



Clinical Review of Cardiogenic Shock After Acute Myocardial Infarction

— Revascularization, Mechanical Circulatory Support, and Beyond —

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Owing to recent advances in early reperfusion and pharmacological therapies, the prognosis of patients with acute myocardial infarction (AMI) has considerably improved over the past decades. However, the mortality rate remains high at ~40–50% after AMI when complicated by cardiogenic shock. Although immediate coronary revascularization of the infarct-related artery has been the only evidence-based treatment, temporary mechanical circulatory support with a microaxial flow pump (Impella) has become another therapeutic option supported by randomized trial data in highly selected patients. Here we summarize the latest evidence concerning clinical challenges in patients with AMI and cardiogenic shock.

Key Words: Acute myocardial infarction; Cardiogenic shock; Mechanical circulatory support

The prognosis of acute myocardial infarction (AMI) has considerably improved over the past decades, owing to recent advances in pharmacological treatment, standardized care, and early reperfusion strategies with percutaneous coronary intervention (PCI).^{1–3} However, even in the current the clinical outcomes of patients with AMI are poor when complicated by cardiogenic shock (CS). To date, short-term mortality rates (during hospitalization or at 30 days) after AMI in patients without CS have been decreasing to <5%, but remain high, ranging from 40% to 50%, in observational and randomized control trial (RCT) data.^{4–12} Although immediate coronary revascularization of the infarct-related artery in patients with ST-segment elevation myocardial infarction (STEMI) has been the only evidence-based treatment strategy in the AMI-CS scenario,⁶ the recent DanGer Shock trial demonstrated the potential survival benefit of a mechanical circulatory support (MCS) device in selected patients in this setting.¹² In this review, we summarize the clinical evidence concerning AMI-CS, particularly focusing on coronary revascularization, MCS devices, and patient care.

Pathophysiology, Epidemiology, and Severity

CS is a hemodynamically complex syndrome characterized by peripheral hypoperfusion and organ dysfunction due to primary cardiac impairment.¹³ In general, CS is defined as

systolic blood pressure (BP) <90 mmHg (for 30 min) or requiring vasoactive agents or MCS to maintain BP.¹⁴ Although often not objective, signs of hypotension and perfusion (e.g., altered mental status and cold, clammy skin and extremities) are also important in the diagnosis of CS. Objective measures may include oliguria with urine output <30 mL/h and levels of atrial lactate >2.0–3.0 mmol/L.^{14,15} There is considerable variability in CS acuity, underlying etiology, volume status, and systemic vascular resistance, for which the term “mixed CS” was recently defined.¹⁶ Mixed CS can be categorized as CS with ≥1 additional shock etiology of such variables, most commonly with low systemic vascular resistance (e.g., inflammatory response-like syndrome).¹⁶ Given the hemodynamic complexities and poor prognosis of patients with (mixed) CS, individualized considerations and treatment strategies are warranted (**Figure**).

Among patients with CS, AMI is the most common etiology, and CS occurs in 5–10% of cases in the setting of AMI.¹⁷ Impaired cardiac output leads to systemic hypoperfusion and maladaptive cycles of ischemia, inflammation, vasoconstriction, and volume overload in patients with AMI-CS, resulting in multiorgan failure and death.¹⁵ In contrast to AMI without CS, short-term mortality rates in patients with AMI-CS remains high even in the current era. Some observational studies have shown better survival rates in recent years,⁴ but other observational and RCT data indicate unchanged mortality rates over past decades

