Contemporary Management of Concomitant Cardiac Arrest and Cardiogenic Shock Complicating Myocardial Infarction

Saraschandra Vallabhajosyula, MD, MSc; Dhiran Verghese, MD; Timothy D. Henry, MD; Jason N. Katz, MD, MHS; William J. Nicholson, MD; Wissam A. Jaber, MD; and Jacob C. Jentzer, MD

Abstract

Cardiogenic shock (CS) and cardiac arrest (CA) are the most life-threatening complications of acute myocardial infarction. Although there is a significant overlap in the pathophysiology with approximately half the patients with CS experiencing a CA and approximately two-thirds of patients with CA developing CS, comprehensive guideline recommendations for management of CA + CS are lacking. This paper summarizes the current evidence on the incidence, pathophysiology, and short- and long-term outcomes of patients with acute myocardial infarction complicated by concomitant CA + CS. We discuss the hemodynamic factors and unique challenges that need to be accounted for while developing treatment strategies for these patients. A summary of expert-based step-by-step recommendations to the approach and treatment of these patients, both in the field before admission and in-hospital management, are presented.

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Acute myocardial infarction (AMI), including ST-elevation myocardial infarction (STEMI) and non–ST-elevation myocardial infarction (NSTEMI), is one of the most common acute cardiovascular conditions, accounting for approximately 800,000 hospitalizations annually in the United States and contributing to substantial morbidity and mortality.13 Cardiogenic shock (CS) and cardiac arrest (CA) are the most life-threatening complications of AMI, occurring in nearly 5% to 10% of all admissions, and together they account for more than 60% to 80% of deaths due to AMI.3,5 Despite advances in the field of acute cardiovascular care, the in-hospital mortality associated with these individual conditions exceeds 30% to 50%.5,8

Acute myocardial infarction leading to left ventricular dysfunction is the most frequent acute trigger for both CS and CA.1,3 Traditionally, these two devastating complications of AMI have been studied in isolation. However, approximately half of the patients with CS from AMI experience a CA and two-thirds of patients with CA have CS requiring vasopressors.6,9-12 The recent expert consensus statement on the classification of CS from the Society of Cardiovascular Angiography and Intervention (SCAI) emphasized the additional risk portended by CA regardless of the severity of CS, describing CA as a “risk modifier” at every stage of CS.13 Prior work on patients admitted to the cardiac intensive care unit has shown CA to result in worse outcomes across the spectrum of cardiogenic shock defined by the SCAI shock stages.7,9

There is a comparative dearth of studies and guideline recommendations specifically focusing on the clinical management of patients with concomitant CA+CS, and in many instances these patients have been systematically excluded from clinical trials.9,11,14-20 It is imperative to further understand the interaction of CA+CS with...
respect to management and standardization of care for these patients, particularly considering the potential for treatments targeting each individual condition to adversely affect management of the other.4

INCIDENCE
Cardiogenic shock is noted to complicate nearly 5% to 10% of AMI admissions, with higher rates observed in STEMI compared with NSTEMI.3,4,21 Older studies on the temporal trends of AMI-CS through the early 2000s showed a decreasing trend of CS in patients with AMI, likely related to the increased use of primary percutaneous coronary intervention (PPCI) for early revascularization.22-25 However, more recent studies have confirmed an increase in the prevalence of CS complicating AMI admissions (Table 1).3,4,26-28 Advanced age, greater comorbidity, higher burden of underlying ischemic substrate, higher prevalence of heart failure, and cardiomyopathy may be some of the factors contributing to the recent increasing prevalence of CS complicating AMI.3 Cardiac arrest appears to complicate approximately 5% of AMI, including 7% to 8% of STEMI and 1% to 2% of NSTEMI admissions.3,11,26-29 As with CS, there has been an increase in the prevalence of in-hospital CA and out-of-hospital CA (OHCA) in patients with AMI (Table 2).3,28,30-33 In two recent large randomized clinical trials enrolling AMI-CS patients, 45% to 54% had preceding AMI-CS, with the prevalence of CA exceeding 90% in some clinical trials in this population.34-36

Data from large registries have shown that 2.4% to 3.4% of AMI patients presented with acute myocardial infarction complicated by cardiogenic shock and cardiac arrest (AMICS-CA).3,38 Analysis of national data noted 2.7% of all STEMI admissions and 0.6% of all NSTEMI admissions to be complicated by a combination of CA+CS.3,28 A single-center analysis of the Minneapolis Heart Institute regional STEMI program noted that 4.1% of STEMI patients had concomitant CA and CS.39 In patients with AMI and CA from contemporary registries, concomitant CS was present in 38% to 45% of the patients, including 43% to 51% with STEMI and 38% with NSTEMI.10-12 Using a national database, our group identified that 30% of STEMI admissions and 11% of NSTEMI admissions with either CS or CA had a combination of both entities.3,28

PATHOPHYSIOLOGY
Cardiac arrest following AMI-CS typically occurs secondary to ventricular tachycardia (VT) or ventricular fibrillation (VF).40 Ventricular arrhythmias are a major potential cause of death in CS.21,41 Patients with STEMI have a higher incidence of ventricular arrhythmias, explaining their higher risk of CA.31 Pulseless electrical activity (PEA) and asystole can occur as manifestations of refractory CS (SCAI shock stage E) or refractory VF.42,43 The presence of CA worsens the trajectory of patients with CS and has been associated with an incremental mortality at each SCAI shock state.7,29

Multiple interacting acute processes superimposed on the underlying structural
heart disease may contribute to post-arrest myocardial dysfunction (PAMD), a reversible cardiac stunning process which can trigger or aggravate CS after CA (Figure 1). Post-arrest myocardial dysfunction has been reported in approximately two-thirds of patients resuscitated from CA, but it can be hard to disentangle clinically from underlying cardiomyopathy or myocardial injury resulting from AMI. Post-arrest myocardial dysfunction after CA can be reversible with spontaneous improvement in cardiac output (CO) and left ventricular (LV) function noted over time, typically following a time course of 12 to 24 hours after return of spontaneous circulation.

