted for 1.7% of cases. The rate of PAC use was 2.8%. A retrospective analysis of the two GUSTO studies correlated PAC use with higher mortality risk but not in those with CS [86], a result that was consistent with other studies [76, 87]. Mortality was attributed to inconsistent interpretation of PAC profile, PAC procedure complications, and aggressive management in response to hemodynamic measurements [86]. In the contemporary MCS era, a recent analysis from a large registry (n = 1414) examined the association of early PAC placement prior to MCS initiation with mortality in CS patients who were categorized according to SCAI stages. In-hospital mortality was significantly lower in the PAC-use groups and across all SCAI stages [75]. The current advances in and the availability of the non-invasive technologies used in the intensive care units and for the diagnosis and monitoring of cardiovascular diseases, have contributed to the decline in PAC use. Echocardiography, for example, is a practical alternative [40] for the diagnosis and monitoring of CS. Moreover, it provides a fast differential diagnosis and excludes mechanical complications [2]. However, evidence that correlates non-invasive monitoring with improved clinical outcomes is scarce [74].

## 5. Management

Early hemodynamic support is essential for patients in shock regardless of the cause. Priorities and goals of therapy usually target four phases. The salvage phase, to obtain acceptable BP through life-saving measures (e.g., coronary revascularization; discussed below); the optimization phase, to ensure adequate cellular oxygenation through hemodynamic resuscitation (e.g., optimizing cardiac output); the stabilization phase, to minimize complications through organ support; and the de-escalation phase, to achieve negative fluid balance [1]. The "VIP" approach succinctly describes the initial resuscitation steps; "ventilate" by administering oxygen, "infuse" by fluid resuscitation, and "pump" to restore cardiac competence. The postscript (i.e., "PS"), follows with "pharmacologic treatment" such as vasoactive agents to improve perfusion and "specific or surgical management" of the primary causes [88].

### *5.1 Hemodynamic support in CS*

Circulatory support, either pharmacologic or nonpharmacologic, should be promptly employed to manage hypotension and maintain tissue perfusion [89]. Fig. 7 summarizes the overall management approach to CS [48, 90, 91].

#### *5.1.1 Pharmacologic circulatory support*

Vasoactive agents (i.e., intravenous inotropes and vasopressors) remain the initial hemodynamic support in CS unresponsive to fluid resuscitation [4, 23], with an administration rate in almost 90% of patients [5, 92]. They preserve end-organ tissue perfusion through increasing myocardial contractility and CO, and decreasing filling pressures [4]. Vasopressors or inoconstrictors, via $\alpha$- and $\beta$-adrenergic receptors, increase SVR and cardiac contractility, respectively [23, 93]. Inotropes and inodilators lead to LV unloading by increasing contractility and reducing SVR [94]. Table 3 describes the hemodynamic effects of the commonly used vasoactive agents [2, 3, 48, 56, 95, 96]. With the exception of levosimendan, inotropic agents increase intracellular calcium, thus increasing myocardial oxygen consumption and the risk of malignant arrhythmias [4, 23]. There is limited evidence available to support the superiority of one agent over another or to guide agent selection [4, 23, 96]. Data from RCTs have shown improved hemodynamic effects with the use of vasoactive agents. Add-on levosimendan improved short-term survival, while dopamine increased mortality. As a result, dopamine is no longer recommended as an initial agent. A new study (DOREMI) that compared milrinone with dobutamine did not find a statistically significant difference with respect to primary or secondary outcomes. Currently, there is no role for NO synthase inhibitors in managing CS complicating acute MI. Table 4 (Ref. [97–111]) presents a summary of the relevant RCTs of the vasoactive agents [96–111]. A recent meta-analysis did not find a mortality benefit with the use of vasopressors and inotropes in CS complicating acute MI [112]. An emerging evidence highlighted the potential role of levosimendan in CS patients requiring venoarterial extracorporeal membrane oxygenation (VA-ECMO), in facilitating VA-ECMO weaning and reducing all-cause mortality [113–115]. Unsurprisingly, the cardiology societal guidelines do not share a universal recommendation for the first-line agent in CS [96]. Two of them recommended norepinephrine as a first-line vasopressor (Class IIb, Level B) [2, 48], another two individualized the approach based on CS phenotype and/or etiology [3, 116], while oth-

**Table 3. Hemodynamic effects of commonly used vasoactive agents.**

| Agent | Target | Effect |
|---|---|---|
| **Vasopressor/inotropes** | | |
| Dopamine | D > $\alpha_1$, $\beta_1$, $\beta_2$<br>Dose-dependent agonism | - Inotropy, dromotropy, chronotropy, and vasoconstriction<br>- ↑ to ↑↑ CO, ↑ to ↑↑ SVR |
| Epinephrine | $\alpha_1 = \beta_1 > \beta_2$ | - Inotropy, chronotropy, dromotropy, and vasoconstriction<br>- ↑↑ CO, ↑↑ SVR |
| Norepinephrine | $\alpha_1 > \beta_1 > \beta_2$ | - Inotropy, chronotropy, dromotropy, and vasoconstriction<br>- ↑ CO, ↑↑SVR |
| **Inodilators** | | |
| Dobutamine | $\beta_1 > \beta_2 > \alpha_1$ | - Inotropy and mild vasodilation<br>- ↑↑ CO, ↓ SVR, ↓ PVR, ↓ MAP |
| Enoximone<br>Milrinone | PDEi | Inotropy and inodilator<br>- ↑ CO, ↓ SVR, ↓ PVR, ↓ MAP |
| Levosimendan | Myofilament $Ca^{2+}$ sensitizer and $K^+$ channel modifier | - Inotropy and inodilator<br>- ↑ CO, ↓ SVR, ↓ PVR, ↓ MAP |

$\alpha$, alpha-adrenergic receptors; $\beta$, beta-adrenergic receptors; $Ca^{2+}$, calcium; CO, cardiac output; D, dopamine receptor; $K^+$, potassium; $Ca^{2+}$, calcium; MAP, mean arterial pressure; PDEi, phosphodiesterase inhibitor; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

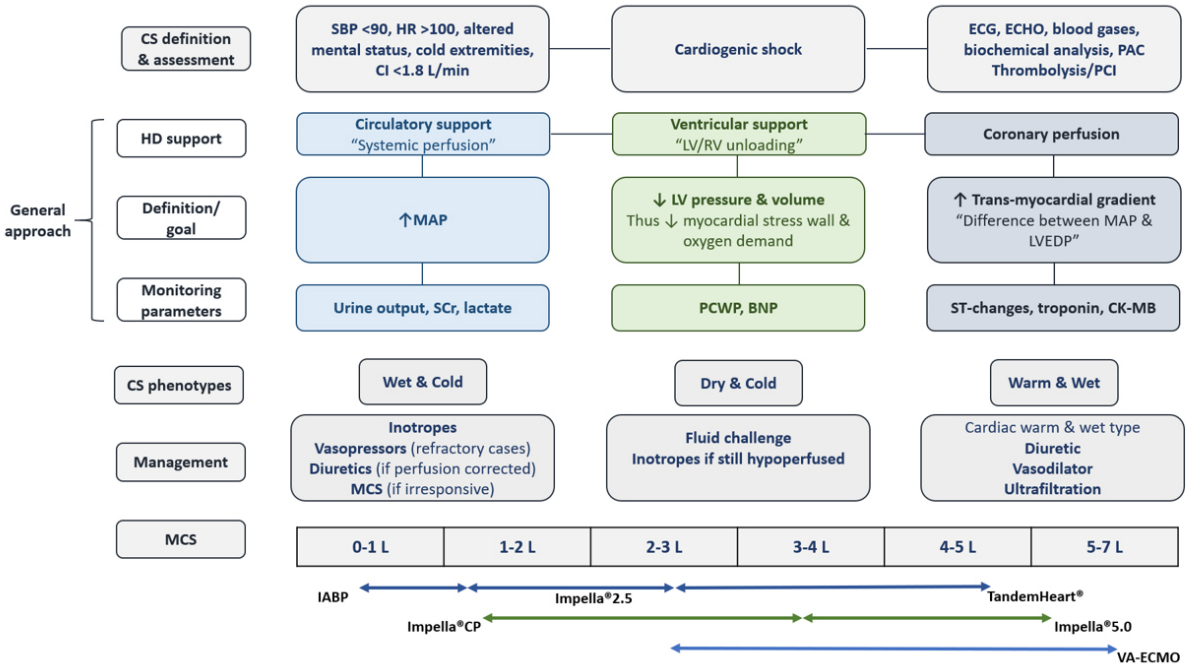


**Fig. 7. Management approach to cardiogenic shock.** BNP, brain natriuretic peptide; CI, cardiac index; CK-MB, creatine kinase-MB; CS, cardiogenic shock; HR, heart rate; ECG, electrocardiogram; ECHO, echocardiogram; HD, hemodynamics; HR, heart rate; IABP, intra-aortic balloon pump; LVEDP, left ventricular end-diastolic pressure; MAP, mean arterial blood pressure; MCS, mechanical circulatory support; PAC, pulmonary artery catheter; PCI, percutaneous coronary intervention; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; SCr, serum creatinine; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

ers did not specify any agent [56, 117, 118]. Given their safety concern, vasoactive agents should not be used for a prolonged duration [4, 92], and the need to escalating their doses should warrant considering temporary MCS [23]. Escalation of vasoactive agents doses [90, 119] and delay in MCS implantation [119] is associated with an increase in mortality [90, 119].

*5.1.2 Nonpharmacologic circulatory support*

The use of temporary MCS devices is in the rise for the purpose of maintaining hemodynamics in CS [4, 119]. They are usually used as a bridge-to-decision for myocardial recovery, heart transplantation, palliation, or a durable ventricular assist device (VAD) [4, 23, 90]. Various devices have been developed and studied after the SHOCK trial which was

