Circulation

AHA SCIENTIFIC STATEMENT

Invasive Management of Acute Myocardial Infarction Complicated by Cardiogenic Shock

A Scientific Statement From the American Heart Association

ABSTRACT: Cardiogenic shock (CS) remains the most common cause of mortality in patients with acute myocardial infarction. The SHOCK trial (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) demonstrated a survival benefit with early revascularization in patients with CS complicating acute myocardial infarction (AMICS) 20 years ago. After an initial improvement in mortality related to revascularization, mortality rates have plateaued. A recent Society of Coronary Angiography and Interventions classification scheme was developed to address the wide range of CS presentations. In addition, a recent scientific statement from the American Heart Association recommended the development of CS centers using standardized protocols for diagnosis and management of CS, including mechanical circulatory support devices (MCS). A number of CS programs have implemented various protocols for treating patients with AMICS, including the use of MCS, and have published promising results using such protocols. Despite this, practice patterns in the cardiac catheterization laboratory vary across health systems, and there are inconsistencies in the use or timing of MCS for AMICS. Furthermore, mortality benefit from MCS devices in AMICS has yet to be established in randomized clinical trials. In this article, we outline the best practices for the contemporary interventional management of AMICS, including coronary revascularization, the use of MCS, and special considerations such as the treatment of patients with AMICS with cardiac arrest.

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Cardiogenic shock (CS) represents an inability of the heart to maintain an effective cardiac output commensurate to the metabolic demands of the body attributable to a primary underlying cardiac pathology. Acute myocardial infarction (AMI) is the most common cause of CS.[1] Although the incidence of ST-segment–elevation myocardial infarction (STEMI) is decreasing, the incidence of CS complicating AMI (AMICS) remains stable (7%–10%) if not increasing, especially among the elderly.[2] An array of acute or acute-on-chronic insults can contribute to its pathogenesis, including exacerbations of ischemic heart disease, valvular disease, cardiomyopathy, pericardial disease, or arrhythmia. Regardless of cause, CS results in a deficiency of end-organ perfusion that is often characterized by hypotension, tachycardia, peripheral vasoconstriction, pulmonary and systemic venous congestion, decreased urine output, altered sensorium, acute liver or kidney injury, and lactic acidosis.[3–5] Although CS remains a clinical diagnosis, objective definitions have been established by clinical trials,[6,7] and a recent document has proposed a novel classification system based on clinical characteristics at presentation.[8]

Mortality associated with AMICS remains high, with 30-day mortality approximating 40% to 45% in contemporary randomized trials.[7,9] After the SHOCK trial (Should We Emergently Revascularize Occluded Coronaries for CS),[6] which demonstrated survival benefit with early revascularization in AMICS at longer follow-up, and with growth in availability of primary percutaneous coronary intervention (PCI), AMICS-associated mortality declined.[10] From 2005 to 2013, this improvement appeared to plateau in an analysis of the National Cardiovascular Data Registry despite increasing rates of PCI.[11] Mechanical circulatory support (MCS) devices are increasingly used in AMICS, but their effect on mortality has yet to be established in randomized clinical trials.[4]

The AMIS registry (AMI in Switzerland) of 83 Swiss hospitals documented a decrease in AMI mortality from 8.7% to 7.3% from 1997 to 2017 (P<0.001 for trend)[12] and a decrease in development of CS in hospital from 7.8% to 3.5% over the same time period. This was offset, however, by an increase in CS at presentation from 2.5% to 4.6%. Overall, in-hospital mortality of all patients with AMICS decreased from 62.2% in 1997 to 36.3% in 2017 (P<0.001 for temporal trend; Figure 1), likely related to the growth in primary PCI. Of note, patients with AMICS who survive to hospital discharge continue to experience a higher rate of mortality after discharge. In a large series of patients ≥65 years of age surviving to hospital discharge in the ACTION registry (Acute Coronary Treatment and Intervention Outcomes Network), mortality was higher at 60 days (9.6% versus 5.5%) and at 1 year (22.4% versus 16.7%) in patients with AMI with CS compared with patients with AMI without CS.[13]