Three major pathways contribute to the specific pathophysiology of PAMD and CS after CA: 1) myocardial dysfunction developing as a result of ischemia-reperfusion injury; 2) cytokine excess and a systemic inflammatory response; and 3) catecholamine-induced myocardial toxicity. Cardiac arrest leads to transient global myocardial ischemia and cellular energy depletion causing intracellular sodium and calcium overload with initiation of cellular apoptosis. Reperfusion after transient ischemia leads to the release of large amounts of toxic reactive oxygen species and a second wave of cellular injury contributing to myocardial stunning and triggering a systemic inflammatory response. The systemic inflammation that follows return of spontaneous circulation (ROSC) leads to pathologic vasodilation, depressed cardiac output,

### TABLE 1. Trends in the Incidence of CS Complications

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Study population</th>
<th>Incidence of CS at start of the study</th>
<th>Incidence of CS towards the end of the study</th>
<th>Trend in incidence of AMI-CS</th>
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<tbody>
<tr>
<td><strong>AMI</strong></td>
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<tr>
<td>Fang et al&lt;sup&gt;22&lt;/sup&gt;</td>
<td>25 years</td>
<td>National Hospital Discharge Survey data — USA</td>
<td>3.9 % of AMI hospitalizations</td>
<td>1.7% of AMI hospitalizations</td>
<td>Decreasing trend</td>
</tr>
<tr>
<td>Jeger et al&lt;sup&gt;23&lt;/sup&gt;</td>
<td>10 years</td>
<td>AMIS plus registry — Switzerland Retrospective analysis from Worcester metropolitan area</td>
<td>Overall rate of CS, 12.9%</td>
<td>Overall rate of CS, 5.5%</td>
<td>Decreasing trend</td>
</tr>
<tr>
<td>Goldberg et al&lt;sup&gt;24&lt;/sup&gt;</td>
<td>30 years</td>
<td>1975-2005 Retrospective analysis from Worcester metropolitan area</td>
<td>7.5% of AMI hospitalizations</td>
<td>4.1% (5.5) of AMI hospitalizations</td>
<td>Stable between 1975-1997 followed by a steady decline 1997-2005</td>
</tr>
<tr>
<td>Awad et al&lt;sup&gt;25&lt;/sup&gt;</td>
<td>8 years</td>
<td>1997-2007 GRACE study — North and South America</td>
<td>≈5.1 % of AMI admissions</td>
<td>≈3.6% of AMI admissions</td>
<td>Decreasing trend</td>
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<tr>
<td>Lauridsen et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>6 years</td>
<td>2010-2015 Danish National Patient Registry</td>
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<td>Increasing trend</td>
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<td><strong>STEMI</strong></td>
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<tr>
<td>Vallabhajosyula et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>18 years</td>
<td>2000-2017 National Inpatient Sample database — USA</td>
<td>4.3% of STEMI admissions</td>
<td>8.6% of STEMI admissions</td>
<td>Steady increase</td>
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<tr>
<td>Babaev et al&lt;sup&gt;27&lt;/sup&gt;</td>
<td>10 years</td>
<td>1995-2004 National Registry of Myocardial Infarction — USA</td>
<td>≈8.5% of STEMI admissions</td>
<td>≈9.5% of STEMI admissions</td>
<td>Slight steady upward trend</td>
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<tr>
<td><strong>NSTEMI</strong></td>
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<tr>
<td>Vallabhajosyula et al&lt;sup&gt;28&lt;/sup&gt;</td>
<td>18 years</td>
<td>2000-2017 National Inpatient Sample Database — USA</td>
<td>1.3% of NSTEMI admissions</td>
<td>2.8% of NSTEMI admissions</td>
<td>Steady increase</td>
</tr>
</tbody>
</table>

<sup>a</sup>AMI, acute myocardial infarction; AMIS, Acute Myocardial Infarction in Switzerland; CS, cardiogenic shock; GRACE, Global Registry of Acute Coronary Events; NSTEMI, non—ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.
function, and multiorgan failure, often in a delayed manner such that patients pass from a low-output stunning phase of PAMD to a mixed vasodilatory shock state later during their clinical course. High levels of inflammatory markers including interleukin 6 and C-reactive protein have been associated with myocardial dysfunction and unfavorable outcomes after CA. The recent IMICA (Interleukin-6 Receptor Antibodies for Modulating the Systemic Inflammatory Response After Out-of-Hospital Cardiac Arrest) trial reported reduction of systemic inflammation and myocardial injury in patients post ROSC by inhibiting the interleukin-6–mediated immune response with the use of tocilizumab; further research is needed to determine whether this approach will improve clinical outcomes. Catecholamine excess (particularly high doses of epinephrine administered during cardiopulmonary resuscitation) can lead to additional myocardial injury and calcium overload, and may provoke a stress-induced cardiomyopathy. Shock after CA has been variably defined in the past as sustained hypotension or the need for vasopressors, yet contemporary definitions of shock emphasize the presence of tissue hypoperfusion and ensuing metabolic derangements (eg, elevated lactate, acute kidney injury, elevated troponin) as the core diagnostic criteria. However, after CA, evidence of tissue hypoperfusion could occur secondary to global ischemia resulting from the no-flow time from CA and cardiopulmonary resuscitation, leading to uncertainty about how to define CS after CA. Despite the considerable overlap in pathophysiology, the severity of shock can be assigned even in intubated/sedated patients, post ROSC, using the recently updated SCAI shock classification. We define post-CA shock as the need for pharmacological and/or mechanical circulatory support to maintain a mean arterial pressure (MAP) greater than or equal to 65 mm Hg for more than 1 hour following ROSC, despite adequate fluid resuscitation, with clinical or biochemical evidence of hypoperfusion.

Patients with AMICS-CA have a dynamic pathophysiology with a rapidly evolving clinical trajectory, often culminating in a downward spiral of progressive circulatory compromise. Acute myocardial infarction CS follows a hemometabolic cascade with the initial hemodynamic insult resulting in metabolic derangements causing multiorgan failure, cellular ischemia, and acidosis, which itself increases the risk of subsequent

<p>| TABLE 2. Trends in the Incidence of CA Complications* |
|---------------------------------|-------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Study population</th>
<th>Incidence of CA at start of the study</th>
<th>Incidence of CA towards the end of the study</th>
<th>Trend in incidence of AMI-CA</th>
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<tbody>
<tr>
<td><strong>AMI</strong></td>
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<tr>
<td>Vallabhajosyula et al37</td>
<td>15 years 2000-2014</td>
<td>National Inpatient Sample — USA</td>
<td>Increasing trend of all administrative codes for CA complicating AMI</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>McManus et al32</td>
<td>8 years 2000-2007</td>
<td>Global Registry of Acute Coronary Events Registry - North and South America, Europe, Australia, and New Zealand</td>
<td>6.8% of AMI admissions</td>
<td>7% of AMI admissions</td>
<td>Stable with minimal increase</td>
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<tr>
<td><strong>STEMI</strong></td>
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<tr>
<td>Vallabhajosyula et al3</td>
<td>18 years 2000-2017</td>
<td>National Inpatient Sample — USA</td>
<td>6.2% of STEMI admissions</td>
<td>7.3% of STEMI admissions</td>
<td>Increase</td>
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<tr>
<td><strong>NSTEMI</strong></td>
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</tr>
<tr>
<td>Vallabhajosyula et al28</td>
<td>18 years 2000-2017</td>
<td>National Inpatient Sample — USA</td>
<td>2.3% of NSTEMI admissions</td>
<td>2.1% of NSTEMI admissions</td>
<td>Stable</td>
</tr>
</tbody>
</table>