**Table 4. Summary of randomized controlled trials of vasoactive agents.**

| Study<br>Sites number (S) | Sample size (N)<br>Follow-up (F/U) | Interventions<br>Population | Conclusion | Jadad scale[a] (0–5) |
|---|---|---|---|---|
| **Vasopressors and inotropes** | | | | |
| De Backer 2010 [97]<br>SOAP II<br>S = 8 | N = 1679<br>CS subgroup (17%)<br>F/U: 28 days | - Dopamine versus norepinephrine<br>- Shock in general | - No difference in death<br>- More adverse events with dopamine use<br>- CS subgroup: higher mortality rate with dopamine use | 5 |
| Levy 2011 [98]<br>S = 1 | N = 30<br>F/U: 26 months | - Epinephrine versus NE – Dobutamine<br>- Dopamine-resistant CS without ACS | - Similar efficacy between groups in term of global hemodynamic effects<br>- Transient lactic acidosis, higher HR and arrhythmia, and inadequate gastric mucosa perfusion with epinephrine<br>- NE-dobutamine may be more reliable and safer | 2 |
| Levy 2018 [99]<br>OptimaCC<br>S = 9 | N = 57<br>F/U: 60 days | - Epinephrine versus NE<br>- CS after acute MI | - Epinephrine use compared with NE was associated with similar effects on arterial pressure and CI but higher incidence of refractory shock | 5 |
| **Inodilators** | | | | |
| García-González 2006 [100]<br>S = 1 | N = 22<br>F/U: at 24 and 30 hr | - Levosimendan versus dobutamine<br>- CS in STEMI patients treated with PPCI | - Levosimendan improved CPO and CI [100]<br>- Levosimendan significantly reduced IVRT, and increased E/A ratio [101]<br>- No difference in improving long-term survival [102] | 1 |
| Fuhrmann 2008 [103]<br>S = 1 | N = 32<br>F/U: at 30 days | - Add-on levosimendan versus enoximone<br>- CS complicating acute MI | - Levosimendan may improve survival compared with enoximone | 3 |
| Husebye 2013 [104]<br>LEAF<br>S = 1 | N = 61<br>CS subgroup (15%)<br>F/U: 42 days | - Levosimendan versus matching placebo<br>- STEMI treated with PPCI complicated by HF | - Levosimendan improved contractility post ischemia<br>- Levosimendan did not increase arrhythmias<br>- Similar results obtained in CS subgroup | 5 |
| Mathew 2021 [105]<br>DOREMI<br>S = 1 | N = 192<br>F/U: index hospitalization | - Milrinone versus dobutamine<br>- CS (SCAI stages B, C, D, or E), including patients with ACS | - No difference in composite of in-hospital death from any cause, resuscitated cardiac arrest, receipt of a cardiac transplant or MCS, nonfatal MI, TIA or stroke, or initiation of RRT (primary outcome)<br>- No difference in the individual components of primary composite outcome (secondary outcomes) | 5 |
| **Nitric oxide synthase inhibitors** | | | | |
| Cotter 2003 [106]<br>LINCS<br>S = 1 | N = 30<br>F/U: at 30 days | - Supportive care plus L-NAME versus supportive care only (no treatment)<br>- ASC complicated by refractory CS | - NOSi significantly reduced mortality and improved MAP and UOP | 1 |

**Table 4. Continued.**

| Study<br>Sites number (S) | Sample size (N)<br>Follow-up (F/U) | Interventions<br>Population | Conclusion | Jadad scale[a] (0–5) |
|---|---|---|---|---|
| Dzavík 2007 [107]<br>SHOCK-2<br>S = 22 | N = 79<br>F/U: 30 days<br>Dose-ranging study (Phase II) | - L-NMMA (in 5 regimens) versus matching placebo (normal saline)<br>- Acute MI complicated by persistent CS | - L-NMMA resulted in modest increases in MAP at 15 min but no differences at 2 hr<br>- No difference in 30-day mortality | 4 |
| Alexander 2007 [108]<br>TRIUMPHb<br>S = 130 | N = 398<br>F/U: 6 months | - Tilarginine (L-NMMA) versus matching Placebo<br>- MI complicated by refractory CS despite opening the IRA | - Tilarginine did not reduce mortality rates<br>- Early mortality rates were high<br>- Note: enrolment was terminated at 398 patients based on a prespecified futility analysis. | 4 |

aJadad scale: 3-item scale examines randomization, blinding, and patient disposition; 5-point score: 0 and 2 (poor quality) and 3 to 5 (good quality) [109–111].

bThe study was terminated prematurely for futility analysis.

Abbreviations: ACS, acute coronary syndrome; CI, cardiac index; CPO, Cardiac power; CS, cardiogenic shock; F/U, follow-up duration; hr, hour; HF, heart failure; HR, heart rate; IRA, infarct-related artery; IVRT, isovolumetric relaxation time; LEAF, LEvosimendan in Acute heart Failure following myocardial infarction; LINCS, L-NAME (a NO synthase inhibitor) In the treatment of refractory Cardiogenic Shock; L-NAME, $N^G$-Nitro-L-Arginine-Methyl Ester; L-NMMA, L-N-monomethyl-arginine; MAP, mean arterial pressure; max, maximum; MCS, mechanical circulatory support; MI, myocardial infarction; NE, norepinephrine; NOSi, nitric oxide synthase inhibitor(s); OpimaCC, Optimizing the use of vasopressor after coronary reperfusion in cardiogenic shock secondary to myocardial infarction; PPCI, primary percutaneous coronary intervention; RRT, renal replacement therapy; SCAI, Cardiovascular Angiography and Interventions; SHOCK-2, SHould we inhibit nitric Oxide synthase in Cardiogenic shocK 2; SOAP II, Sepsis Occurrence in Acutely Ill Patients; STEMI, ST elevation myocardial infarction; TIA, transient ischemic attack; TRIUMPH, Tilarginine Acetate Injection in a Randomized International Study in Unstable MI Patients With Cardiogenic Shock; UOP, urine output.

conducted when only intra-aortic balloon pump (IABP) device was available [13]. The devices included axial LV-to-aorta pumps (Impella®), left atrium (LA)-to-aorta assist devices (TandemHeart®), right atrium (RA)-to-aorta pump (VA-ECMO) and devices for RV support [13, 119]. The devices are usually classified according to the pump type: volume-displacement pumps (i.e., IABP), continuous-flow pumps (i.e., Impella®) or centrifugal-flow (i.e., TandemHeart®, VA-ECMO) MCS [120]. In the National Cardiovascular Data Registry, 2.4% and 0.7% of percutaneous coronary intervention (PCI) cases were provided IABP and other MCS devices, respectively. IABP was mostly (63.3%) initiated after the start of PCI, while the other MCS devices were mostly (77.6%) inserted prior to PCI [121]. MCS devices reduce ventricles pressure and volume (i.e., unloading). These devices have potential ability to perverse vital organs perfusion, support circulation, amplify coronary perfusion, contain infarct size, reduce congestion and pulmonary edema by decreasing intracardiac filling pressures, and decrease LV volumes, wall stress, and myocardial oxygen demand [120]. Centres' initial experiences with MCS devices demonstrated their benefit [37, 52, 122–124]. However, mortality benefit was not shown in the subsequent pivotal RCTs [36, 38], or meta-analyses [125, 126]. Table 5 (Ref. [4, 23, 36–38, 52, 90, 119, 120, 124, 127–133]) summarizes the features and evidence from pivotal studies of the available temporary MCS devices.

The best evidence for IABP use informing about mortality benefit comes from the IABP-SHOCK II trial [39, 130, 131] which did not show any benefit, leading to downgrading of guidelines' recommendations on routine IABP use [134]. However, IABP may improve outcomes in the presence of mechanical complications. Thus, the guidelines consider IABP for those patients [56]. Multiple observational studies [135–137], RCTs [138–140], and meta-analyses [141–144] have concluded the lack of mortality benefit as well. As compared with IABP, Impella®LP 2.5 significantly improved hemodynamics but not 30-day mortality (46%) in the pilot ISAR-SHOCK study [37]. Whereas, 30-day mortality rate was higher (64.2%) in those who received Impella®LP 2.5 in a multicentre registry [145]. Routine use of Impella®CP, in the exploratory IMPRESS study, did not show 30-day or six-month mortality benefit [36]. In addition, findings from two meta-analyses of RCTs did not report statistical difference in 30-day [126, 146] or six-month mortality when compared with IABP [146]. Evidence from observational studies on Impella® devices use versus IABP support showed conflicting results (i.e., increased harm such as in-hospital mortality and major bleeding [147], improved survival with early initiation of MCS [148, 149] or lack of association with 30-day mortality [150]). Similarly, studies on patients undergoing high-risk PCI, but not presenting with CS, showed inconsistent results with the use of Impella® devices [151–156]. When acute MI patients presenting with CS were randomized to either TandemHeart® or IABP support, the former device improved hemodynamic parameters but not 30-day mortality [52, 124, 126]. The reported rates of 30-day and six-month mortality were more than 40% [157]. There are few published non-comparative studies that described the experience with TandemHeart® device in patients undergoing high-risk PCI including those who developed CS [158–160]. The evidence for VA-ECMO use in acute MI complicated with CS, including those who experienced cardiac arrest, is based on observational studies. In the cardiac arrest setting, VA-ECMO may be considered in patients who are refractory to cardiopulmonary resuscitation (CPR) (i.e., extracorporeal CPR (E-CPR)). A recent systematic review of cohort studies concluded that the use of VA-ECMO in CS complicating acute MI may have survival benefit [161]. The first mortality risk score, ENCOURAGE score, has been proposed to dictate the decision on the indication of VA-ECMO in acute MI patients based on pre-ECMO factors that have been correlated with mortality [162]. The EURO SHOCK (NCT03813134) is a multi-center, open-label, RCT that is underway and compares early initiation of VA-ECMO plus standard pharmacological therapy after acute PCI with standard pharmacological therapy alone. The primary endpoint is 30-day mortality. In addition, analysis of the cost-effectiveness will be conducted [163]. Earlier cohort studies in patients with ACS complicated by refractory CS or cardiac arrest who were on ECMO, concluded that in-hospital survival rate was improved [164, 165], and early initiation of ECMO would result in better outcomes and successful ECMO weaning [165]. In the aforementioned setting, the results of two meta-analyses of observational studies showed that ECMO has improved survival [166, 167]. However, one of the meta-analyses showed favourable neurological outcomes [167], while the other one reported a significantly higher complications rate, (i.e., neurological deficit and kidney impairment) [166]. Several studies found that E-CPR in acute MI patients with CS and cardiac arrest resulted in acceptable survival rates and improved outcomes [71, 168–170]. Nonetheless, prior-ECMO support in patients with VAD was associated with postoperative complications especially RV and respiratory failure [172]. Finally, combining IABP with VA-ECMO is gaining more interest and has been associated with successful VA-ECMO weaning and improved mortality rates [173].

Acute RV dysfunction or failure may eventuate from different clinical setting such as acute MI, decompensated heart failure, fulminant myocarditis, orthotopic heart transplant, or following left VAD (LVAD) procedure [90, 174]. RV failure contributes to CS via three ways: RV infarction due to obstruction of proximal right coronary artery in the absence of LV failure; elevated pulmonary vascular resistance and/or PCWP leading to elevated pulmonary afterload; and RV failure complicating primary LV failure [59]. RV failure is associated with increased mortality and morbidity [59, 120]. The approach for managing RV failure includes treating the cause, sustaining adequate preload, decreasing RV afterload and improving RV contractility [120]. This is achieved by inotropic