In recent years, multiple centers have developed critical pathways and protocols to organize acute invasive care for AMICS with promising results.[14,15] Whereas randomized controlled trials have examined discrete elements of care, including strategies for coronary revascularization,[6,9] vasopressor selection,[16,17] and MCS,[7,18] no contemporary trial has validated a comprehensive algorithm for acute care delivery. In particular, important uncertainties remain in the appropriate use, selection, and management of MCS devices in patients with AMICS. Recognizing these gaps in knowledge, we set out in this scientific statement to critically appraise current evidence, identify areas of consensus and controversy, propose best practices, and highlight necessary areas for future research in the acute invasive management of AMICS.

DEFINING SHOCK

The shock state, although generally characterized as a lack of end-organ perfusion, has been notoriously difficult to define and classify, largely because the syndrome of shock can be heterogeneous with varying timelines of development. The National Cardiovascular Data Registry's CathPCI registry, for example, defines shock as >30 minutes of systolic blood pressure <90 mm Hg, cardiac index <2.2 L·min^{-1}·m^{-2} determined to be secondary to cardiac dysfunction, or the requirement for inotropic or vasopressor agents or MCS.[11] Selected statewide databases use different definitions (eg, systolic blood pressure <80 mm Hg despite vasopressors). Heterogeneity of definitions propagates uncertainty in comparisons of outcomes across the nation. Furthermore, these definitions may fail to capture patients in preshock or early shock who are at risk for hemodynamic deterioration or mortality.

To address this gap, the Society for Cardiovascular Angiography and Intervention (SCAI) has introduced a classification scheme for a patient's hemodynamic state.[8] Recent publications validated this classification.[19,20] In a series of 10 004 patients admitted to the Mayo Clinic cardiac intensive care unit, 43.1% had acute coronary syndromes, 46.1% had heart failure, and 12.1% presented with cardiac arrest.[19] After multivariable adjustment, there was a stepwise increase in risk of hospital mortality with increments of SCAI shock stages A to E. In a separate series of 1007 patients presenting with CS or large AMI (51% with a preceding cardiac arrest), a stepwise increase in 30-day mortality was again observed in shock stages A to E (Figure 2).[20] An important aspect of the SCAI classification is a cardiac arrest modifier. At every stage of SCAI shock, the presence of cardiac arrest significantly increases mortality. Hence, this classification appears useful to risk-stratify hospitalized patients, and its gradual universal adoption may reasonably enhance country-wide shock metrics. Future studies are required to prospectively test the clinical utility of this classification scheme and to