*AMI, acute myocardial infarction; CA, cardiac arrest; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.
CA (eg, hemodynamic collapse resulting in PEA). The severe acidosis that characterizes the post-arrest period can worsen this hemodynamic cascade, explaining why CA has been shown to worsen organ failure and acidosis in patients with CS. In AMI-CS, systemic hypotension impairs blood flow to an already ischemic myocardium which further worsens myocardial function, increases electrical instability, and predisposes patients to develop ventricular arrhythmias and pump failure. Arrhythmias often rapidly worsen hemodynamics and induce further damage to an already compromised myocardium if not corrected early.

**CLINICAL COURSE AND OUTCOMES**

Although the no-flow time during CA effects all organs, it has the most significant impact on the nervous system, as the brain is extremely sensitive to oxygen deprivation. Cardiac arrest presents the highest early upfront mortality in AMI, with the primary cause of death being neurological, secondary to anoxic brain injury (ABI). Multiple factors including the arrest rhythm, location of the arrest, bystander cardiopulmonary resuscitation (CPR), duration of resuscitation, and neurological status determine the degree of AMI and prognosis of patients after CA. Although deaths within the first 24 hours after ROSC typically result from refractory shock and worsening hemodynamics leading to multiorgan failure and recurrent CA, less than one-third of those dying after admission to an intensive care unit following OHCA are due to a cardiovascular or circulatory etiology.

Pre-hospital and in-hospital mortality after CA is substantial, with only 10% of patients who have OHCA surviving to hospital discharge. In a registry study of AMI patients, those with CA represented only 7.5% of the total population but accounted for 36.5% of all deaths. Among patients who survive the index hospitalization, CA has not been associated with an increased subsequent mortality and patients without permanent neurological injury do well long term. In a study by Josiassen et al, patients with out-of-hospital CA+CS had higher lactate levels at admission.

**FIGURE 1. Pathophysiology of cardiac arrest and cardiogenic shock complicating acute myocardial infarction.**
compared with those with only CS; this has been reported in other analysis as well. Importantly, CA was associated with a more rapid normalization of lactate, mixed venous oxygen saturation, and lower need for vasoactive medications, likely due to more rapid LV recovery from transient stunning compared to a more prolonged depression of LV function with CS. Elderly patients who survive to hospital discharge after CA do not have a higher 1-year mortality rate or higher readmission compared with AMI survivors without CA. In the IABP SHOCK (Intra-aortic Balloon Pump in Cardiogenic Shock) trial and registry, 50% of AMI-CS was complicated by pre-hospital CA and patients with CA complicating AMI-CS had a statistically significant higher 30-day mortality but similar 12-month mortality. This emphasizes the high upfront risk without a significant subsequent mortality risk portended by CA.64

On the other hand, CS survivors often require a continued interaction with the health care system due to heart failure, need for medication titration, and management of coronary revascularization.65 The 1-year survival of patients in the IABP-SHOCK trial was 50%, which is significantly lower than the 1-year survival of patients with AMI without CS; however, most survivors only experienced mild New York Heart Association functional class I/II heart failure symptoms.66,37 In a landmark analysis that included patients with STEMI who survived to hospital discharge, Omer et al noted that patients with CA had stable outcomes up to 5 years, whereas those with CS had an increased 5-year mortality. The prognosis of patients with CS who suffer CA is

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Study population</th>
<th>Patient population</th>
<th>CA+CS</th>
<th>CA alone</th>
<th>CS alone</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vallabhajosyula et al</td>
<td>8.5 years</td>
<td>OptumLabs Data Warehouse</td>
<td>AMI</td>
<td>48.8</td>
<td>35.9</td>
<td>24.1</td>
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</tr>
<tr>
<td>Ostenfeld et al</td>
<td>5 years</td>
<td>Denmark Tertiary care center</td>
<td>AMI</td>
<td>63</td>
<td>—</td>
<td>56</td>
<td>—</td>
</tr>
<tr>
<td>Lauridsen et al</td>
<td>6 years</td>
<td>Danish National Patient Registry</td>
<td>AMI</td>
<td>57</td>
<td>—</td>
<td>67</td>
<td>—</td>
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<tr>
<td>STEMI</td>
<td></td>
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<tr>
<td>Gupta et al</td>
<td>1 year</td>
<td>NCDR-CathPCI Registry</td>
<td>STEMI</td>
<td>40.3</td>
<td>9</td>
<td>20.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Vallabhajosyula et al</td>
<td>18 years</td>
<td>National Inpatient Sample</td>
<td>STEMI</td>
<td>53.6</td>
<td>37.8</td>
<td>31.3</td>
<td>—</td>
</tr>
<tr>
<td>Scholz et al</td>
<td>10 years</td>
<td>FITT-STEMI Trial</td>
<td>STEMI</td>
<td>45</td>
<td>16</td>
<td>39</td>
<td>3</td>
</tr>
<tr>
<td>Omer et al</td>
<td>10 years</td>
<td>MHI regional STEMI program</td>
<td>STEMI</td>
<td>44</td>
<td>19</td>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>NSTEMI</td>
<td></td>
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</tr>
<tr>
<td>Gupta et al</td>
<td>1 year</td>
<td>NCDR-CathPCI Registry</td>
<td>NSTEMI</td>
<td>38.5</td>
<td>6.6</td>
<td>13.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Vallabhajosyula et al</td>
<td>18 years</td>
<td>National Inpatient Sample</td>
<td>NSTEMI</td>
<td>59.5</td>
<td>46.4</td>
<td>28.5</td>
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</tbody>
</table>

AMI, acute myocardial infarction; CA, cardiac arrest; CS, cardiogenic shock; FITT-STEMI, Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction; MHI, Minneapolis Heart Institute; NCDR-CathPCI, National Cardiovascular Data Registry; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.
determined by the extent of ABI and severity and reversibility of CS and organ failure.\(^\text{18}\)

Patients with AMICS-CA are a high-risk group with a mortality substantially exceeding patients with CA or CS alone. In fact, this cohort of patients has the highest in-hospital and long-term mortality.\(^\text{4}\)