**Table 5. Temporary mechanical circulatory support devices.**

| MCS device | Description | Hemodynamic effects | Characteristics | Pivotal/RCT (PICO) |
|---|---|---|---|---|
| **LV support** | | | | |
| **IABP** | - **Device**: counterpulsation pump placed in descending aorta<br>- Has 2 major components, balloon catheter and pump console to control the balloon<br>- **CO support/flow**: 0.3–0.5 L/min<br>- **Mechanism**: balloon inflation and deflation (aorta)<br>- **Insertion**: femoral artery, axillary artery<br>- **Cannula size**: 7–9 Fr (arterial)<br>- **Implantation**: percutaneous<br>- Timing of balloon inflation and deflation is based on ECG or pressure triggers | - LV unloading (modest)<br>- Cardiac power ↑<br>- Afterload ↓<br>- MAP ↑<br>- LVEDP ↓<br>- LV preload -<br>- Coronary perfusion ↑ | - **Advantages**: easy insertion, low cost, rare vascular complications<br>- **Disadvantages**: increase in CO is small, requires native heart beat and stable rhythm, arrhythmias mitigate its usefulness<br>- **Complications**: spinal cord ischemia, infection, bleeding, retroperitoneal haematoma, limb ischemia, compartment syndrome, vascular trauma, stroke, thrombocytopenia<br>- **Contraindications**: AR, severe PAD or aortic disease | Thiele 2012 (IABP-SHOCK II) [38]<br>- N = 600<br>- **P**: CS complicating acute MI (STEMI/NSTEMI) and early revascularization.<br>- **I&C**: IABP versus conventional treatment<br>- **O-efficacy**: no difference in 30-day mortality (39.7% vs. 41.3%)<br>- **Long F/U**: no difference in mortality at 12 months [130] and 6.2 years [131] |
| **Impella®LP 2.5** | - **Device:** micro-axial pump that decompresses LV and pumps blood into ascending aorta<br>- **CO support/flow**: 1.0–2.5 L/min<br>- **Mechanism**: axial flow continuous pump (LV-to-Aorta)<br>- **Insertion**: femoral artery, axillary artery<br>- **Cannula size**: 12–14 Fr<br>- **Implantation**: percutaneous<br>- **Max implant duration**: 7–10 day | - LV unloading<br>- Cardiac power ↑↑<br>- Afterload ↓<br>- MAP ↑↑<br>- LVEDP ↓↓<br>- LV preload ↓↓<br>- Coronary perfusion ↑ | - **Advantages**: axillary approach allows long-term support<br>- Do not require ECG or arterial waveform triggering<br>- **Complications**: haemolysis, valvular lesions, device migration, CNS hemorrhage, CNS infarction, brain death, seizures<br>- **Contraindications**: mechanical aortic valve or LV thrombus, AR or stenosis, severe PAD | Seyfarth 2008 (ISAR-SHOCK) [37]<br>- 2-center, pilot, N = 26<br>- **P**: CS post-acute MI<br>- **I&C**: Impella®LP 2.5 versus IABP<br>- **O-efficacy**: significant improvement in CI after 30 min with Impella®. Mortality at 30-day was 46% in both groups<br>- **O-safety**: haemolysis and transfusion significantly higher with Impella®LP 2.5 |
| **Impella®CP** | - **Device:** micro-axial pump that decompresses LV and pumps blood into ascending aorta<br>- **CO support/flow**: 3.7–4.0 L/min<br>- **Mechanism**: axial flow continuous pump (LV-to-Aorta)<br>- **Insertion**: femoral artery, axillary artery<br>- **Cannula size**: 12–14 Fr<br>- **Implantation**: percutaneous<br>- **Max implant duration**: 7–10 day | - As above | - As above | Ouweneel 2017 (IMPRESS) [36]<br>- N = 48<br>- **P**: CS post-acute MI<br>- **I&C**: Impella®CP versus IABP<br>- **O-safety**: more bleeding events and haemolysis with Impella®CP<br>- **O-efficacy**: no difference in 30-day survival and 6-month mortality ( 50%) in both groups |
| **Impella®LP 5.0** | - **CO support/flow**: 5.0 L/min<br>- **Mechanism**: axial flow continuous pump (LV-to-Aorta)<br>- **Insertion**: femoral or axillary artery<br>- **Cannula size**: 21–22 Fr<br>- **Implantation**: surgical cutdown of artery prior to insertion of sheath<br>- **Max implant duration**: 2–3 week | - As above | - As above | - No RCTs |

**Table 5. Continued.**

| MCS device | Description | Hemodynamic effects | Characteristics | Pivotal/RCT (PICO) |
|---|---|---|---|---|
| **Impella® 5.5** | - **CO support/flow**: 5.5–6.0 L/min<br>- **Mechanism**: axial flow continuous pump (LV-to-Aorta)<br>- **Insertion**: femoral or axillary artery | - LV unloading<br>- Cardiac power ↑↑<br>- Afterload ↓↓<br>- Coronary perfusion ↑ | - As above | - No RCTs |
| **TandemHeart® LV-FA** | - **Device**: centrifugal pump with inflow cannula placed in LA and outflow cannula in one or both femoral arteries across interatrial septum.<br>- Pumps blood from LA to iliofemoral arterial system<br>- Has 4 components: a 21-F transseptal cannula, a centrifugal pump, a femoral arterial cannula, and a control console<br>- **CO support/flow**: 2.5–5.0 L/min<br>- **Mechanism**: centrifugal flow continuous pump (LA-to-Aorta)<br>- **Insertion**: femoral artery or femoral vein<br>- **Cannula size**: 12–19 Fr (arterial), 21 Fr (venous)<br>- **Implantation**: transeptal puncture<br>- **Max implant duration**: 2–3 week | - LV unloading<br>- Cardiac power ↑↑<br>- Afterload ↑<br>- MAP ↑↑<br>- LVEDP ↓↓<br>- LV preload ↓↓<br>- Coronary perfusion - | - **Advantages:** does not require ECG or arterial waveform triggering<br>- **Disadvantages:** need for transseptal puncture, risk of dislodgement of LA cannula<br>- **Complications:** air embolism, cardiac perforation, tamponade, residual atrial septal defect, massive RV-to-aorta shunt, thrombo-or air-embolism, haemolysis, vascular trauma, limb ischemia<br>- **Contraindications**: profound coagulopathies, bleeding diatheses e.g., HIT or DIC, RA or LA thrombus, severe PAD | Thiele 2005 [124]<br>- N = 41<br>- **P**: CS post-acute MI<br>- **I&C**: TandemHeart® versus IABP<br>- **O-efficacy**: hemodynamic improvement is greater with TandemHeart®. Mortality at 30 days were similar (43% vs. 45%)<br>- **O-safety**: significantly more limb ischemia, blood transfusions, DIC in TandemHeart® arm<br><br>Burkhoff 2006 [52]<br>- 12-center, N = 42<br>- **P**: refractory CS (post-acute MI; 70%)<br>- **I&C**: TandemHeart® versus IABP<br>- **O-efficacy**: significantly greater increases in CI and greater decreases in PCWP over first 16 hours with TandemHeart®. Survival at 30-day was not significantly different (53% vs. 64%)<br>- **O-safety**: no difference in severe adverse events or bleeding |
| **RV support** | | | | |
| **CentriMag®** | - **Device**: centrifugal pump with magnetically levitated propeller<br>- Has centrifugal pump, electric motor, and console.<br>- **CO support/flow**: up to 9.9 L/min<br>- **Mechanism**: centrifugal-flow<br>- **Insertion**: femoral-to-femoral bypass | - RV unloading | - **Advantages**: easy insertion and maintenance, reliable, low thrombosis risk<br>- **Complications**: infection, Bleeding, Systemic heparinization required, Limited patient mobility, Arrhythmia | - No RCTs |
| **Impella®RP** | - **Device**: axial catheter-based pump or RV assist device that pumps blood from RA to PA<br>- **CO support/flow**: 4.0–5.0 L/min<br>- **Mechanism**: axial flow continuous pump (RA-to-PA)<br>- **Insertion**: femoral vein<br>- **Cannula size**: 22 Fr (venous) | - RV unloading | - **Advantages**: need for only single venous access site | Anderson 2015 (RECOVER RIGHT) [132]<br>- 15-center, prospective, non-RCT, N = 30<br>- **P**: refractory RV failure following acute MI, cardiotomy or LVAD implantation<br>- **I&C**: Impella®RP versus none<br>- **O-efficacy**: immediate hemodynamics improvement with significant increase in cardiac index and decrease in CVP. Overall survival at 30 days was 73.3%. All patients discharged were alive at 180 days |

**Table 5. Continued.**

| MCS device | Description | Hemodynamic effects | Characteristics | Pivotal/RCT (PICO) |
|---|---|---|---|---|
| **PROTEK Duo®** | - **Device**:<br>- **CO support/flow**:<br>- **Mechanism**: extracorporeal centrifugal-flow (RA-to-PA)<br>- **Insertion**: superior vena cava<br>- **Cannula size**: double lumen, 29 or 31 Fr | - RV unloading | - | - No RCTs |
| **TandemHeart® RA-PA** | - **CO support/flow**: 4.0 L/min<br>- **Mechanism**: extracorporeal centrifugal-flow continuous pump (RA-to-PA)<br>- **Insertion**: internal jugular vein<br>- **Cannula size**: 29 Fr (venous) | - RV unloading | - **Complications**: infection, bleeding, ischemia of lower extremities | - No RCTs |
| **LV and RV support** | | | | |
| **VA-ECMO** | - **Device:** heart-lung bypass machine<br>- Has centrifugal pump and membrane oxygenation<br>- V-V for oxygenation only or V-A for oxygenation and circulatory support<br>- **CO support/flow**: 7.0 L/min<br>- **Mechanism**: centrifugal flow continuous pump (RA-to-Aorta)<br>- **Insertion**: femoral vein or femoral artery<br>- **Cannula size**: 14–19 Fr (arterial), 17–21 Fr (venous)<br>- **Implantation**: percutaneous or surgical cutdown<br>- **Max implant duration**: 3–4 week | - RV unloading<br>- Cardiac power ↑↑↑<br>- Afterload ↑↑↑<br>- MAP ↑↑<br>- LVEDP ↔<br>- LV preload ↓<br>- Coronary perfusion - | - **Advantages**: metabolic derangement and deleterious systemic effects of CS can be corrected within hours of initiation<br>- **Disadvantages**: afterload increase may worsen PCWP and LV function, vasodilators or MCS e.g., IABP or Impella® may be needed to reduce afterload<br>- **Complications**: air embolism, LV dilation, LV blood stasis, pulmonary edema, circuit clots, haemolysis, acquired von Willebrand disease, HIT, VTE, GI or pulmonary bleeding, sepsis, DIC<br>- **Contraindications**: significant aortic insufficiency, severe PAD | - No RCTs |

Abbreviations: AR, aortic valve regurgitation; CI, cardiac index; CNS, central nervous system; CO, cardiac output; CS, cardiogenic shock; CVP, central venous pressure; DIC, disseminated intravascular coagulation; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; FA, femoral artery; Fr, French; F/U, follow-up; GI, gastrointestinal; HIT, heparin induced thrombocytopenia; IABP, intra-aortic balloon pump; IMPRESS, IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; LA, left atrium; LV, left ventricle or ventricular; LVAD, left ventricular assist device; LVEDP, left ventricle end-diastolic pressure; MAP, mean arterial blood pressure; Max, maximum; MCS, mechanical circulatory support; MI, myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; PA, pulmonary artery; PAD, peripheral artery disease; PCWP, pulmonary capillary wedge pressure; PICO, population, intervention, comparison, and outcomes; RA, right atrium; RCTs, randomized controlled trials; RECOVER RIGHT, Impella RP Right Ventricular Heart Failure Trial; RV, right ventricle; SHOCK-IABP II, Intraaortic Balloon Pump in Cardiogenic Shock II; STEMI, ST-segment elevation myocardial infarction; V-A, veno-arterial; VTE, venous thromboembolism; V-V, Veno-veno.

therapy, pulmonary vasodilation, and optimized volume status [174]. When medical therapy is insufficient, temporary MCS or destination therapy should be considered [120, 174]. Historically, MCS support has been limited to IABP [120]. At-present, examples of RV-support devices include CentriMag®, PROTEK Duo®, and Impella®RP [23, 90, 129, 133]. The CentriMag® ventricular assist system provides temporary right, left, or biventricular support. A preliminary study showed that CentriMag®, in patients with CS, provided temporary support with low rates of device-related complications without device failure events [175]. PROTEK Duo® catheter has an extracorporeal pump, and its use in the setting LVAD implantation and CS due to severe pulmonary hypertension has been described in case reports [133]. TandemHeart® adapted for RV support improved hemodynamic status without any reported intra-procedure mortality [176]. Following the promising initial experiences, Impella®RP device in the pivotal RECOVER RIGHT trial promptly improved hemodynamic parameters in patients with life-threatening RV failure and all patients were alive at 180 days follow-up [132].