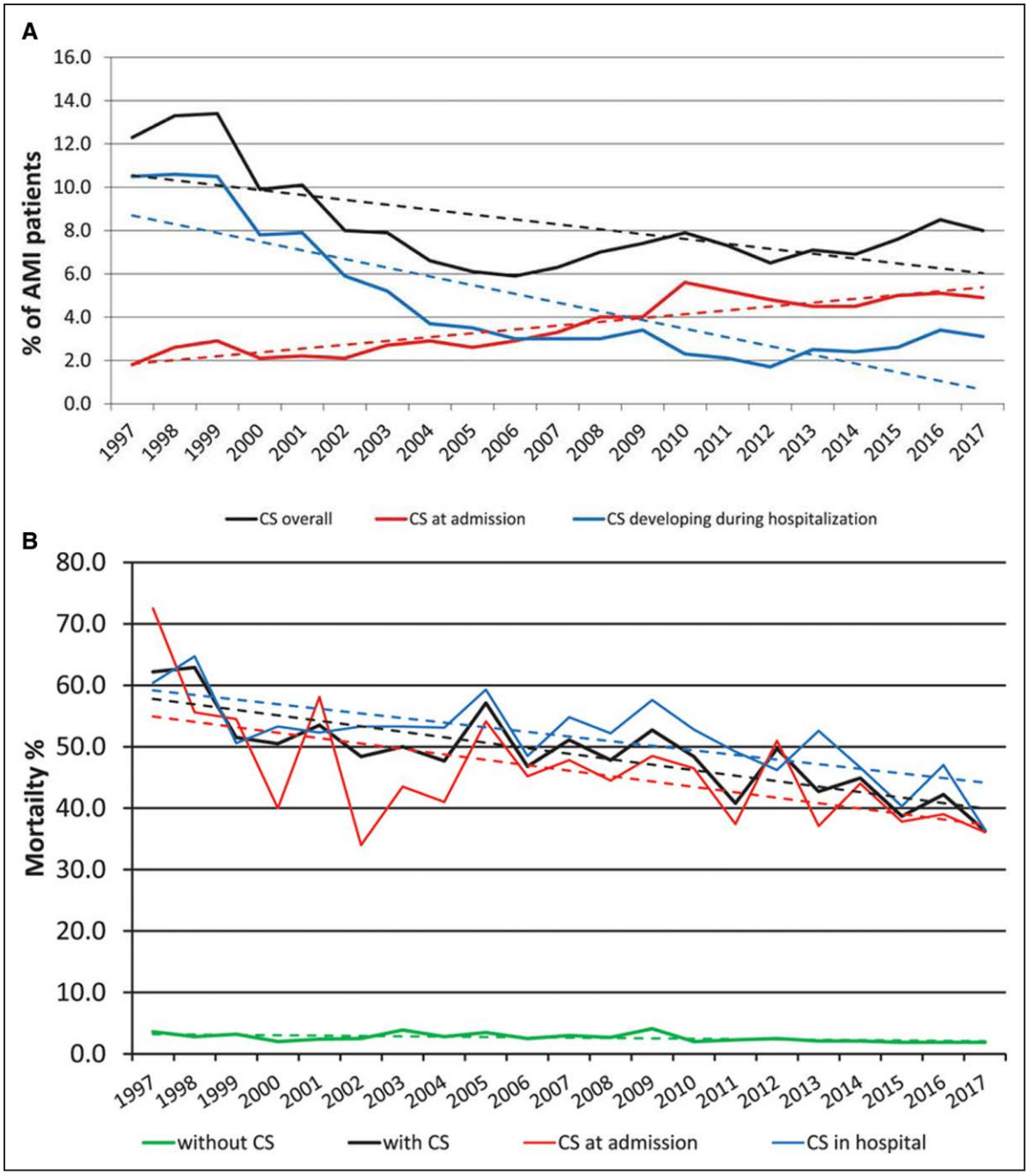

Figure 1. Incidence and outcomes of cardiogenic shock complicating acute myocardial infarction.
A, Trends in incidence of overall cardiogenic shock (CS), CS at admission, and CS developing during hospitalization in patients with acute myocardial infarction (AMI; n=51 842). Values indicate incidence of CS as a percentage of overall AMI cases. Dotted lines indicate trend lines. **B**, Trends in incidence of in-hospital mortality in patients with AMI according to presence and onset of CS. Values indicate incidence of in-hospital mortality. Dotted lines indicate trend lines. Adapted with permission from Hunziker et al.[12] Copyright © 2019, American Heart Association, Inc.

study the relative predictive value of each element used to define specific SCAI stages.

TRIAGE TO INVASIVE MANAGEMENT

On AMICS recognition, viable patients with spontaneous circulation should be brought to the cardiac catheterization laboratory of a PCI-capable hospital as soon as possible. Early echocardiography and laboratory examination (arterial blood gas, lactate) are important and can be performed in the cardiac catheterization laboratory with limited delay, taking advantage of the patient transfer in time for preparation.

Classification, stabilization, and diagnostic evaluation of AMICS are prerequisites to tailored invasive therapy. Stable patients with risk factors for shock (stage A) or early shock (stage B) can generally proceed directly to coronary angiography and culprit lesion