### Outcomes in AMICS-CA

Cardiac arrest is a major risk factor for mortality among patients with CS, and likewise CS is a major risk factor for mortality among patients with CA.\(^\text{7,9,18}\) In-hospital and long-term outcomes are exponentially complicated with the combination of both CA+CS in patients with AMI. Patients with AMICS-CA have the highest in-hospital mortality, frequently exceeding 40% to 50%, and those who survive to hospital discharge continue to experience an increased mortality after discharge due to the residual risk associated with their underlying heart disease.\(^\text{4,5}\) Patients with AMICS-CA have higher rates of cardiac and noncardiac organ failure, organ support therapies, longer in-hospital stay, higher long-term mortality, higher health care resource use, readmissions, and higher post-acute care use compared to AMI with CS or CA alone.\(^\text{3,4,28,67}\) In patients with STEMI and NSTEMI alike, the in-hospital mortality is highest in those with CS+CA (Table 3).\(^\text{3,28,33,39,68}\) In patients with AMICS-CA, the neurological injury, need for mechanical ventilation, prolonged duration of immobilization, trauma secondary to resuscitation, end-organ damage, heart failure, and long-term medications lead to a much higher use of post-acute care resources.\(^\text{65}\)

Cardiac arrest complicates one of three CS hospitalizations, and the prevalence of CA increases significantly with the increasing stage of CS.\(^\text{7,9,69}\) Furthermore, CA is associated with an increased mortality at each level of CS severity within the SCAI shock classification and should be considered as a risk modifier at every stage.\(^\text{7,9,13,69}\) Importantly, patients who develop CA as a complication of CS (ie, in-hospital CA) and CA patients who develop CS after ROSC are similarly high-risk groups whose prognosis is determined both by the severity of CS and the circumstances surrounding CA.\(^\text{70,71}\) A 12-year study assessing CA complicating CS observed improved outcomes in isolated CS patients but not in those CS admissions complicated by CA over the study period.\(^\text{69}\) Although in-hospital survival was lower for CS patients complicated with CA, the 1-year post-discharge survival rate, analyzed for hospital survivors, was similar in both groups, showing the high upfront risk without an increase in subsequent mortality when CA complicates CS.\(^\text{69}\) Clinical trials of mechanical circulatory support (MCS) devices in CS have included mostly patients with CA, and the presence of anoxic brain injury in enrolled patients with CA could have attenuated the benefit of MCS and masked a potentially beneficial impact of the MCS; future trials in CS populations should stratify randomization by the presence of CA.\(^\text{18,72}\)

Hypotension occurs in up to 66% of patients with CA and can be secondary to transient myocardial stunning, use of sedative medications in comatose patients, as well as CS secondary to myocardial ischemia and myocardial dysfunction. The true incidence and outcomes of CS in patients with CA post-ROSC is heterogenous due to varying definitions and inconsistent cardiac functional assessment in published studies, although most studies have shown worse outcomes in patients with shock after CA.\(^\text{54,55,57,38,72}\) Low MAP, elevated blood lactate, and higher requirements of vasopressors after CA is associated with worse short- and long-term outcomes and increased mortality.\(^\text{44,73}\) Shock with persistently low cardiac index at 24 hours after ROSC is associated with a higher early mortality from multiorgan dysfunction.\(^\text{39}\)

### MANAGEMENT

Standard management approaches to CA and AMI-CS individually have been elaborated in well-constructed professional society consensus guidelines.\(^\text{19,20}\) However, to a great extent, these guidelines have not described the challenges specific to management of patients with both conditions. This is essential...
insofar as specific clinical features or treatments of either condition can influence the use or efficacy of certain treatments for the other. In some cases, a treatment that may be the standard-of-care for one condition might actually worsen the other condition or have potential risks in patients with both. As an example, because ABI drives mortality to a substantial degree among patients with CA+CS, treatments targeting ABI are warranted. However, the presence of ABI may modify the benefit of standard therapies for CS such as revascularization or MCS.

Supportive Management
Supportive management of CS includes optimization of fluid status, restoration of adequate hemodynamics and organ perfusion using vasopressors and inotropes, and support of organ failure. A similar approach is taken for patients with CA, and should be taken for patients with CA+CS. One particular challenge in caring for patients with CA+CS is the exacerbation of hemodynamic instability and shock severity caused by PAMD and the systemic inflammatory response syndrome resulting from CA, which can further aggravate organ failure, lower vascular resistance, and worsen shock, necessitating higher vasopressor doses.7 Capillary leak and other factors developing after CA can lower filling pressures, requiring fluid resuscitation even in patients with CS.39 Most crucially, shock after CA can evolve from an early cardiogenic phenotype with PAMD and stunning into a mixed or predominantly vasodilatory pathophysiology over the first 8 to 24 hours. Emphasis should be placed on continuous clinical assessment of the patient’s perfusion status,

FIGURE 2. Algorithm for management of concomitant cardiac arrest and cardiogenic shock complicating acute myocardial infarction. CO, cardiac output; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ECPELLA, extracorporeal membrane oxygenation plus Impella; MAP, mean arterial pressure; MCS, mechanical circulatory support; PEEP, positive end expiratory pressure; ROSC, return of spontaneous circulation; TTM, targeted temperature management; UO, urine output.
with frequent serial biomarker monitoring to complement clinical judgement. Apart from direct evidence of end-organ dysfunction, the most commonly monitored biomarkers for assessing the severity of perfusion deficits are lactate and mixed venous oxygen saturation. As described above, in patients with AMICS-CA, shock is often due to a combination of vasoplegia and CS. Guidelines recommend pulmonary artery catheter (PAC) monitoring in patients with an uncertain mechanism of shock and patients with CS who do not respond to initial therapy. The use of a PAC provides continuous hemodynamic profiling, facilitating optimization of volume status, differentiation of right-sided, left-sided, and biventricular dysfunction, as well as aids in the selection, titration, and weaning of pharmacological and MCS support to restore CO. A large multicenter registry noted lower in-hospital mortality across all SCAI stages in patients who received comprehensive hemodynamic profiling with a PAC. To continually optimize hemodynamics and titrate therapies effectively, invasive hemodynamic monitoring with a PAC is valuable in our estimation and, despite the use of several minimally invasive devices for monitoring of CO, the PAC remains the gold standard for complete hemodynamic assessment (Figure 2). Although the use of PAC is controversial for many patients, recent studies have highlighted its importance in patients with CS, and this applies to patients with AMICS-CA as well. Based on available published evidence, we prefer an approach which titrates norepinephrine as the first-line vasopressor to target an adequate MAP (typically greater than 65 to 70 mm Hg) and independently titrates dobutamine as the first-line inotrope to target an adequate cardiac index (typically >2.2 L/min per m²) and cardiac power output (ideally >0.6 W) with normal and systemic oxygen delivery (evidenced by mixed venous oxygen saturation ≥60% to 65%) and normalization of lactate and urine output (Figure 2). Although normalization of the cardiac index using inotropes is logical, we believe that it is more important to normalize systemic oxygen delivery and restore perfusion. In post-arrest patients, a higher MAP goal of 80 to 100 mm Hg has been proposed to mitigate secondary brain injury due to impaired cerebral blood flow autoregulation; however, this approach has not been shown to improve neurological outcomes, and the potential adverse effects of higher vasoactive drug doses in patients with CS should be considered. Most patients with CA+CS are intubated and mechanically ventilated, and a lung-protective ventilation strategy targeting a low tidal volume of 6 to 8 mL/kg is prudent; either high or low levels of oxygen and CO₂ in the blood have been associated with poor outcomes after CA, so maintaining normal levels is ideal. Hyper-ventilation can be used to correct severe acidosis, but this may cause cerebral vasodilation that could exacerbate ABI; untreated acidosis may compromise cardiovascular function, so administering alkali therapy may be necessary.