Taken together, a retrospective study documented a five-year experience of MCS devices as a bridge-to-decision in patients with refractory CS. Acute MI was the etiology of CS in 49% of patients. Initially, the use of temporary VAD was in 49% and VA-ECMO in 51% of patients. Implantable VAD and heart transplantation were performed in 26% and 11% of patients, respectively. Survival to discharge from hospital was 49% [177]. There are few controversial questions related to temporary MCS in the care of CS patients, the main ones focus on device selection and time of device initiation [4, 23]. Device selection in patients with severe hemodynamic instability, should be guided by several factors such as, patient's hemodynamic status, advantages and disadvantages of the device, its technical feasibility, and the overall goals of therapy. As a general approach, IABP is usually the initial choice given the familiarity with it. However, the pharmacologic support is usually required but not with the Impella® devices. Thus, as a next step Impella®LP 2.5 or CP may offer a more powerful support. With the continuous deterioration, TandemHeart®, VA-ECMO, or Impella®LP 5.0 can be considered. Early insertion and initiation of MCS device and before PCI can result in significant hemodynamic improvement and mitigate ischemia and the worsening cardiac function [120]. The recent European guidelines recommended the short-term use of MCS in selected patients with ACS and CS, and did not recommend routine IABP use [118, 178], which should be considered in patients with mechanical complications [56, 178]. Destination therapy with durable MCS (i.e., LVAD) or heart transplantation is warranted in refractory CS despite revascularization, inotropic therapy and temporary MCS [4].

### *5.2 Management of acute MI*

Early, successful myocardial revascularization in ACS complicated by CS is the only therapy with proven mortality benefit [21, 32, 179]. Over 23 years from 1975 to 1997, despite the non-significant change in the rate of CS complicating acute MI, the survival rate increased in parallel with the increased use of coronary reperfusion strategies [29].

#### *5.2.1 Pharmacologic revascularization*

Thrombolytic or fibrinolytic therapy should be considered for STEMI patients if timely PCI is delayed or not feasible [90, 180]. Furthermore, data on the efficacy of thrombolytics in CS patients is very limited as they were frequently excluded from the respective clinical trials [181]. In Cath-PCI registry, there was a significant reduction in thrombolysis use, from 4% to 1.2%, between 2005 and 2013, respectively [35].

#### *5.2.2 Non-pharmacologic revascularization*

In patients presenting with ACS complicated by CS, emergency coronary angiography is recommended [118, 178]. The landmark SHOCK trial has shown significant six-month mortality benefit on long-term follow up [182], but not at 30 days, with early revascularization using either PCI or coronary artery bypass grafting (CABG) [21]. In Cath-PCI registry, the number of patients who underwent PCI for acute MI complicated by CS increased dramatically between 2005 and 2013 [35]. Currently, immediate CABG has been reported in less than 4% of patients [90]. Emergency CABG is usually indicated when coronary arteries are not amenable to PCI [118, 178].

#### *5.2.3 PCI strategy*

The majority of patients with CS (i.e., >80%) has coronary angiographic findings of multivessel or left main disease, which subject them to higher mortality risk compared to those with single-vessel disease [90]. The revascularization strategy for multivessel disease has been debatable. The pivotal CULPRIT-SHOCK trial concluded that PCI of culprit lesion alone significantly reduced death or severe renal impairment at 30 days, compared with immediate PCI to multiple vessels [39]. However, death rate did not differ significantly at one year of follow-up [183]. Based on CULPRIT-SHOCK results, routine revascularization of the non-culprit lesions has been downgraded to Class III [118], and emergency PCI of the culprit lesion is a Class I recommendation [118, 178]. Two meta-analyses have shown that culprit-only PCI was associated with short-term but not longer-term mortality benefit as compared with multivessel PCI [184, 185]. Whereas, another two meta-analyses did not find significant difference in mortality [186, 187]. The recent COMPLETE trial that enrolled STEMI patients with multivessel artery disease who underwent successful culprit-lesion PCI found that complete revascularization with staged PCI of all suitable non-culprit lesions was superior to culprit-only PCI. However, only 10% of the patients presented with Killip class II or more [188].

#### *5.2.4 Other PCI aspects*

Patients with acute MI complicated with CS are usually excluded from studies examining PCI arterial access site, stent type or aspiration thrombectomy. Trans-radial access has

been endorsed by the AHA and advocated by CS care centres as the access of preference [189, 190]. Trans-radial access has been associated with lower rates of mortality, major adverse cardiac and cerebrovascular events [191, 192], and major bleeding [191]. In Cath-PCI registry, the use of radial access significantly increased from 0.4% to 4.2% between 2005 and 2013, respectively [35]. Interestingly, in a study from England and Wales the increase in radial access use with primary PCI was from 24.6% in 2007 to 76.5% in 2014 [193]. Routine aspiration thrombectomy is not recommended as there is no convincing evidence to support it in CS [189]. Drug-eluting stents, apparently, are favoured over bare-metal stents despite the indefinite evidence in CS [189, 194–196].

#### *5.2.5 Medications for treatment of ACS with CS*

Recommendations for pharmacologic therapy in CS are similar to those for ACS without CS, since there are no dedicated RCTs in CS. Antithrombotic therapy (i.e., antiplatelets and anticoagulation) is a must prior, during, and after PCI [2, 90, 189]. Once the shock status is resolved, beta-blockers and renin-angiotensin system inhibitors should be considered as tolerated [2].

#### *5.2.6 Other considerations*

Interventional cardiologist ideally collaborates with general cardiologist, cardiothoracic surgeon, intensivist, heart failure specialist, and specialized nurses in a multidisciplinary approach (i.e., the shock team) [4, 90, 119] to decide on the most effective acute interventions and destination therapy as appropriate [90, 119].

## 6. Risk assessment

Initial risk stratification and prognosis of patients with CS can be assessed by several risk scores. However, not all of them were validated [2, 59]. IABP-SHOCK and CardShock scores were investigated. The IABP-SHOCK score stratifies the risk of 30-day mortality (low, intermediate, high) by using six variables (age, prior stroke, Thrombolysis In Myocardial Infarction flow grade post PCI, serum levels of lactate, creatinine, and glucose) [197]. The CardShock score estimates the risk of short-term mortality (low, intermediate, high) by using seven variables (age, prior CABG, previous MI, ACS etiology, LV ejection fraction, lactate level, confusion) [5].

## 7. Challenges

The evidence for management of patients presenting with MI and CS is usually extrapolated from trials that enrolled hemodynamically stable MI patients. Although not optimal, it is considered an acceptable approach given the lack of other alternatives [189]. Conducting RCTs in CS patients is difficult because CS includes broad spectrum of patients of variable etiologies and severities with consequent variability of treatment outcomes [13]. Some unanswered clinical questions include, initial selection of a vasoactive agent [96], most appropriate MCS device strategy [23], or routine use of MCS devices as adjunct to coronary revascularization. Trials are underway that address some of these issues [120].

## 8. Summary

Acute MI with myocardial dysfunction is the most frequent cause of CS. It is characterized by circulatory collapse and inadequate end-organ tissue perfusion due to impaired CO. CS triggers unfavourable compensatory mechanisms that create a vicious cycle which is difficult to reverse and eventually leads to death. Interrupting this vicious cycle and restoring hemodynamic stability is the fundamental comprehensive treatment of CS. Although it has been declined over time, the mortality rate is still unacceptably high despite the advancement in MCS modalities and coronary revascularization practices. Early identification of CS, rapid diagnosis, and prompt initiation of therapy may improve prognosis. Clinical assessment with physical examination and early invasive hemodynamics, helps in the identification of CS phenotype, risk stratification, and severity classification according to SCAI taxonomy. Thus, this can guide a tailored and optimized therapeutic approach in critically ill patients. To date there is no pharmacological or nonpharmacological intervention that showed a mortality benefit.

Vasoactive agents are considered the initial management of hemodynamic instability. There is no convincing evidence of the superiority of one agent over another. The current availability of MCS devices has broadened the therapeutic choices for hemodynamic support. Their early initiation instead of escalating the doses of vasoactive agents may mitigate further deterioration. Appropriate MCS device should be carefully selected and paired with the right patient at the right time. Device selection process should be dictated by several factors. Early coronary revascularization, by PCI or CABG, is the cornerstone therapy which improves mortality in patients with acute MI complicated by CS. Adequately powered RCTs are urgently needed to address the controversial and unanswered questions.

## Abbreviations

CardShock, Cardiogenic Shock; COMPLETE, The Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI; DOREMI, Dobutamine Compared with Milrinone; ENCOURAGE, prEdictioN of Cardiogenic shock OUtcome foR AMI patients salvaGed by VA-ECMO; GUSTO, Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded coronary arteries; IMPRESS, IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; RECOVER RIGHT, Impella RP Right Ventricular Heart Failure Trial; SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock; SHOCK-IABP II, Intraaortic Balloon Pump in Cardiogenic Shock II.

## Author contributions

RK: design, literature search, literature summaries, writing, tables summary, figures, revision, and responses to reviewers. SE: design, general writing and critical revision.

## Ethics approval and consent to participate

Not applicable.


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## Conflict of interest

The authors declare no conflict of interest.

## References


[1] Vincent J, De Backer D. Circulatory Shock. New England Journal of Medicine. 2013; 369: 1726–1734.

[2] Zeymer U, Bueno H, Granger CB, Hochman J, Huber K, Lettino M, *et al.* Acute Cardiovascular Care Association position statement for the diagnosis and treatment of patients with acute myocardial infarction complicated by cardiogenic shock: a document of the Acute Cardiovascular Care Association of the European Society of Cardiology. European Heart Journal. 2020; 9: 183–197.

[3] van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, *et al.* Contemporary Management of Cardiogenic Shock: a Scientific Statement from the American Heart Association. Circulation. 2017; 136: e232–e268.

[4] Tehrani BN, Truesdell AG, Psotka MA, Rosner C, Singh R, Sinha SS, *et al.* A Standardized and Comprehensive Approach to the Management of Cardiogenic Shock. JACC: Heart Failure. 2020; 8: 879–891.

[5] Harjola V, Lassus J, Sionis A, Køber L, Tarvasmäki T, Spinar J, *et al.* Clinical picture and risk prediction of short-term mortality in cardiogenic shock. European Journal of Heart Failure. 2015; 17: 501–509.

[6] Holmes DR, Bates ER, Kleiman NS, Sadowski Z, Horgan JHS, Morris DC, *et al.* Contemporary reperfusion therapy for cardiogenic shock: the GUSTO-I trial experience. The GUSTO-I Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. Journal of the American College of Cardiology. 1995; 26: 668–674.

[7] Holmes DR, Berger PB, Hochman JS, Granger CB, Thompson TD, Califf RM, *et al.* Cardiogenic shock in patients with acute ischemic syndromes with and without ST-segment elevation. Circulation. 1999; 100: 2067–2073.

[8] Anderson ML, Peterson ED, Peng SA, Wang TY, Ohman EM, Bhatt DL, *et al.* Differences in the profile, treatment, and prognosis of patients with cardiogenic shock by myocardial infarction classification: a report from NCDR. Circulation. Cardiovascular Quality and Outcomes. 2013; 6: 708–715.