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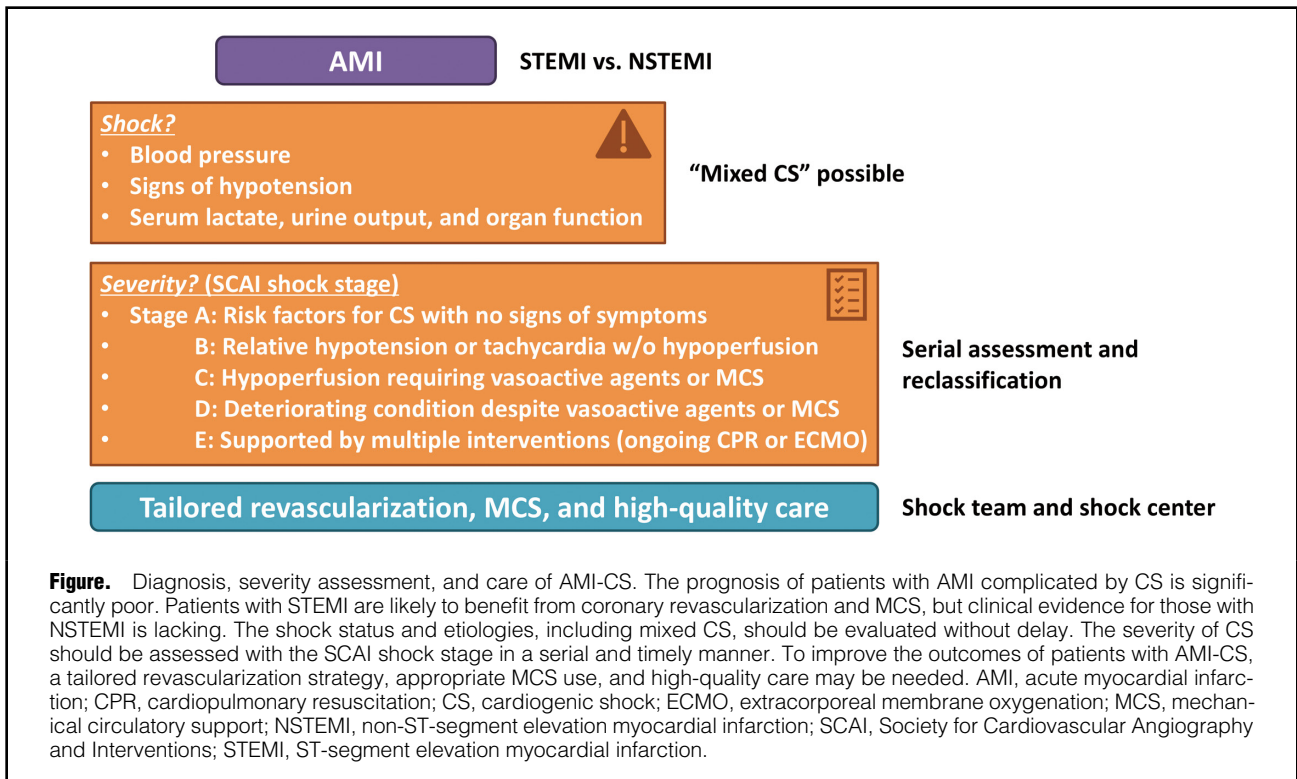
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from 40% to 50% after AMI-CS.^{6-12,18} In addition, AMI-CS may have worse clinical outcomes than CS related to heart failure.¹⁹ A population-based cohort study in Canada showed that even among survivors to discharge, >40% of patients required increased support in care from their baseline, and nearly 50% were readmitted and approximately 15% died within 1 year after AMI-CS.²⁰ These findings highlight the need to improve short- and long-term morbidity and mortality with better medical treatment and care of patients with AMI-CS.

In order to universally define the clinical severity, and enhance care and research trials, of CS, the Society for Cardiovascular Angiography and Interventions (SCAI) shock stage was developed in 2019.²¹ The diagnostic ability of the SCAI shock classification has been validated by multiple groups across a broad spectrum of CS.²¹ Subsequently in 2023, the Shock Academic Research Consortium (SHARC) further proposed standardized definitions for CS research and MCS devices.²² Although the original SCAI shock classification system lacked uniform criteria for each stage, a novel approach using clinical variables (BP, clinical presentation, and treatment intensity) and biomarkers (lactate, alanine transaminase, and pH) was proposed to define CS stages.²³ Importantly, because the severity of CS (e.g., SCAI shock stage) changes in most patients within the first 24–72h, timely reassessment and reclassification, including response to therapy, should be considered to convey better treatment strategies and decision-making (Figure).^{24,25}