**Targeted Temperature Management**

Targeted temperature management (TTM) has been shown to be associated with improved survival and neurological function in CA patients and remains the standard-of-care for those who are persistently comatose after resuscitation from CA, although the temperature goals during TTM have changed recently. The early trials of TTM after CA did not include patients with concomitant CS. In the subsequent TTM trials, hypothermia (33 °C in both TTM and TTM-2) was not found to be superior to normothermia (36 °C in TTM and 37.5 °C in TTM-2); these studies excluded patients with severe or refractory CS. However, in the TTM trial, temperatures were achieved with a suite of targeted interventions in similar percentage of subjects in both the groups and, in the TTM-2 trial, 46% of the patients in the normothermia groups received cooling with a temperature...
Furthermore, approximately 15% of patients in both groups in the TTM-2 trial had recorded temperatures above 37.7°C. Moderate hypothermia of 31°C was not superior when compared with a mild hypothermia of 34°C in the (CAPITAL CHILL) trial. The key crucial message from these trials is the need for close temperature monitoring with pharmacotherapy, device cooling, and a targeted temperature management protocol for comatose patients after ROSC. The goal temperature during TTM can be personalized to the individual patient based on the discretion of the treating physician. There are known adverse hemodynamic effects of lower targeted temperatures during TTM, making a higher target temperature of (36°C to 37.5°C) reasonable for patients with concomitant CS, in our opinion.

The American Heart Association and the European Resuscitation Council guidelines recommend TTM for patients with inhospital and OHCA and with any arrest rhythm. More specific to the AMICS-CA population, the German-Austrian S3 guidelines recommend cooling of body temperature for at least 24 hours for all resuscitated comatose patients with AMI-CS. Targeted temperature management, particularly at lower target temperatures, causes a reduction in CO associated with a reduction in heart rate and an increased vascular resistance, which may lead to increased vasopressor requirements and impaired lactate clearance. Targeted temperature management is not beneficial per se among patients with AMI-CS without CA, but presumably can still be of benefit for patients with CA despite its adverse hemodynamic effects. In patients with AMICS-CA, TTM should be initiated as early as possible, but this can be challenging for patients with AMI-CS as they often require percutaneous coronary intervention (PCI) and MCS device placement. We emphasize the importance of close temperature monitoring in patients with AMICS-CA with a strict goal to prevent fever and suggest a higher goal temperature (36°C to 37.5°C) recognizing that the set

**FIGURE 3.** Poor prognostic markers for cardiac arrest and cardiogenic shock complicating acute myocardial infarction. ABI, anoxic brain injury; ACC, American college of cardiology; CA, cardiac arrest; CABG, coronary artery bypass graft; CKD, chronic kidney disease; CLIP, Cystatin C, Lactate, Interleukin-6, Pro-B-type natriuretic peptide; CPR, cardiopulmonary resuscitation; CS, cardiogenic shock; ESRD, end stage renal disease; IABP-SHOCK II, Intra-aortic Balloon Pump in Cardiogenic Shock II trial; INTCAR, International Cardiac Arrest Registry; MI, myocardial infarction; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; SCAI, Society of Cardiovascular Angiography and Intervention; TIMI, thrombolysis in myocardial infarction grade flow.
goal for a targeted temperature management protocol should be personalized to the individual patient.

Reperfusion and Revascularization
Given the dynamic and complex nature of patients with AMICS-CA, management should be focused with an emphasis on the overall prognosis, probability of meaningful neurological recovery, and candidacy for revascularization. Patients with persistent shock after ROSC and a Glasgow Coma Scale of greater than or equal to 8 should be immediately triaged to the catheterization laboratory. However, neurologic prognostication for comatose CA patients is notoriously difficult during the very early post-ROSC period when decisions regarding coronary angiography and revascularization must be made (Figure 3). Although the presence of a multitude of high-risk clinical features, listed in a recent American College of Cardiology (ACC) consensus statement, can identify patients with CA who are unlikely to survive, declaring futility in such cases is extremely controversial. Guidelines recommend short door-to-balloon time and early PCI in cases of STEMI and high-risk NSTEMI; patients with AMICS-CA clearly qualify. There appears to be a higher survival benefit from early reperfusion in the cohort of AMICS-CA compared with hemodynamically stable patients. This emphasizes the need for immediate PCI in patients with AMICS-CA. Use of invasive hemodynamic monitoring with a PAC, MCS, and TTM should be performed with the goal to achieve revascularization at the earliest and safest manner possible (Figure 3). Although this approach remains controversial, there are proponents of performing hemodynamic stabilization, potentially including PAC and temporary MCS placement, before coronary angiography in patients with AMICS. However, caution must be taken when diagnosing STEMI based on an electrocardiogram performed immediately after ROSC due to the potential for metabolic disturbances resulting from CA to create transient ST-segment changes.

Fibrinolytic Therapy. There is no evidence for fibrinolysis in the AMICS-CA population, and PPCI is preferred whenever possible. Patients with AMICS-CA due to STEMI who present to non–PCI-capable facilities may benefit from a pharmacoinvasive approach with prompt transfer to a PCI-capable center for angiography and subsequent management. An invasive approach with PPCI remains the best practice in STEMI complicated by CA+CS.