[9] Hasdai D, Harrington RA, Hochman JS, Califf RM, Battler A, Box JW, *et al.* Platelet glycoprotein IIb/IIIa blockade and outcome of cardiogenic shock complicating acute coronary syndromes without persistent ST-segment elevation. Journal of the American College of Cardiology. 2000; 36: 685–692.

[10] Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, *et al.* Trends in Coronary Angiography, Revascularization, and Outcomes of Cardiogenic Shock Complicating Non-ST-Elevation Myocardial Infarction. American Journal of Cardiology. 2016; 117: 1–9.

[11] Babaev A, Frederick PD, Pasta DJ, Every N, Sichrovsky T, Hochman JS. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. Journal of the American Medical Association. 2005; 294: 448–454.

[12] Webb JG, Sleeper LA, Buller CE, Boland J, Palazzo A, Buller E, *et al.* Implications of the timing of onset of cardiogenic shock after acute myocardial infarction: a report from the SHOCK Trial Registry. should we emergently revascularize Occluded Coronaries for cardiogenic shocK? Journal of the American College of Cardiology. 2000; 36: 1084–1090.

[13] Baran DA, Grines CL, Bailey S, Burkhoff D, Hall SA, Henry TD, *et al.* SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheterization and Cardiovascular Interventions. 2019; 94: 29–37.

[14] Agress CM, Binder MJ. Cardiogenic shock. American Heart Journal. 1957; 54: 458–477.

[15] Ginsberg F, Parrillo JE. Cardiogenic shock: a historical perspective. Critical Care Clinics. 2009; 25: 103–14, viii.

[16] Malach M, Rosenberg BA. Acute myocardial infarction in a city hospital. III. Experience with shock. American Journal of Cardiology. 1960; 5: 487–492.

[17] Weisse AB. The elusive clot: the controversy over coronary thrombosis in myocardial infarction. Journal of the History of Medicine and Allied Sciences. 2006; 61: 66–78.

[18] Alves J, Saddala P, Maddaleni M. Cardiogenic shock historical perspective. 2014. Available at: https://www.wikidoc.org/index.php/Cardiogenic_shock_historical_perspective (Accessed: 18 May 2021).

[19] Scholz KH, Maier SKG, Maier LS, Lengenfelder B, Jacobshagen C, Jung J, *et al.* Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. European Heart Journal. 2018; 39: 1065–1074.

[20] Backhaus T, Fach A, Schmucker J, Fiehn E, Garstka D, Stehmeier J, *et al.* Management and predictors of outcome in unselected patients with cardiogenic shock complicating acute ST-segment elevation myocardial infarction: results from the Bremen STEMI Registry. Clinical Research in Cardiology. 2018; 107: 371–379.

[21] Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, *et al.* Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. should we Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. New England Journal of Medicine. 1999; 341: 625–634.

[22] Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A, *et al.* Improved Outcomes Associated with the use of Shock Protocols: Updates from the National Cardiogenic Shock Initiative. Catheterization and Cardiovascular Interventions. 2019; 93: 1173–1183.

[23] Bellumkonda L, Gul B, Masri SC. Evolving Concepts in Diagnosis and Management of Cardiogenic Shock. American Journal of Cardiology. 2018; 122: 1104–1110.

[24] Griffith GC, Wallace WB, Cochran B, Nerlich WE, Frasher WE. The treatment of shock associated with myocardial infarction. Circulation. 1954; 9: 527–532.

[25] Hunt D, Sloman G, Christie D, Penington C. Changing patterns and mortality of acute myocardial infarction in a coronary care unit. British Medical Journal. 1977; 1: 795–798.

[26] Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. American Journal of Cardiology. 1967; 20: 457–464.
[27] Goldberg RJ, Gore JM, Alpert JS, Osganian V, de Groot J, Bade J, *et al.* Cardiogenic shock after acute myocardial infarction. Incidence and mortality from a community-wide perspective, 1975 to 1988. New England Journal of Medicine. 1991; 325: 1117–1122.
[28] Lee L, Bates ER, Pitt B, Walton JA, Laufer N, O'Neill WW. Percutaneous transluminal coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogenic shock. Circulation. 1988; 78: 1345–1351.
[29] Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal Trends in Cardiogenic Shock Complicating Acute Myocardial Infarction. New England Journal of Medicine. 1999; 340: 1162–1168.
[30] Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-Year Trends (1975 to 2005) in the Magnitude of, Management of, and Hospital Death Rates Associated with Cardiogenic Shock in Patients with Acute Myocardial Infarction. Circulation. 2009; 119: 1211–1219.
[31] GUSTO investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. New England Journal of Medicine. 1993; 329: 673–682.
[32] Hochman JS, Boland J, Sleeper LA, Porway M, Brinker J, Col J, *et al.* Current spectrum of cardiogenic shock and effect of early revascularization on mortality. Results of an International Registry. SHOCK Registry Investigators. Circulation. 1995; 91: 873–881.
[33] Hochman JS, Buller CE, Sleeper LA, Boland J, Dzavik V, Sanborn TA, *et al.* Cardiogenic shock complicating acute myocardial infarction–etiologies, management and outcome: a report from the SHOCK Trial Registry. Should we emergently revascularize Occluded Coronaries for cardiogenic shocK? Journal of the American College of Cardiology. 2000; 36: 1063–1070.
[34] Goldberg RJ, Gore JM, Thompson CA, Gurwitz JH. Recent magnitude of and temporal trends (1994–1997) in the incidence and hospital death rates of cardiogenic shock complicating acute myocardial infarction: the second national registry of myocardial infarction. American Heart Journal. 2001; 141: 65–72.
[35] Wayangankar SA, Bangalore S, McCoy LA, Jneid H, Latif F, Karrowni W, *et al.* Temporal Trends and Outcomes of Patients Undergoing Percutaneous Coronary Interventions for Cardiogenic Shock in the Setting of Acute Myocardial Infarction: a Report from the CathPCI Registry. JACC. Cardiovascular Interventions. 2016; 9: 341–351.
[36] Ouweneel DM, Eriksen E, Sjauw KD, van Dongen IM, Hirsch A, Packer EJS, *et al.* Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock after Acute Myocardial Infarction. Journal of the American College of Cardiology. 2017; 69: 278–287.
[37] Seyfarth M, Sibbing D, Bauer I, Fröhlich G, Bott-Flügel L, Byrne R, *et al.* A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. Journal of the American College of Cardiology. 2008; 52: 1584–1588.
[38] Thiele H, Zeymer U, Neumann F, Ferenc M, Olbrich H, Hausleiter J, *et al.* Intraaortic balloon support for myocardial infarction with cardiogenic shock. New England Journal of Medicine. 2012; 367: 1287–1296.
[39] Thiele H, Akin I, Sandri M, Fuernau G, de Waha S, Meyer-Saraei R, *et al.* PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock. New England Journal of Medicine. 2017; 377: 2419–2432.
[40] Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. Circulation. 2008; 117: 686–697.
[41] Elbadawi A, Elgendy IY, Mahmoud K, Barakat AF, Mentias A, Mohamed AH, *et al.* Temporal Trends and Outcomes of Mechanical Complications in Patients with Acute Myocardial Infarction. JACC: Cardiovascular Interventions. 2019; 12: 1825–1836.
[42] Menon V, Webb JG, Hillis LD, Sleeper LA, Abboud R, Dzavik V, *et al.* Outcome and profile of ventricular septal rupture with cardiogenic shock after myocardial infarction: a report from the SHOCK Trial Registry. Should we emergently revascularize Occluded Coronaries in cardiogenic shocK? Journal of the American College of Cardiology. 2000; 36: 1110–1116.
[43] Alonso DR, Scheidt S, Post M, Killip T. Pathophysiology of cardiogenic shock. Quantification of myocardial necrosis, clinical, pathologic and electrocardiographic correlations. Circulation. 1973; 48: 588–596.
[44] McCallister BD, Christian TF, Gersh BJ, Gibbons RJ. Prognosis of myocardial infarctions involving more than 40% of the left ventricle after acute reperfusion therapy. Circulation. 1993; 88: 1470–1475.
[45] Kohsaka S, Menon V, Lowe AM, Lange M, Dzavik V, Sleeper LA, *et al.* Systemic inflammatory response syndrome after acute myocardial infarction complicated by cardiogenic shock. Archives of Internal Medicine. 2005; 165: 1643–1650.
[46] Prondzinsky R, Unverzagt S, Lemm H, Wegener N, Schlitt A, Heinroth KM, *et al.* Interleukin-6, -7, -8 and -10 predict outcome in acute myocardial infarction complicated by cardiogenic shock. Clinical Research in Cardiology. 2012; 101: 375–384.
[47] Hochman JS. Cardiogenic shock complicating acute myocardial infarction: expanding the paradigm. Circulation. 2003; 107: 2998–3002.
[48] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, *et al.* 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2016; 37: 2129–2200.
[49] Jones TL, Nakamura K, McCabe JM. Cardiogenic shock: evolving definitions and future directions in management. Open Heart. 2020; 6: e000960.
[50] Binder MJ, Ryan JA, Marcus S, Mugler F, Strange D, Agress CM. Evaluation of therapy in shock following acute myocardial infarction. American Journal of Medicine. 1955; 18: 622–632.
[51] Hochman JS, Sleeper LA, Godfrey E, McKinlay SM, Sanborn T, Col J, *et al.* Should we Emergently Revascularize Occluded Coronaries for Cardiogenic ShocK: an international randomized trial of emergency PTCA/CABG—trial design. American Heart Journal. 1999; 137: 313–321.
[52] Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. American Heart Journal. 2006; 152: 469.e1–469.e8.
[53] Thiele H, Schuler G, Neumann F, Hausleiter J, Olbrich H, Schwarz B, *et al.* Intraaortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock: design and rationale of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial. American Heart Journal. 2012; 163: 938–945.
[54] Thiele H, Desch S, Piek JJ, Stepinska J, Oldroyd K, Serpytis P, *et al.* Multivessel versus culprit lesion only percutaneous revascularization plus potential staged revascularization in patients with acute myocardial infarction complicated by cardiogenic shock: Design and rationale of CULPRIT-SHOCK trial. American Heart Journal. 2016; 172: 160–169.
[55] Menon V, White H, LeJemtel T, Webb JG, Sleeper LA, Hochman JS. The clinical profile of patients with suspected cardiogenic shock due to predominant left ventricular failure: a report from the SHOCK Trial Registry. Journal of the American College of Cardiology. 2000; 36: 1071–1076.
[56] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment el-