Coronary Revascularization

Although several therapeutic strategies, such as inotropes, glycoprotein IIb/IIIa inhibitors, nitric oxide synthase inhi-

bition, and hypothermia, have been tested in RCT settings with small sample sizes, few have shown a clinically significant benefit in patients with AMI complicated by CS.¹⁴ Nonetheless, the pivotal SHOCK trial demonstrated that emergency coronary revascularization by PCI or coronary artery bypass grafting reduced all-cause deaths after STEMI with CS.⁶ This landmark RCT included 302 patients with STEMI complicated by CS from 1993 to 1998 and randomized them into emergency revascularization (as soon as possible and within 6h) or medical therapy (Table 1). Intra-aortic balloon pumping (IABP) and thrombolytic therapy were recommended and delayed revascularization (≥ 54 h after randomization) was allowed in the medical therapy group.⁶ In fact, revascularization procedures were performed in 86.8% and 25.3% of the revascularization and medical therapy groups, respectively. The primary endpoint of the SHOCK trial, the superiority in 30-day mortality in the revascularization group, was not met, but the survival benefit of revascularization was shown at 6 months and thereafter up to 6 years.^{6,26} In the current guidelines, immediate coronary angiography and PCI of the infarct-related artery are recommended in patients with CS complicating acute coronary syndrome (ACS), although the effectiveness of revascularization is uncertain. ST-segment elevation is not shown on ECG.²⁷ Because RCTs in the field of AMI-CS are likely to enroll lower-risk patients, leading to lower mortality rates on more aggressive treatment as compared with observational studies,²⁸ whether the evidence from RCTs can be extrapolated to real-world clinical practice is always debatable. However, the survival benefit of PCI was confirmed in observational studies of STEMI and CS even in the elderly.²⁹ Additionally, in recent decades, skills and knowledge in PCI have improved considerably.³⁰⁻⁷⁹ Another important RCT in

Table 1. Key Randomized Control Trials of Coronary Revascularization in AMI-CS		
	SHOCK ⁶	CULPRIT-SHOCK ⁷
Publication year	1999	2017
Sample size	302	686
No. of study sites	30	83
Region	USA, Canada, and others	Europe (11 countries)
Intervention	Emergency revascularization	Immediate MV-PCI
Control	Medical therapy	Culprit-only PCI
Study population	STEMI	AMI
Key inclusion criteria	End-organ malperfusion ^b	MV-CAD
SBP (mmHg)	<90	<90
Lactate level (mmol/L)	NA	>2.0
Key exclusion criteria	NA	CPR >30 min
Baseline characteristics		
Age (years)	65.8 ^c	70 ^f
STEMI	100%	62.5%
CA or resuscitation	28.3%	53.6%
Mechanical ventilation	78–88%	81.3%
SBP (mmHg)	86.5–89.0 ^c	100 ^f
Heart rate (beats/min)	100.1–103.3 ^c	90–91 ^f
Lactate level (mmol/L)	NA	5 ^g
LAD or LMCA ^a	57.4–63.6% ^d	49.8%
LVEF (%)	29.1–32.5 ^c	30–33 ^f
Mortality rate	46.7% vs. 56.0% ^e	51.6% vs. 43.3% ^e
Primary results	Survival benefit of emergency revascularization was not significant at 30 days but evident at 6 months	More deaths and RRT in the MV-PCI group
Safety results	No safety concerns of revascularization	Bleeding and RRT rates were numerically higher in the MV-PCI group

^aCulprit coronary artery; ^bCool extremities or urine output <30 mL/h and heart rate \geq 60 beats/min; ^cMean; ^dAnterior myocardial infarction; ^eAt 30 days; ^fMedian; ^gApproximate value. AMI, acute myocardial infarction; CA, cardiac arrest; CAD, coronary artery disease; CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; LAD, left anterior descending coronary artery; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MV, multivessel; NA, not applicable; PCI, percutaneous coronary intervention; RRT, renal replacement therapy; SBP, systolic blood pressure; STEMI, ST-segment elevation myocardial infarction.