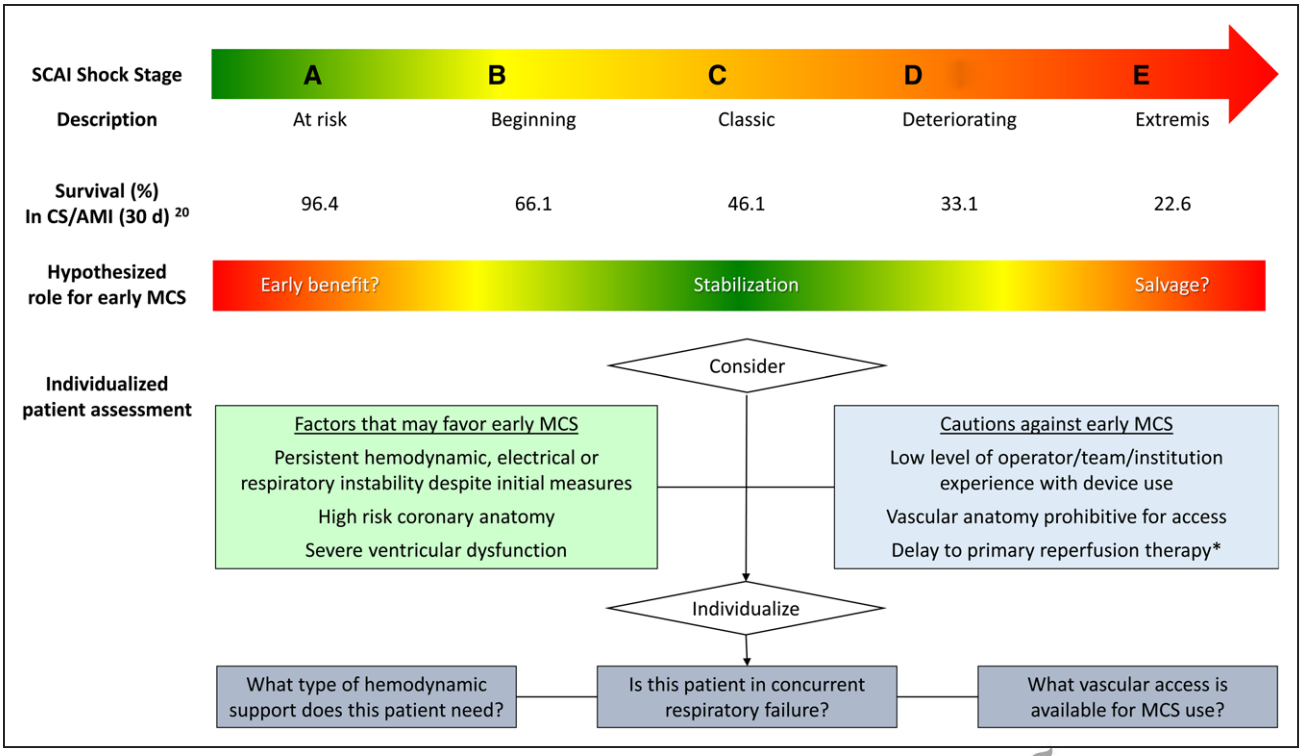

Figure 2. Consideration of early mechanical circulatory support (MCS) in the context of shock classification.
Clinical description, reported 30-day mortality,[20] and hypothesized roles for early MCS in patients with cardiogenic shock (CS) complicating acute myocardial infarction (AMI) as categorized by the Society for Cardiovascular Angiography and Intervention (SCAI) classification.[8] Considerations are proposed for the use and individualization of MCS devices. *Implications of time delay incurred during MCS initiation before primary reperfusion therapy are uncertain pending dedicated trials in the setting of CS complicating AMI.

revascularization with continuous reassessment for signs and symptoms of progression of shock. Patients presenting in shock (stages C–E) may first require acute stabilization with attention to blood pressure, end-organ perfusion status, oxygenation, and acid-base status. Especially in cases of STEMI, any necessary stabilization efforts must be expedited to minimize delay to reperfusion therapy.[21,22] Selected patients with late or extreme forms of shock (stage E) for whom invasive management is inconsistent with goals of care and unlikely to provide benefit should instead be evaluated for palliative care. It is important to note that early engagement of palliative care services and aggressive early invasive management are not mutually exclusive. Whereas only 4.5% of patients hospitalized for AMICS between 2000 and 2014 in the National Inpatient Sample received palliative care services,[23] it is likely that more patients across the spectrum of AMICS can benefit from early engagement in discussion of values and goals of care in parallel with invasive measures.