evation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal. 2018; 39: 119–177.
[57] Forrester JS, Diamond GA, Swan HJ. Correlative classification of clinical and hemodynamic function after acute myocardial infarction. American Journal of Cardiology. 1977; 39: 137–145.
[58] Ng VG, Lansky AJ, Meller S, Witzenbichler B, Guagliumi G, Peruga JZ, *et al.* The prognostic importance of left ventricular function in patients with ST-segment elevation myocardial infarction: the HORIZONS-AMI trial. European Heart Journal. Acute Cardiovascular Care. 2014; 3: 67–77.
[59] Brener MI, Rosenblum HR, Burkhoff D. Pathophysiology and Advanced Hemodynamic Assessment of Cardiogenic Shock. Methodist DeBakey Cardiovascular Journal. 2020; 16: 7–15.
[60] Nohria A, Tsang SW, Fang JC, Lewis EF, Jarcho JA, Mudge GH, *et al.* Clinical assessment identifies hemodynamic profiles that predict outcomes in patients admitted with heart failure. Journal of the American College of Cardiology. 2003; 41: 1797–1804.
[61] Stevenson LW. Design of therapy for advanced heart failure. European Journal of Heart Failure. 2005; 7: 323–331.
[62] Kapur NK, Thayer KL, Zweck E. Cardiogenic Shock in the Setting of Acute Myocardial Infarction. Methodist DeBakey Cardiovascular Journal. 2020; 16: 16–21.
[63] Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, *et al.* ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure): Developed in Collaboration With the International Society for Heart and Lung Transplantation; Endorsed by the Heart Failure Society of America. Circulation. 2001; 104: 2996–3007.
[64] Stevenson LW, Pagani FD, Young JB, Jessup M, Miller L, Kormos RL, *et al.* INTERMACS profiles of advanced heart failure: the current picture. the Journal of Heart and Lung Transplantation. 2009; 28: 535–541.
[65] Jentzer JC, van Diepen S, Barsness GW, Henry TD, Menon V, Rihal CS, *et al.* Cardiogenic Shock Classification to Predict Mortality in the Cardiac Intensive Care Unit. Journal of the American College of Cardiology. 2019; 74: 2117–2128.
[66] Jentzer JC, Baran DA, van Diepen S, Barsness GW, Henry TD, Naidu SS, *et al.* Admission Society for Cardiovascular Angiography and Intervention shock stage stratifies post-discharge mortality risk in cardiac intensive care unit patients. American Heart Journal. 2020; 219: 37–46.
[67] Hanson ID, Tagami T, Mando R, Kara Balla A, Dixon SR, Timmis S, *et al.* SCAI shock classification in acute myocardial infarction: Insights from the National Cardiogenic Shock Initiative. Catheterization and Cardiovascular Interventions. 2020; 96: 1137–1142.
[68] Baran DA, Long A, Badiye AP, Stelling K. Prospective validation of the SCAI shock classification: Single center analysis. Catheterization and Cardiovascular Interventions. 2020; 96: 1339–1347.
[69] Thayer KL, Zweck E, Ayouty M, Garan AR, Hernandez-Montfort J, Mahr C, *et al.* Invasive Hemodynamic Assessment and Classification of in-Hospital Mortality Risk among Patients with Cardiogenic Shock. Circulation: Heart Failure. 2020; 13: e007099.
[70] Schrage B, Dabboura S, Yan I, Hilal R, Neumann JT, Sörensen NA, *et al.* Application of the SCAI classification in a cohort of patients with cardiogenic shock. Catheterization and Cardiovascular Interventions. 2020; 96: E213–E219.
[71] Pareek N, Dworakowski R, Webb I, Barash J, Emezu G, Melikian N, *et al.* SCAI cardiogenic shock classification after out of hospital cardiac arrest and association with outcome. Catheterization and Cardiovascular Interventions. 2021; 97: E288–E297.
[72] Califf RM, Bengtson JR. Cardiogenic shock. New England Journal of Medicine. 1994; 330: 1724–1730.
[73] Saxena A, Garan AR, Kapur NK, O'Neill WW, Lindenfeld J, Pinney SP, *et al.* Value of Hemodynamic Monitoring in Patients with Cardiogenic Shock Undergoing Mechanical Circulatory Support. Circulation. 2020; 141: 1184–1197.
[74] Rossello X, Vila M, Rivas-Lasarte M, Ferrero-Gregori A, Sans-Roselló J, Duran-Cambra A, *et al.* Impact of Pulmonary Artery Catheter Use on Short- and Long-Term Mortality in Patients with Cardiogenic Shock. Cardiology. 2017; 136: 61–69.
[75] Garan AR, Kanwar M, Thayer KL, Whitehead E, Zweck E, Hernandez-Montfort J, *et al.* Complete Hemodynamic Profiling with Pulmonary Artery Catheters in Cardiogenic Shock is Associated with Lower in-Hospital Mortality. JACC: Heart Failure. 2020; 8: 903–913.
[76] Gore JM, Goldberg RJ, Spodick DH, Alpert JS, Dalen JE. A community-wide assessment of the use of pulmonary artery catheters in patients with acute myocardial infarction. Chest. 1987; 92: 721–727.
[77] Koo KKY, Sun JCJ, Zhou Q, Guyatt G, Cook DJ, Walter SD, *et al.* Pulmonary artery catheters: evolving rates and reasons for use. Critical Care Medicine. 2011; 39: 1613–1618.
[78] Vallabhajosyula S, Shankar A, Patlolla SH, Prasad A, Bell MR, Jentzer JC, *et al.* Pulmonary artery catheter use in acute myocardial infarction-cardiogenic shock. ESC Heart Failure. 2020; 7: 1234–1245.
[79] Shah MR, Hasselblad V, Stevenson LW, Binanay C, O'Connor CM, Sopko G, *et al.* Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. Journal of the American Medical Association. 2005; 294: 1664–1670.
[80] Binanay C, Califf RM, Hasselblad V, O'Connor CM, Shah MR, Sopko G, *et al.* Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. Journal of the American Medical Association. 2005; 294: 1625–1633.
[81] Richard C, Warszawski J, Anguel N, Deye N, Combes A, Barnoud D, *et al.* Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial. Journal of the American Medical Association. 2003; 290: 2713–2720.
[82] Rhodes A, Cusack RJ, Newman PJ, Grounds RM, Bennett ED. A randomised, controlled trial of the pulmonary artery catheter in critically ill patients. Intensive Care Medicine. 2002; 28: 256–264.
[83] Sionis A, Rivas-Lasarte M, Mebazaa A, Tarvasmäki T, Sans-Roselló J, Tolppanen H, *et al.* Current Use and Impact on 30-Day Mortality of Pulmonary Artery Catheter in Cardiogenic Shock Patients: Results from the CardShock Study. Journal of Intensive Care Medicine. 2020; 35: 1426–1433.
[84] Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIb investigators. A comparison of recombinant hirudin with heparin for the treatment of acute coronary syndromes. New England Journal of Medicine. 1996; 335: 775–782.
[85] Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. New England Journal of Medicine. 1997; 337: 1118–1123.
[86] Cohen MG, Kelly RV, Kong DF, Menon V, Shah M, Ferreira J, *et al.* Pulmonary artery catheterization in acute coronary syndromes: insights from the GUSTO IIb and GUSTO III trials. American Journal of Medicine. 2005; 118: 482–488.
[87] Zion MM, Balkin J, Rosenmann D, Goldbourt U, Reicher-Reiss H, Kaplinsky E, *et al.* Use of pulmonary artery catheters in patients with acute myocardial infarction. Analysis of experience in 5,841 patients in the SPRINT Registry. SPRINT Study Group. Chest. 1990; 98: 1331–1335.
[88] Weil MH. The "VIP" approach to the bedside management of shock. Journal of the American Medical Association. 1969; 207: 337.
[89] Squara P, Hollenberg S, Payen D. Reconsidering Vasopressors for Cardiogenic Shock. Chest. 2019; 156: 392–401.

[90] Hajjar LA, Teboul J. Mechanical Circulatory Support Devices for Cardiogenic Shock: State of the Art. Critical Care. 2019; 23: 76.
[91] Kapur NK, Davila CD, Jumean MF. Integrating Interventional Cardiology and Heart Failure Management for Cardiogenic Shock. Interventional Cardiology Clinics. 2017; 6: 481–485.
[92] Thiele H, Ohman EM, de Waha-Thiele S, Zeymer U, Desch S. Management of cardiogenic shock complicating myocardial infarction: an update 2019. European Heart Journal. 2019; 40: 2671–2683.
[93] Gamper G, Havel C, Arrich J, Losert H, Pace NL, Müllner M, *et al.* Vasopressors for hypotensive shock. Cochrane Database of Systematic Reviews. 2016; 2: CD003709.
[94] Schumann J, Henrich EC, Strobl H, Prondzinsky R, Weiche S, Thiele H, *et al.* Inotropic agents and vasodilator strategies for the treatment of cardiogenic shock or low cardiac output syndrome. Cochrane Database of Systematic Reviews. 2018; 1: CD009669.
[95] Vahdatpour C, Collins D, Goldberg S. Cardiogenic Shock. Journal of the American Heart Association. 2019; 8: e011991
[96] Kaddoura R, Elmoheen A, Badawy E, Eltawagny MF, Seif MA, Bashir K, *et al.* Vasoactive pharmacologic therapy in cardiogenic shock: a critical review. Journal of Drug Assessment. 2021; 10: 68–85.
[97] De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, *et al.* Comparison of dopamine and norepinephrine in the treatment of shock. New England Journal of Medicine. 2010; 362: 779–789.
[98] Levy B, Perez P, Perny J, Thivilier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. Critical Care Medicine. 2011; 39: 450–455.
[99] Levy B, Clere-Jehl R, Legras A, Morichau-Beauchant T, Leone M, Frederique G, *et al.* Epinephrine Versus Norepinephrine for Cardiogenic Shock after Acute Myocardial Infarction. Journal of the American College of Cardiology. 2018; 72: 173–182.
[100] García-González MJ, Domínguez-Rodríguez A, Ferrer-Hita JJ, Abreu-González P, Muñoz MB. Cardiogenic shock after primary percutaneous coronary intervention: Effects of levosimendan compared with dobutamine on haemodynamics. European Journal of Heart Failure. 2006; 8: 723–728.
[101] Dominguez-Rodriguez A, Samimi-Fard S, Garcia-Gonzalez MJ, Abreu-Gonzalez P. Effects of levosimendan versus dobutamine on left ventricular diastolic function in patients with cardiogenic shock after primary angioplasty. International Journal of Cardiology. 2008; 128: 214–217.
[102] Samimi-Fard S, García-González MJ, Domínguez-Rodríguez A, Abreu-González P. Effects of levosimendan versus dobutamine on long-term survival of patients with cardiogenic shock after primary coronary angioplasty. International Journal of Cardiology. 2008; 127: 284–287.
[103] Fuhrmann JT, Schmeisser A, Schulze MR, Wunderlich C, Schoen SP, Rauwolf T, *et al.* Levosimendan is superior to enoximone in refractory cardiogenic shock complicating acute myocardial infarction. Critical Care Medicine. 2008; 36: 2257–2266.
[104] Husebye T, Eritsland J, Müller C, Sandvik L, Arnesen H, Seljeflot I, *et al.* Levosimendan in acute heart failure following primary percutaneous coronary intervention-treated acute ST-elevation myocardial infarction. Results from the LEAF trial: a randomized, placebo-controlled study. European Journal of Heart Failure. 2013; 15: 565–572.
[105] Mathew R, Di Santo P, Jung RG, Marbach JA, Hutson J, Simard T, *et al.* Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock. New England Journal of Medicine. 2021; 385: 516–525.
[106] Cotter G, Kaluski E, Milo O, Blatt A, Salah A, Hendler A, *et al.* LINCS: L-NAME (a no synthase inhibitor) in the treatment of refractory cardiogenic shock: a prospective randomized study. European Heart Journal. 2003; 24: 1287–1295.
[107] Dzavík V, Cotter G, Reynolds HR, Alexander JH, Ramanathan K, Stebbins AL, *et al.* Effect of nitric oxide synthase inhibition on haemodynamics and outcome of patients with persistent cardiogenic shock complicating acute myocardial infarction: a phase II dose-ranging study. European Heart Journal. 2007; 28: 1109–1116.
[108] Alexander JH, Reynolds HR, Stebbins AL, Dzavik V, Harrington RA, Van de Werf F, *et al.* Effect of tilarginine acetate in patients with acute myocardial infarction and cardiogenic shock: the TRIUMPH randomized controlled trial. Journal of the American Medical Association. 2007; 297: 1657–1666.
[109] Moher D, Jadad AR, Nichol G, Penman M, Tugwell P, Walsh S. Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. Controlled Clinical Trials. 1995; 16: 62–73.
[110] Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, *et al.* Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials. 1996; 17: 1–12.
[111] Clark HD, Wells GA, Huët C, McAlister FA, Salmi LR, Fergusson D, *et al.* Assessing the quality of randomized trials: reliability of the Jadad scale. Controlled Clinical Trials. 1999; 20: 448–452.
[112] Karami M, Hemradj VV, Ouweneel DM, den Uil CA, Limpens J, Otterspoor LC, *et al.* Vasopressors and Inotropes in Acute Myocardial Infarction Related Cardiogenic Shock: A Systematic Review and Meta-Analysis. Journal of Clinical Medicine. 2020; 9: 2051.
[113] Burgos LM, Seoane L, Furmento JF, Costabel JP, Diez M, Vrancic M, *et al.* Effects of levosimendan on weaning and survival in adult cardiogenic shock patients with veno-arterial extracorporeal membrane oxygenation: systematic review and meta-analysis. Perfusion. 2020; 35: 484–491.
[114] Kaddoura R, Omar AS, Ibrahim MIM, Alkhulaifi A, Lorusso R, Elsherbini H, *et al.* Effectiveness of Levosimendan on Veno-Arterial Extracorporeal Membrane Oxygenation Management and Outcome: A Systematic Review and Meta-Analysis. Journal of Cardiothoracic and Vascular Anesthesia. 2021; 35: 2483–2495.
[115] Patel SJ, Augoustides JG. Levosimendan and Venoarterial ECMO—a Promising Application. Journal of Cardiothoracic and Vascular Anesthesia. 2021; 35: 2496–2498.
[116] O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, *et al.* 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013; 127: e362–e425.
[117] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, *et al.* 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. 2013; 128: e240–e327.
[118] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal. 2019; 40: 87–165.
[119] Guerrero-Miranda CY, Hall SA. Cardiogenic Shock in Patients with Advanced Chronic Heart Failure. Methodist DeBakey Cardiovascular Journal. 2020; 16: 22–26.
[120] Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, *et al.* 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. Journal of the American College of Cardiology. 2015; 65: e7–e26.
[121] Masoudi FA, Ponirakis A, de Lemos JA, Jollis JG, Kremers M, Messenger JC, *et al.* Trends in U.S. Cardiovascular Care: 2016 Re-