terms of revascularization is the CULPRIT-SHOCK trial, in which the clinical benefit of immediate multivessel PCI was tested in patients with AMI-CS (Table 1).⁷ Immediate complete revascularization in the setting of CS may intuitively improve clinical outcomes in patients with AMI and multivessel coronary disease, but the trial demonstrated no benefit, and even harm, of the immediate multivessel PCI strategy.⁷ Several important limitations of the CULPRIT-SHOCK trial (e.g., crossover phenomenon, chronic total occlusion, and staged PCI) should be acknowledged,⁸⁰ but the evidence is compelling. Therefore, although immediate PCI is a valuable and standard-of-care strategy in patients with AMI-CS, routine complete revascularization should be avoided in those with multivessel coronary disease.

MCS

To theoretically improve clinical outcomes, temporary MCS devices, including IABP, extracorporeal membrane oxygenation (ECMO), and a microaxial left ventricular assist device (Impella, Abiomed, Danvers, USA), have been utilized in clinical practice. IABP is still one of the most frequently used MCS devices globally,⁸¹ and ECMO may be unavoidable in some patient populations (e.g., refractory cardiac arrest). However, no significant benefit of these devices has been confirmed in patients with AMI-CS in RCT settings. The key RCTs, such as the IABP-

SHOCK II, IMPRESS, EURO SHOCK, and the ECLS-SHOCK trials, have failed to demonstrate survival benefit of MCS devices in patients with AMI complicated by CS (Table 2).^{8–11} Additionally, MCS devices, particularly ECMO and Impella, are associated with increased risks of major bleeding and vascular complications (Table 2). Thus, the 2023 European guidelines indicated that short-term MCS may be considered in patients with ACS and severe/refractory CS (Class IIb, Level of Evidence C).²⁷ In this context, the DanGer Shock trial successfully showed the potential survival benefit of the Impella device in patients with STEMI and CS.¹² This pivotal trial included a total of 360 patients at 14 European centers over 10 years, suggesting that the study population in the DanGer Shock was highly selected. Notable differences in the inclusion criteria between the DanGer Shock trial and other key RCTs of MCS devices include an exclusively STEMI population, higher cutoff value of systolic BP levels, and the threshold of left ventricular ejection fraction, but the greatest difference may be comatose after out-of-hospital cardiac arrest as an exclusion criterion in the DanGer Shock trial (Table 2). Indeed, the rates of cardiac arrest or resuscitation and mechanical ventilation at baseline were considerably lower in the DanGer Shock trial than in other RCTs (Table 2). The use of the Impella CP was associated with lower mortality rates than for usual care alone at 180 days in patients with STEMI and CS

	IABP-SHOCK II⁸	IMPRESS⁹	EURO SHOCK¹⁰	ECLS-SHOCK¹¹	DanGer Shock¹²
Publication year	2012	2017	2023	2023	2024
Sample size	600	48	35	417	355
No. of study sites	37	2	15	44	14
Region	Germany	The Netherlands and Norway	Europe (6 countries)	Germany and Slovenia	Europe (3 countries)
Intervention	IABP	Impella CP	VA-ECMO	VA-ECMO	Impella CP
Control	Standard care	IABP	Standard care	Standard care	Standard care
Study population	AMI	STEMI	AMI	AMI	STEMI
Key inclusion criteria	End-organ malperfusion ^b	Mechanical ventilation	CS after primary PCI	End-organ malperfusion ^b	LVEF <45%
SBP (mmHg)	<90	<90	<90	<90	<100
Lactate level (mmol/L)	>2.0	NA	NA	>3.0	>2.5
Key exclusion criteria	CPR >30 min	NA	Ongoing CPR pH <7	CPR >45 min	Comatose after OHCA Right HF
Baseline characteristics					
Age (years)	69–70 ^c	58–59 ^e	67–68 ^c	62–63 ^c	67–69 ^c
STEMI	68.9%	100%	NA	67.2%	100%
CA or resuscitation	45.0%	91.7%	48.6%	77.7%	20.3%
Mechanical ventilation	82.0%	100%	71.4%	88.9%	17.7%
SBP (mmHg)	89–90 ^c	81–84 ^e	82–95 ^c	95–97 ^c	82–84 ^c
Heart rate (beats/min)	92 ^c	81–83 ^e	NA	90–95 ^c	94–95 ^c
Lactate level (mmol/L)	3.6–4.7 ^c	7.5–8.9 ^e	8.1–10.2 ^{e,g}	6.8–6.9 ^c	4.5–4.6 ^c
LAD or LMCA ^a	52.4%	70.8%	61.8%	57.8%	71.8%
LVEF (%)	35 ^c	NA ^f	20–25 ^c	30 ^c	25 ^c
Mortality rate	39.7% vs. 41.3% ^d	45.8% vs. 50.0% ^d	43.8% vs. 61.1% ^d	47.8% vs. 49.0% ^d	45.8% vs. 58.5% ^h
Primary results	IABP did not reduce 30-day mortality	Impella CP and IABP were similar in 30-day mortality	VA-ECMO did not reduce 30-day mortality	VA-ECMO did not reduce 30-day mortality	Impella reduced 180-day mortality
Safety results	No safety concerns of IABP	More bleeding in the Impella group	More bleeding in the VA-ECMO group	More bleeding and vascular complications in the VA-ECMO group	More bleeding and other complications in the Impella group