Early Invasive Strategy in CA+CS. Early culprit vessel revascularization is the only established mortality-reducing therapy for CS based on randomized studies. The seminal SHOCK trial (including 28% of patients with CA) showed that early revascularization with PCI or coronary artery bypass graft was associated with lower short- and long-term mortality in patients with AMICS, particularly for patients who were revascularized sooner. In patients with AMI-CS and multivessel coronary artery disease (CAD), the CULPRIT-SHOCK trial, which included approximately 54% of patients with CA, showed that culprit vessel—only PCI was associated with a lower 30-day and 1-year mortality and had fewer complications than acute multivessel PCI. Geri et al, evaluating the effect of an early invasive strategy for OHCA (including post-arrest CS in 59% of cases), reported a lower short-term and long-term mortality in patients treated with early coronary angiography and PCI (within 6 hours). By contrast, the COACT (Coronary Angiography after Cardiac Arrest) study found no difference in mortality in hemodynamically stable CA patients without STEMI when randomized to early vs delayed coronary angiography; this study does not directly apply to CA+CS patients, as the trial excluded patients with CS and approximately 64% of the deaths were attributed to ABI. Similarly, in the recent TOMAHAWK trial, immediate angiography provided no benefit over a delayed strategy in OHCA without STEMI, although patients with CS as well as those requiring immediate angiography were excluded in the trial. The PEARL (Early Coronary
Angiography Versus Delayed Coronary Angiography) trial conducted in OHCA patients without STEMI (including only 14% patients with shock) was an underpowered study which also did not show a benefit from early coronary angiography.\(^{104}\) Current American and European consensus guidelines recommend emergent coronary angiography for patients with OHCA with STEMI or suspected AMI (regardless of the presence of coma) as well as for patients with AMI complicated by hemodynamic or electric instability including CS and recurrent ventricular arrhythmias.\(^{8,105}\) For patients with AMICS-CA, the German-Austrian guidelines recommend early catheterization with a goal to PCI.\(^{105}\) Patients with OHCA and multivessel CAD who recover after a culprit vessel—only PCI strategy are likely to benefit from delayed PCI to the nonculprit vessel during or shortly following the index hospitalization.\(^{77,106}\) We recommend an early invasive approach for patients with AMI (STEMI and NSTEMI) complicated by concomitant CA+CS, although caution is warranted for comatose patients with a multitude of adverse prognostic markers.\(^{94}\) In the event of multivessel CAD on coronary angiography, we advocate for a staged approach with delayed PCI to the nonculprit vessels. For patients who remain unstable or deteriorate after culprit vessel PCI, it may be reasonable to consider immediate PCI for high-risk nonculprit vessels with severe proximal stenosis (not chronic total occlusions), particularly if there are angiographic features suggesting thrombus or plaque rupture.

Mechanical Circulatory Support
Mechanical circulatory support has become a mainstay of therapy for patients with CS with compromised CO despite vasoactive drug therapy.\(^{107}\) The ability to support or completely replace native cardiac function with readily deployable percutaneous ventricular support devices in patients with AMICS-CA has allowed hemodynamic stabilization of these extremely unstable patients, including those patients with refractory VF.\(^{107}\) Mechanical circulatory support devices should be used to improve cerebral and systemic perfusion and break the deleterious hemometabolic shock cycle. Although hemodynamic support has the potential to improve end-organ perfusion and mitigate the metabolic derangements noted with CS, it will not necessarily reverse established ABI after CA.\(^{18}\) Therefore, it is not coincidental that randomized trials of temporary MCS devices that have included a large number of CA patients failed to show a reduction in mortality; rather than an indictment of MCS devices per se, this may simply reflect the inability of MCS to ameliorate established ABI after CA. A broader brain-focused resuscitation strategy with hemodynamic and ventilatory support coupled with TTM may lessen secondary brain injury after CA, and such comprehensive strategies should be considered in patients with concomitant AMICS-CA. There is insufficient evidence and lack of consensus on the timing of MCS insertion. Most trials randomized patients to MCS after revascularization and some experts argue that the lack of benefits noted may have been influenced by the timing of device insertion.\(^{19,33,108}\) Some observational studies have shown promising results when MCS was deployed before revascularization,\(^{97,109}\) whereas others noted no benefit.\(^{110}\) Mechanical circulatory support can provide beneficial support during PCI in critically ill patients with CA+CS. We recommend early (before revascularization) MCS insertion, when feasible without a delay to reperfusion, in this cohort of patients with persistent hemodynamic compromise despite initial stabilization with vasopressors and inotropes, as well as in those receiving active CPR. Device selection should be based on specific CS profiles with the exception of patients with ongoing CPR in whom extracorporeal membrane oxygenation (ECMO) has shown to be beneficial.\(^{111,112}\) In accordance with the American Heart Association (AHA) and other clinical practice guidelines, we recommend that temporary MCS selection should be based on device availability, multidisciplinary team familiarity, and patient-specific needs.\(^{5,19,113}\) Specific recommendations for individual
MCS devices are beyond the scope of this review, but we believe that the degree of hemodynamic support provided should be tailored to the severity of CS using the SCAI shock classification.

**Intra-aortic Balloon Pump.** Intra-aortic balloon pump remains the most commonly used MCS device for CS as well as for patients with AMICS-CA, with reported use in 5% of patients with simultaneous pathologies.\(^6,114\) The IABP is easily deployed; however, clinical trials have not shown a survival benefit in CS patients. Approximately 45% of patients in the IABP-SHOCK II (Intra-aortic Balloon Pump in Cardiogenic Shock II) trial had CA before randomization, and the use of IABP showed no survival benefit compared with guideline-recommended optimal medical therapy (including in the CA subgroup).\(^34\) The lack of benefit from IABP could have been due to its modest hemodynamic effects, competing risks of death from neurological and cardiovascular causes, and the uncertain effects of hemodynamic stabilization on ABI; the high severity of shock observed in this trial may have been beyond the capability of the IABP to reverse.\(^18\) Intra-aortic balloon counterpulsation in CS showed only a modest and inconsistent increase in CO and the IABP trial found no significant difference in CO, cardiac power output, or systemic vascular resistance with the use of IABP compared with vasoactive drugs alone.\(^66,37\)

With the advent of more advanced MCS devices, the role of IABP is limited to LV unloading for patients receiving ECMO and post–myocardial infarction mechanical complications such as mitral regurgitation or ventricular septal defects.