port from 4 ACC National Cardiovascular Data Registries. Journal of the American College of Cardiology. 2017; 69: 1427–1450.
[122] Moulopoulos S, Stamatelopoulos S, Petrou P. Intraaortic balloon assistance in intractable cardiogenic shock. European Heart Journal. 1986; 7: 396–403.
[123] Jurmann MJ, Siniawski H, Erb M, Drews T, Hetzer R. Initial experience with miniature axial flow ventricular assist devices for postcardiotomy heart failure. the Annals of Thoracic Surgery. 2004; 77: 1642–1647.
[124] Thiele H, Sick P, Boudriot E, Diederich K, Hambrecht R, Niebauer J, *et al.* Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. European Heart Journal. 2005; 26: 1276–1283.
[125] Cheng JM, den Uil CA, Hoeks SE, van der Ent M, Jewbali LSD, van Domburg RT, *et al.* Percutaneous left ventricular assist devices vs. intra-aortic balloon pump counterpulsation for treatment of cardiogenic shock: a meta-analysis of controlled trials. European Heart Journal. 2009; 30: 2102–2108.
[126] Thiele H, Jobs A, Ouweneel DM, Henriques JPS, Seyfarth M, Desch S, *et al.* Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials. European Heart Journal. 2017; 38: 3523–3531.
[127] Roffi M, Patrono C, Collet J, Mueller C, Valgimigli M, Andreotti F, *et al.* 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European Heart Journal. 2016; 37: 267–315.
[128] Combes A, Price S, Slutsky AS, Brodie D. Temporary circulatory support for cardiogenic shock. Lancet. 2020; 396: 199–212.
[129] Hsu P, Parker J, Egger C, Autschbach R, Schmitz-Rode T, Steinseifer U. Mechanical circulatory support for right heart failure: current technology and future outlook. Artificial Organs. 2012; 36: 332–347.
[130] Thiele H, Zeymer U, Neumann F, Ferenc M, Olbrich H, Hausleiter J, *et al.* Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet. 2013; 382: 1638–1645.
[131] Thiele H, Zeymer U, Thelemann N, Neumann FJ, Hausleiter J, Abdel-Wahab M, *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.
[132] Anderson MB, Goldstein J, Milano C, Morris LD, Kormos RL, Bhama J, *et al.* Benefits of a novel percutaneous ventricular assist device for right heart failure: the prospective RECOVER RIGHT study of the Impella RP device. the Journal of Heart and Lung Transplantation. 2015; 34: 1549–1560.
[133] Kapur NK, Esposito ML, Bader Y, Morine KJ, Kiernan MS, Pham DT, *et al.* Mechanical Circulatory Support Devices for Acute Right Ventricular Failure. Circulation. 2017; 136: 314–326.
[134] Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, *et al.* ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal. 2012; 33: 2569–2619.
[135] Barron HV, Every NR, Parsons LS, Angeja B, Goldberg RJ, Gore JM, *et al.* The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock complicating acute myocardial infarction: data from the National Registry of Myocardial Infarction 2. American Heart Journal. 2001; 141: 933–939.
[136] Zeymer U, Bauer T, Hamm C, Zahn R, Weidinger F, Seabra-Gomes R, *et al.* Use and impact of intra-aortic balloon pump on mortality in patients with acute myocardial infarction complicated by cardiogenic shock: results of the Euro Heart Survey on PCI. EuroIntervention. 2011; 7: 437–441.
[137] Curtis JP, Rathore SS, Wang Y, Chen J, Nallamothu BK, Krumholz HM. Use and Effectiveness of Intra-Aortic Balloon Pumps among Patients Undergoing High Risk Percutaneous Coronary Intervention: Insights from the National Cardiovascular Data Registry. Circulation: Cardiovascular Quality and Outcomes. 2012; 5: 21–30.
[138] Ohman EM, Nanas J, Stomel RJ, Leesar MA, Nielsen DWT, O'Dea D, *et al.* Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS Trial. Journal of Thrombosis and Thrombolysis. 2005; 19: 33–39.
[139] Prondzinsky R, Lemm H, Swyter M, Wegener N, Unverzagt S, Carter JM, *et al.* Intra-aortic balloon counterpulsation in patients with acute myocardial infarction complicated by cardiogenic shock: the prospective, randomized IABP SHOCK Trial for attenuation of multiorgan dysfunction syndrome. Critical Care Medicine. 2010; 38: 152–160.
[140] Perera D, Stables R, Thomas M, Booth J, Pitt M, Blackman D, *et a.* Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. Journal of the American Medical Association. 2010; 304: 867–874.
[141] Sjauw KD, Engström AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, *et al.* A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? European Heart Journal. 2009; 30: 459–468.
[142] Romeo F, Acconcia MC, Sergi D, Romeo A, Muscoli S, Valente S, *et al.* The outcome of intra-aortic balloon pump support in acute myocardial infarction complicated by cardiogenic shock according to the type of revascularization: a comprehensive meta-analysis. American Heart Journal. 2013; 165: 679–692.
[143] Unverzagt S, Buerke M, de Waha A, Haerting J, Pietzner D, Seyfarth M, *et al.* Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. Cochrane Database of Systematic Reviews. 2015; 3: CD007398.
[144] Ahmad Y, Sen S, Shun-Shin MJ, Ouyang J, Finegold JA, Al-Lamee RK, *et al.* Intra-aortic Balloon Pump Therapy for Acute Myocardial Infarction: a Meta-analysis. JAMA Internal Medicine. 2015; 175: 931–939.
[145] Lauten A, Engström AE, Jung C, Empen K, Erne P, Cook S, *et al.* Percutaneous left-ventricular support with the Impella-2.5-assist device in acute cardiogenic shock: results of the Impella-EUROSHOCK-registry. Circulation. Heart Failure. 2013; 6: 23–30.
[146] Ouweneel DM, Eriksen E, Seyfarth M, Henriques JPS. Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump for Treating Cardiogenic Shock: Meta-Analysis. Journal of the American College of Cardiology. 2017; 69: 358–360.
[147] Dhruva SS, Ross JS, Mortazavi BJ, Hurley NC, Krumholz HM, Curtis JP, *et al.* Association of Use of an Intravascular Microaxial Left Ventricular Assist Device vs Intra-aortic Balloon Pump with in-Hospital Mortality and Major Bleeding among Patients with Acute Myocardial Infarction Complicated by Cardiogenic Shock. Journal of the American Medical Association. 2020; 323: 734.
[148] O'Neill WW, Schreiber T, Wohns DHW, Rihal C, Naidu SS, Civitello AB, *et al.* The current use of Impella 2.5 in acute myocardial infarction complicated by cardiogenic shock: results from the USpella Registry. Journal of Interventional Cardiology. 2014; 27: 1–11.
[149] Basir MB, Schreiber T, Dixon S, Alaswad K, Patel K, Almany S, *et al.* Feasibility of early mechanical circulatory support in acute myocardial infarction complicated by cardiogenic shock: the Detroit cardiogenic shock initiative. Catheterization and Cardiovascular