^aCulprit coronary artery; ^bAltered mental status, cold, clammy skin and extremities, and oliguria with urine output <30 mL/h; ^cMedian; ^dAt 30 days; ^eMean; ^fLVEF <20% in 32.5% and 20–40% in 40.0%; ^gPeak level; ^hAt 180 days. HF, heart failure; IABP, intra-aortic balloon pump; OHCA, out-of-hospital cardiac arrest; VA-ECMO, venoarterial extracorporeal membrane oxygenation. Other abbreviations as in Table 1.

(45.8% vs. 58.5%, $P=0.04$).¹² However, the survival benefit of the Impella was not significant at 30 days, which is a conventional timeframe in previous RCTs, and the device was clearly associated with increased risks of major complications.¹² The results of the DanGer Shock trial may be a milestone in the field of CS but should be cautiously interpreted, as Thiele et al. mentioned.⁸² Subsequently, Thiele et al. showed a patient-level meta-analysis using data from 9 RCTs of ECMO and the Impella device in patients with AMI-CS, in which active MCS device use did not result in a better survival rate at 180 days.⁸³ However, when focusing only on patients with STEMI and CS without risk of hypoxic brain injury, a reduction in mortality rate by use of the MCS devices was found. Thus, they concluded that MCS devices (ECMO and Impella) should be restricted to such patients only.⁸³ Given that several well-designed observational studies have consistently demonstrated no benefit (or even harm) of the Impella device in real-world clinical settings,^{84,85} Impella use may not be recommended outside the DanGer Shock trial population. A recent registry study showed that among patients admitted to a contemporary cardiac intensive care unit, ~30% with STEMI-CS and ~5% of those with any CS presentation would meet the major eligibility criteria for the DanGer

Shock trial.⁸⁶ To facilitate patient selection for MCS devices, dedicated risk scores for IABP, ECMO, and the Impella have been developed (Table 3).^{87–89} The indication of MCS device, particularly for the Impella, may not be appropriate in patients with considerably high scores on such risk-predicting models or in those with impaired consciousness after cardiac arrest.⁹⁰ In addition, data are scarce on MCS using Impella plus ECMO.⁹¹ Taken together, MCS devices are potentially useful in patients with AMI complicated by CS, among which the Impella device may be promising in improving clinical outcomes in highly and appropriately selected patient populations.