**Percutaneous Ventricular Assist Devices.** Percutaneous left ventricular assist devices (pLVADs), including Impella and TandemHeart, provide greater augmentation of the CO compared with IABP.\(^14,113-117\) Although the early Impella 2.5 might have provided only marginally higher augmentation of the CO, the Impella CP and Impella 5.0 provide significant hemodynamic augmentation.\(^108,116,118\) There has been a significant increase in the use of pLVAD in CS as well as AMICS-CA over the years.\(^114,119\) These devices offer substantial LV support but require native right ventricular function unless a second pLVAD to support the right heart is placed.\(^107\) In a nationwide study of AMI, pLVAD and other MCS devices were more often used in the cohort with CA+CS compared with CA or CS alone.\(^6\) Similar trends were noted with more frequent use of pLVAD in both STEMI and NSTEMI in the CA+CS cohort.\(^3,28\)

Despite an increase in the CO and cardiac index with the pLVAD, there has been no observed survival benefit with the use of pLVAD devices when compared with IABP.\(^107\) The IMPRESS (Impella Versus IABP Reduces Mortality in STEMI Patients Treated With Primary PCI in Severe Cardiogenic Shock) trial that compared the Impella CP with IABP included 92% of patients with a CA before enrollment showed similar 50% mortality at 6 months in both groups.\(^34\) Unfortunately, the number of patients included in the study and a subsequent meta-analysis were small and may have been underpowered to detect a difference.\(^34,110,120\) Registry data on Impella use in patients with CA+CS after ROSC have confirmed similar rates of survival close to 40% to 50% at 1 month.\(^97\) A meta-analysis of the trials comparing MCS with IABP showed improved MAP and decreased lactate but comparable cardiac index and pulmonary capillary wedge pressure with the use of pLVAD devices.\(^120\)

Caution is warranted considering that the pLVADs have been associated with higher rates of noncardiac complications in randomized trials and retrospective studies, with greater rates of vascular, hematologic, and ischemic complications including bleeding, thrombocytopenia, ischemic extremities, and acute kidney injury.\(^108,120,121\) Further studies are needed to identify patient-specific factors that may better delineate optimal candidates for pLVAD and IABP and to establish guideline-directed use of these MCS devices.\(^121\) The substantially higher cost of pLVADs compared with either vasoactive drugs or IABP suggests caution...
when using these devices in CA+CS patients with suspected ABI who may die of ABI despite hemodynamic stabilisation. High-risk prognostic features from the INTCAR (International Cardiac Arrest Registry) study and the proposed criteria for selecting patients for invasive cardiovascular procedures by Rab et al. can be used for patients with CA+CS. The concept is valid insofar as patients with multiple predictors of severe ABI may be less likely to benefit from invasive cardiovascular therapies (including PCI). Patients who show signs of intact neurological function such as spontaneous purposeful movements or a localizing motor response to pain would be better candidates than patients who are either unresponsive to pain or have a reflex response, necessitating both careful examination and clinical judgement in the context of prognosis.

**Extracorporeal Membrane Oxygenation.** The potential role for ECMO in the treatment of AMICS-CA is of particular interest. Venoarterial ECMO provides complete biventricular hemodynamic and respiratory support, which is often necessary for patients with SCAI shock stage E or ongoing CA. A meta-analysis of observational studies by Ouweneel et al. noted that ECMO use in CA+CS was associated with improved 30-day and long-term survival, including favorable neurological outcomes. The efficacy and safety of ECMO is currently being validated in the ECLS-SHOCK (Extracorporeal life support in patients with acute myocardial infarction complicated by cardiogenic shock) trial. In patients receiving ECMO, Kagawa et al. reported an improved survival in those undergoing intra-arrest PCI compared with patients who received a delayed PCI. In AMI complicated by CA or CS, several studies reported significant advantages of ECMO over other MCS devices including the ability to provide both respiratory and biventricular support, to ensure higher systemic flow rates, the ease of deployment, and the relatively lower costs of care.

Initiation of extracorporeal membrane oxygenation during cardiopulmonary resuscitation (ECPR) in the two-thirds of CA patients who remain refractory to CPR and advanced cardiac life support (ACLS) can restore circulation and allow coronary angiography and PCI to help facilitate ROSC. In patients with VT/VF and concomitant shock, the use of ECMO-assisted (extracorporeal) CPR (during ongoing chest compressions using a mechanical device) initiated before angiography improved the capability to achieve ROSC and increased rates of neurologically meaningful in-hospital survival. The ARREST (Advanced Reperfusion Strategies for Patients With Out-of-hospital Cardiac Arrest and Refractory Ventricular Fibrillation) trial was prematurely terminated because of the noted superiority of ECPR compared with standard ACLS further showing a significant benefit with the use of ECMO and early an early invasive approach in patients with refractory VT/VF without ROSC. Unfortunately, the larger Prague OHCA trial was terminated early due to futility and did not meet criteria for a significant improvement in overall neurologically intact survival for ECPR vs conventional therapy in refractory CA. The trial was underpowered to detect clinically relevant differences between the groups as suggested by the wide confidence interval for the primary outcome. Furthermore, patients in the invasive strategy arm had higher rates of TTM, diagnostic angiography, and PCI. With only two trials showing conflicting results, there is a need for further research to assess the role of ECPR in refractory CA.

The use of ECMO is associated with a substantial risk of complications including bleeding, thrombosis, infections, and limb ischemia. To prevent circuit thrombosis, an activated partial thromboplastin time of 60 to 80 seconds can be used with a lower goal of 40 to 60 seconds in patients who are at a higher risk of bleeding. The use of a reperfusion catheter to perfuse the limb distal to the ECMO cannula entry site is likely to lower the rate of limb ischemia. The countercurrent flow of the ECMO generates an increased afterload against an already compromised LV which
can progressively lead to LV distension and pulmonary edema. Left ventricular venting achieved with the use of concomitant IABP, pLVAD, a direct LV catheter, or atrial septostomy provides decompression for patients on ECMO. Extracorporeal membrane oxygenation plus Impella is increasingly being used for LV venting and has shown promising results with higher rates weaning from ECMO and destination therapy for these patients. Use of ECMO in patients with AMICS-CA necessitates very careful patient selection, incorporating factors such as the quality and duration of CPR, the circumstances of the arrest (ie, witnessed or bystander CPR) and the arrest rhythm; most ECPR programs only include patients with witnessed VT/VF, bystander CPR, and a short overall time before ECMO deployment.

REGIONALIZED SYSTEMS OF CARE

Management of patients with CA and/or CS is complex, time-sensitive, and requires a multidisciplinary treatment team with coordinated care. Hospital and physician volumes have been positively associated with better outcomes and improved survival. Regionalized systems of care have been successfully implemented for time-sensitive conditions including STEMI, stroke, trauma, aortic dissection, CS alone, and CA alone. A regionalized system of care pathway with a hub-and-spoke model has been implemented and validated in multiple
studies for both isolated CA and isolated CS with improved survival noted with direct transfer to specialized centers with multidisciplinary teams and advanced hemodynamic support. We recommend a similar hub-and-spoke approach for CA+CS in AMI (Figure 4).