Interventions. 2018; 91: 454–461.
[150] Schrage B, Ibrahim K, Loehn T, Werner N, Sinning JM, Pappalardo F, *et al.* Impella Support for Acute Myocardial Infarction Complicated by Cardiogenic Shock. Circulation. 2019; 139: 1249–1258.
[151] Valgimigli M, Steendijk P, Serruys PW, Vranckx P, Boomsma F, Onderwater E, *et al.* Use of Impella Recover(R) LP 2.5 left ventricular assist device during high-risk percutaneous coronary interventions; clinical, haemodynamic and biochemical findings. EuroIntervention. 2006; 2: 91–100.
[152] Dixon SR, Henriques JPS, Mauri L, Sjauw K, Civitello A, Kar B, *et al.* A Prospective Feasibility Trial Investigating the Use of the Impella 2.5 System in Patients Undergoing High-Risk Percutaneous Coronary Intervention (the PROTECT I Trial). JACC: Cardiovascular Interventions. 2009; 2: 91–96.
[153] Maini B, Naidu SS, Mulukutla S, Kleiman N, Schreiber T, Wohns D, *et al.* Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: the USpella Registry. Catheterization and Cardiovascular Interventions. 2012; 80: 717–725.
[154] O'Neill WW, Kleiman NS, Moses J, Henriques JPS, Dixon S, Massaro J, *et al.* A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation. 2012; 126: 1717–1727.
[155] Dangas GD, Kini AS, Sharma SK, Henriques JPS, Claessen BE, Dixon SR, *et al.* Impact of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump on prognostically important clinical outcomes in patients undergoing high-risk percutaneous coronary intervention (from the PROTECT II randomized trial). American Journal of Cardiology. 2014; 113: 222–228.
[156] Cohen MG, Ghatak A, Kleiman NS, Naidu SS, Massaro JM, Kirtane AJ, *et al.* Optimizing rotational atherectomy in high-risk percutaneous coronary interventions: insights from the PROTECT II study. Catheterization and Cardiovascular Interventions. 2014; 83: 1057–1064.
[157] Kar B, Gregoric ID, Basra SS, Idelchik GM, Loyalka P. The percutaneous ventricular assist device in severe refractory cardiogenic shock. Journal of the American College of Cardiology. 2011; 57: 688–696.
[158] Thomas JL, Al-Ameri H, Economides C, Shareghi S, Abad DG, Mayeda G, *et al.* Use of a percutaneous left ventricular assist device for high-risk cardiac interventions and cardiogenic shock. Journal of Invasive Cardiology. 2010; 22: 360–364.
[159] Bagai J, Webb D, Kasasbeh E, Crenshaw M, Salloum J, Chen J, *et al.* Efficacy and safety of percutaneous life support during high-risk percutaneous coronary intervention, refractory cardiogenic shock and in-laboratory cardiopulmonary arrest. Journal of Invasive Cardiology. 2011; 23: 141–147.
[160] Alli OO, Singh IM, Holmes DR, Pulido JN, Park SJ, Rihal CS. Percutaneous left ventricular assist device with TandemHeart for high-risk percutaneous coronary intervention: the Mayo Clinic experience. Catheterization and Cardiovascular Interventions. 2012; 80: 728–734.
[161] Zavalichi MA, Nistor I, Nedelcu A, Zavalichi SD, Georgescu CMA, Stătescu C, *et al.* Extracorporeal Membrane Oxygenation in Cardiogenic Shock due to Acute Myocardial Infarction: a Systematic Review. BioMed Research International. 2020; 2020: 1–9.
[162] Muller G, Flecher E, Lebreton G, Luyt C, Trouillet J, Bréchot N, *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 Medicine. 2016; 42: 370–378.
[163] Banning AS, Adriaenssens T, Berry C, Bogaerts K, Erglis A, Distelmaier K, *et al.* Veno-arterial extracorporeal membrane oxygenation (ECMO) in patients with cardiogenic shock: rationale and design of the randomised, multicentre, open-label EURO SHOCK trial. EuroIntervention. 2021; 16: e1227–e1236.
[164] Sakamoto S, Taniguchi N, Nakajima S, Takahashi A. Extracorporeal life support for cardiogenic shock or cardiac arrest due to acute coronary syndrome. Annals of Thoracic Surgery. 2012; 94: 1–7.
[165] Kim H, Lim S, Hong J, Hong Y, Lee CJ, Jung J, *et al.* Efficacy of veno-arterial extracorporeal membrane oxygenation in acute myocardial infarction with cardiogenic shock. Resuscitation. 2012; 83: 971–975.
[166] Xie A, Phan K, Tsai Y, Yan TD, Forrest P. Venoarterial extracorporeal membrane oxygenation for cardiogenic shock and cardiac arrest: a meta-analysis. Journal of Cardiothoracic and Vascular Anesthesia. 2015; 29: 637–645.
[167] Ouweneel DM, Schotborgh JV, Limpens J, Sjauw KD, Engström AE, Lagrand WK, *et al.* Extracorporeal life support during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis. Intensive Care Medicine. 2016; 42: 1922–1934.
[168] Chen Y, Chao A, Yu H, Ko W, Wu I, Chen RJ, *et al.* Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. Journal of the American College of Cardiology. 2003; 41: 197–203.
[169] Chen Y, Lin J, Yu H, Ko W, Jerng J, Chang W, *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: 554–561.
[170] Thiagarajan RR, Brogan TV, Scheurer MA, Laussen PC, Rycus PT, Bratton SL. Extracorporeal Membrane Oxygenation to Support Cardiopulmonary Resuscitation in Adults. Annals of Thoracic Surgery. 2009; 87: 778–785.
[171] Kagawa E, Dote K, Kato M, Sasaki S, Nakano Y, Kajikawa M, *et al.* Should we emergently revascularize occluded coronaries for cardiac arrest?: rapid-response extracorporeal membrane oxygenation and intra-arrest percutaneous coronary intervention. Circulation. 2012; 126: 1605–1613.
[172] Maxhera B, Albert A, Ansari E, Godehardt E, Lichtenberg A, Saeed D. Survival predictors in ventricular assist device patients with prior extracorporeal life support: selecting appropriate candidates. Artificial Organs. 2014; 38: 727–732.
[173] Aso S, Matsui H, Fushimi K, Yasunaga H. The Effect of Intraaortic Balloon Pumping under Venoarterial Extracorporeal Membrane Oxygenation on Mortality of Cardiogenic Patients: an Analysis Using a Nationwide Inpatient Database. Critical Care Medicine. 2016; 44: 1974–1979.
[174] Mandawat A, Rao SV. Percutaneous Mechanical Circulatory Support Devices in Cardiogenic Shock. Circulation. Cardiovascular Interventions. 2018; 10: e004337.
[175] John R, Long JW, Massey HT, Griffith BP, Sun BC, Tector AJ, *et al.* Outcomes of a multicenter trial of the Levitronix CentriMag ventricular assist system for short-term circulatory support. Journal of Thoracic and Cardiovascular Surgery. 2011; 141: 932–939.
[176] Kapur NK, Paruchuri V, Jagannathan A, Steinberg D, Chakrabarti AK, Pinto D, *et al.* Mechanical circulatory support for right ventricular failure. JACC: Heart Failure. 2013; 1: 127–134.
[177] Takayama H, Truby L, Koekort M, Uriel N, Colombo P, Mancini DM, *et al.* Clinical outcome of mechanical circulatory support for refractory cardiogenic shock in the current era. Journal of Heart and Lung Transplantation. 2013; 32: 106–111.
[178] Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al.* 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2020; 42: 1289–1367.
[179] Berger PB, Holmes DR, Stebbins AL, Bates ER, Califf RM, Topol EJ. Impact of an aggressive invasive catheterization and revascularization strategy on mortality in patients with cardiogenic shock in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial. An observational study. Circulation. 1997; 96: 122–127.
[180] French JK, Feldman HA, Assmann SF, Sanborn T, Palmeri ST, Miller D, *et al.* Influence of thrombolytic therapy, with or with-

out intra-aortic balloon counterpulsation, on 12-month survival in the SHOCK trial. American Heart Journal. 2003; 146: 804–810.
[181] Col NF, Gurwitz JH, Alpert JS, Goldberg RJ. Frequency of inclusion of patients with cardiogenic shock in trials of thrombolytic therapy. American Journal of Cardiology. 1994; 73: 149–157.
[182] Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, *et al.* Early Revascularization and Long-term Survival in Cardiogenic Shock Complicating Acute Myocardial Infarction. Journal of the American Medical Association. 2006; 295: 2511.
[183] Thiele H, Akin I, Sandri M, de Waha-Thiele S, Meyer-Saraei R, Fuernau G, *et al.* One-Year Outcomes after PCI Strategies in Cardiogenic Shock. New England Journal of Medicine. 2018; 379: 1699–1710.
[184] Tarantini G, D'Amico G, Tellaroli P, Colombo C, Brener SJ. Meta-Analysis of the Optimal Percutaneous Revascularization Strategy in Patients with Acute Myocardial Infarction, Cardiogenic Shock, and Multivessel Coronary Artery Disease. American Journal of Cardiology. 2017; 119: 1525–1531.
[185] de Waha S, Jobs A, Eitel I, Pöss J, Stiermaier T, Meyer-Saraei R, *et al.* Multivessel versus culprit lesion only percutaneous coronary intervention in cardiogenic shock complicating acute myocardial infarction: a systematic review and meta-analysis. European Heart Journal Acute Cardiovascular Care. 2018; 7: 28–37.
[186] Kolte D, Sardar P, Khera S, Zeymer U, Thiele H, Hochadel M, *et al.* Culprit Vessel-only Versus Multivessel Percutaneous Coronary Intervention in Patients with Cardiogenic Shock Complicating ST-Segment-Elevation Myocardial Infarction: a Collaborative Meta-Analysis. Circulation: Cardiovascular Interventions. 2017; 10: e005582.
[187] Bertaina M, Ferraro I, Omedè P, Conrotto F, Saint-Hilary G, Cavender MA, *et al.* Meta-Analysis Comparing Complete or Culprit only Revascularization in Patients with Multivessel Disease Presenting with Cardiogenic Shock. American Journal of Cardiology. 2018; 122: 1661–1669.
[188] Mehta SR, Wood DA, Storey RF, Mehran R, Bainey KR, Nguyen H, *et al.* Complete Revascularization with Multivessel PCI for Myocardial Infarction. New England Journal of Medicine. 2019; 381: 1411–1421.
[189] Marquis-Gravel G, Zeitouni M, Kochar A, Jones WS, Sketch MH, Rao SV, *et al.* Technical consideration in acute myocardial infarction with cardiogenic shock: a review of antithrombotic and PCI therapies. Catheterization and Cardiovascular Interventions. 2020; 95: 924–931.
[190] Mason PJ, Shah B, Tamis-Holland JE, Bittl JA, Cohen MG, Safirstein J, *et al.* An Update on Radial Artery Access and Best Practices for Transradial Coronary Angiography and Intervention in Acute Coronary Syndrome: a Scientific Statement from the American Heart Association. Circulation: Cardiovascular Interventions. 2018; 11: e000035.
[191] Mamas MA, Anderson SG, Ratib K, Routledge H, Neyses L, Fraser DG, *et al.* Arterial access site utilization in cardiogenic shock in the United Kingdom: is radial access feasible? American Heart Journal. 2014; 167: 900–8.e1.
[192] Pancholy SB, Palamaner Subash Shantha G, Romagnoli E, Kedev S, Bernat I, Rao SV, *et al.* Impact of access site choice on outcomes of patients with cardiogenic shock undergoing percutaneous coronary intervention: a systematic review and meta-analysis. American Heart Journal. 2015; 170: 353–361.
[193] Rashid M, Rushton CA, Kwok CS, Kinnaird T, Kontopantelis E, Olier I, *et al.* Impact of Access Site Practice on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention Following Thrombolysis for ST-Segment Elevation Myocardial Infarction in the United Kingdom: an Insight from the British Cardiovascular Intervention Society Dataset. JACC: Cardiovascular Interventions. 2017; 10: 2258–2265.
[194] Champion S, Gaüzère BA, Lefor Y. Drug-eluting stents should not be used in ST-elevated myocardial infarction with cardiogenic shock. Archives of Internal Medicine. 2012; 172: 1613–1614.
[195] Ledwoch J, Fuernau G, Desch S, Eitel I, Jung C, de Waha S, *et al.* Drug-eluting stents versus bare-metal stents in acute myocardial infarction with cardiogenic shock. Heart. 2017; 103: 1177–1184.
[196] Chen D, Mao C, Tsai M, Chen S, Lin Y, Hsieh I, *et al.* Clinical outcomes of drug-eluting stents versus bare-metal stents in patients with cardiogenic shock complicating acute myocardial infarction. International Journal of Cardiology. 2016; 215: 98–104.
[197] Pöss J, Köster J, Fuernau G, Eitel I, de Waha S, Ouarrak T, *et al.* Risk Stratification for Patients in Cardiogenic Shock After Acute Myocardial Infarction. Journal of the American College of Cardiology. 2017; 69: 1913–1920.