Medical Care in CS

In patients with ACS, particularly when complicated by CS, critical care involves management and treatment before hospitalization. For instance, prehospital 12-lead ECG performed in collaboration with emergency medical services may be associated with better ACS care.^{92–99} In the hospitalization setting, team-based management in experienced centers has been shown to improve outcomes in high-mortality conditions such as trauma, sepsis, stroke, and cardiac arrest.¹⁰⁰ In patients with AMI complicated by

Table 3. Dedicated Risk Scores for MCS Devices			
	IABP-SHOCK II risk score ⁸⁷	SAVE-score ⁸⁸	J-PVAD risk score ⁸⁹
Publication year	2017	2015	2024
MCS device	IABP	VA-ECMO	Impella
Data source	IABP-SHOCK II trial	ELSO registry	J-PVAD
Derivation cohort	AMI-CS (n=480)	CS (n=3,846)	CS (n=1,701)
No. of items	6	12	12
Components	Age; Previous stroke; BG; Creatinine; Lactate; TIMI flow grade	Etiology; Age; BW; Organ failure; CKD; Intubation duration; Inspiratory pressure; CA; DBP; PP; HCO ₃ ; Constant value	Age; Sex; BMI; Myocarditis; IHCA; VA-ECMO; MAP; Lactate; LDH; T-Bil; Creatinine; Albumin
Outcome	30-day mortality	In-hospital mortality	In-hospital mortality
C-statistic	0.73–0.79 ^a	0.68 ^b	0.76 ^b

^aInternal and external validation. ^bInternal validation. BG, blood glucose; BMI, body mass index; BW, body weight; CKD, chronic kidney disease; DBP, diastolic blood pressure; ELSO, Extracorporeal Life Support Organization; IABP, intra-aortic balloon pump; IHCA, in-hospital cardiac arrest; J-PVAD, Japanese registry for Percutaneous Ventricular Assist Device; LDH, lactate dehydrogenase; MAP, mean arterial pressure; MCS, mechanical circulatory support; PP, pulse pressure; SAVE, survival after veno-arterial-ECMO; T-Bil, total bilirubin; TIMI, Thrombolysis in Myocardial Infarction. Other abbreviations as in Tables 1,2.

CS, a tailored revascularization strategy and appropriate MCS are often needed. Because these therapeutic strategies require resource-intensive skills and expertise, high-quality care may play a significant role in this patient population (Figure). The concept of a “shock team”, consisting of specialists in critical care cardiology and MCS devices, advanced heart failure and transplant cardiology, interventional cardiology, cardiac surgery, and others, has been introduced, and the clinical effectiveness of this approach has been reported.^{101,102} An observational study in North America indicated that in centers with a shock team, invasive hemodynamic monitoring and use of advanced MCS devices (e.g., ECMO and Impella) were more frequent and short-term mortality rates were lower in patients with CS, as compared with institutions without shock teams.¹⁰² The National Cardiogenic Shock Initiative in the USA was a single-arm, prospective observation showing that treatment strategies based on a dedicated protocol for AMI-CS, including early (upfront) MCS device use, immediate PCI, invasive hemodynamic monitoring, weaning or escalation of support, and high-quality care in the intensive care unit, resulted in a relatively low mortality rate during hospitalization (i.e., 29%).¹⁰³ Similarly, the concept of “shock center” is another approach to improving the quality of care in AMI-CS. An administrative database study demonstrated an association between lower CS case volume and higher in-hospital mortality rates in shock patients.¹⁰⁴ In addition, volume-outcome relationships have been reported in primary PCI and with the use of MCS devices.^{105–108} Therefore, appropriate institutional distribution and a regionalized shock network (i.e., “hub and spoke” model) need to be established, including transfer to shock centers at the prehospital level of emergency medical services, for the improved prognosis of patients with AMI and CS (Figure). The potential of other care strategies in AMI-CS (e.g., BP control) will be tested in future clinical studies.¹⁰⁹

Conclusions

Immediate PCI for coronary recanalization and MCS with the Impella device may improve outcomes of patients with AMI complicated by CS, as supported by RCT data. However, the clinical evidence is largely restricted to selected patient populations. For instance, such evidence

is lacking in patients with non-STEMI. Beyond revascularization and MCS, high-quality care at the institutional and regional levels with a multidisciplinary approach is relevant. Further research and action are needed to ameliorate the clinical outcomes of this vulnerable patient population.

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