For the purpose of this review, the term “cardiac arrest and shock center” (CASC) will be used to indicate the specialized hub center. The CASC must have the ability to provide contemporary, comprehensive, evidence-based management for CS and post-CA care 24 hours a day, 7 days a week. The hub centers must be equipped to provide emergent PCI and revascularization, TTM, PAC monitoring, and MCS including plLVAD and ECMO support. Multidisciplinary, collaborative, team-based approaches for management should be instituted and should include key stakeholders including cardiothoracic surgeons, interventional cardiologists, advanced heart failure specialists, neurologists, critical care cardiologists, and intensivists. Palliative care services and ethics teams should be promptly involved as discussions of values and goals of care in parallel with invasive measures can significantly benefit patient management. We recommend the implementation of a 3-tier system (Figure 4) as suggested for patients with CS. Physicians with hybrid training in more than one subspecialty (such as interventional cardiology, critical care cardiology, and advanced heart failure) have the ability to identify the need for complex procedures and provide a unique perspective to manage acute complex cardiovascular states in the cardiac intensive care unit. Prior consensus statements advocate a single cardiac intensive care unit within each CASC to be designated as the receiving unit to consolidate clinical volume and professional experience. Early recognition is key to improve outcomes for patients with CS and, once diagnosed, the goal should be to achieve a first medical contact to revascularization time of 60 minutes or less. After acute stabilization, AMICS-CA patients need close monitoring and management of heart failure, noncardiac organ dysfunction, neuroprognostication, rehabilitation, and advanced planning and discussion of goals of care. We advocate for direct transfer to a CASC for patients with OHCA resuscitated in the field and identified by emergency medical services to be in CS. Respecting the revascularization threshold, direct transfer to a PCI-capable level II center may be considered if the estimated first medical contact—revascularization goal set by the ACC/AHA is likely to be exceeded. Similarly, we recommend that patients who remain in CS post resuscitation and CS patients experiencing CA at lower acuity sites to be transferred promptly to a CASC that can offer ECMO.

FUTURE DIRECTIONS

Future clinical trials of CS patients should take into account the unique challenges and poor outcomes of patients with concomitant CA and result reporting should be stratified by presence or absence of CA and ABI; indeed, some interventions may be more or less effective in CS patients with CA. A recent systematic review of AMI-CS trials showed a significant underreporting of key baseline characteristics and outcome predictors with as low as 0% reporting of baseline neurological status, 28% reporting use of TTM, and 33% reporting the cause of death. For CA patients included in CS studies, more extensive data on arrest circumstances, arrest rhythm, neurological status, TTM, critical care therapies, cause of death, and withdrawal of care algorithms should be standardized and reported clearly. Capturing granular data on CA will help enhance our understanding of the response to different treatment algorithms in patients with CS stratified across the spectrum of CA and ABI severity.

Future studies should elucidate the unique pathophysiology and test targeted therapies in patients with concomitant CS and CA with the goal of improving the poor survival in this patient population. Prespecified subgroup analyses of CA in future AMI-CS trials are crucial to accurately appraise the effect of novel therapies, identify the cause and predictors of death, and benefit of traditional therapies in this vulnerable patient population. The role of
anti-inflammatory therapies to potentiate the effect of vasopressors and accelerate shock reversal in post-arrest CS should be assessed in future randomized control trials. Early studies have shown a potential role of circulating dipeptidyl peptidase 3 as an early prognosticator for the development of refractory CS and adverse outcomes, but this needs further validation. The use of neuroimaging, TTM, MCS, ECMO therapies, and withdrawal of care algorithms should be standardized in patients with AMICS-CA during clinical trials. Functional neurological status at the time of randomization as well as functional outcomes assessed by cerebral performance category or modified Rankin scale should be reported. Development and validation of contemporary prediction scores incorporating clinical, imaging, and biomarkers could serve as a cornerstone to identifying patients in whom intensive invasive management strategies are likely to show a benefit. Identifying the appropriate timing of escalation of hemodynamic support along with the pharmacomechanical continuum would be extremely beneficial. Examining treatment strategies in patients with AMICS-CA across the SCAI CS acuity spectrum would help identify groups of patients in which novel therapies could be efficacious or potentially futile.  

CONCLUSION
Patients with AMICS-CA constitute a uniquely high-risk population with poor short- and long-term outcomes. Management of these patients requires skilled multidisciplinary teams with close monitoring and frequent evaluation of management strategies. Prompt revascularization is of utmost importance and should be prioritized. Mechanical circulatory support devices should be deployed early to improve end-organ perfusion, prevent hemometabolic deterioration, and facilitate coronary angiography and PCI. Patients with AMICS-CA are likely to benefit from titration of vasopressors and inotropes using information acquired by invasive hemodynamic monitoring with PACs. Patients who are comatose should be managed with a lung-protective ventilation strategy, and TTM should be used with a goal to prevent fevers. Given the complexity of care and time-sensitive multipronged approach required to optimize outcomes, a regional system of care pathway, with a hub-and-spoke model, should be established to improve survival.

POTENTIAL COMPETING INTERESTS
The authors report no potential competing interests.

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Abbreviations and Acronyms: ABI, anoxic brain injury; ACLS, advanced cardiac life support; AMI, acute myocardial infarction; AMICS-CA, acute myocardial infarction complicated by cardiogenic shock and cardiac arrest; CA, cardiac arrest; CAD, coronary artery disease; CASC, cardiac arrest and shock center; CS, cardiogenic shock; ECMO, extra corporeal membrane oxygenation; ECPR, extra corporeal membrane oxygenation—assisted cardiopulmonary resuscitation; IABP, intra-aortic balloon pump; MAP, mean arterial pressure; MCS, mechanical circulatory support; NSTEMI, non–ST-segment elevation myocardial infarction; OHCA, out of hospital cardiac arrest; PAC, pulmonary artery catheter; PAMD, post arrest myocardial dysfunction; PEA, pulseless electrical activity; pLVAD, percutaneous left ventricular assist device; PPCI, primary percutaneous coronary intervention; ROSC, return of spontaneous circulation; SCAI, society for cardiovascular angiography and interventions; STEMI, ST-segment elevation myocardial infarction; TTM, targeted temperature management; VF, ventricular fibrillation; VT, ventricular tachycardia

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