INITIAL STABILIZATION

Blood Pressure

The minimum necessary dose of vasopressor should be used to maintain mean arterial blood pressure >65 mm Hg, favoring norepinephrine as first-line therapy.[16,17] Alternative agents may be preferred in addition to or instead of norepinephrine in specific circumstances such as unstable bradycardia, in which case the increased chronotropic effect of dopamine or epinephrine may be desired; dynamic left ventricular (LV) outflow tract obstruction, for which a pure vasopressor such as phenylephrine or vasopressin may be preferred; or refractory hypoxemia or acidosis, in which case efficacy of catecholamine vasopressors may be attenuated, favoring the use of vasopressin. Of note, the mean arterial blood pressure target of 65 mm Hg is not well established, obligating attentiveness to clinical perfusion status. Caution is required in the progressive escalation of vasopressor and inotrope therapy, noting that higher levels of pharmacological support are associated with higher mortality in observational studies, although this may reflect in part the severity of illness.[24] Ongoing studies are evaluating the adjunctive role of milrinone, levosimendan, and dobutamine in different shock settings. However, these inotropic agents may be of limited value for initial stabilization in AMICS because of an increased risk for worsening myocardial ischemia.

Respiratory Function

AMICS predisposes to hypoxemia (resulting from cardiogenic pulmonary edema) and metabolic acidosis

(caused by lactic acidosis and acute kidney injury), placing patients at risk for acute respiratory failure. In a series of 439 436 admissions for AMICS captured in the National Inpatient Sample, 57% of patients received a diagnosis of acute respiratory failure and 43% underwent mechanical ventilation.[25] Worsening hypoxemia and acidosis increase susceptibility to ventricular fibrillation and may increase risk of death during attempted coronary revascularization. Increased work of breathing to compensate for ventilation-perfusion mismatch and metabolic acidosis may further contribute to progression of AMICS. Hence, strong consideration should be given to early endotracheal intubation and mechanical ventilation. Caution is advised in patients with AMICS and predominant right ventricular failure, including patients with right ventricular myocardial infarction, noting that initiation of positive pressure ventilation can abruptly lower systemic arterial pressure. Early intubation and ventilatory support may facilitate revascularization because of improved oxygenation, greater sedation, and enhanced metabolic profile.

DIAGNOSTIC EVALUATION

Physical Examination

Focused physical examination can provide immediate insight into a patient's hemodynamics. Rales and patient unwillingness to lie supine can indicate pulmonary venous congestion. Jugular venous distension suggests systemic venous congestion. Cool and clammy extremities, rapid thready pulses, and altered level of consciousness may represent hypoperfusion. A systolic murmur obligates investigation for mechanical complications. Anxiety and tachycardia are ominous markers of sympathetic activation and may portend subsequent hemodynamic deterioration after sympatholytic interventions, including not only sedation and analgesia but also reperfusion.

Echocardiography

Emergency echocardiography in AMICS should be available 24 h/d and performed as soon as possible, either before or simultaneously with invasive evaluation. The focus should be on left and right ventricular systolic function, significant valvular stenosis or regurgitation, pericardial effusion/tamponade, and evidence of mechanical complications, including septal, papillary muscle, or free wall rupture. Attention should be paid to evidence of intracardiac thrombus. Early surgical consultation should be considered for mechanical complications.

Left-Sided Heart Catheterization

Left-sided heart catheterization should be performed with careful attention to the access technique to reduce risk of bleeding complications. Documenting LV end-diastolic pressure should be considered before contrast administration because elevated LV end-diastolic pressure has been associated with increased short- and long-term mortality and the development of heart failure.[26,27] Selective coronary (or bypass graft) angiography should identify the culprit lesion and define the complete extent of disease. Consideration should be given to deferring contrast ventriculography when a diagnostic echocardiogram is available, especially with severe elevation in LV end-diastolic pressure or renal insufficiency.

Right-Sided Heart Catheterization

Right-sided heart catheterization provides access to quantitative data to sharpen characterization of individual patient hemodynamics over time. No randomized trial has been performed to validate the routine use of right-sided heart catheterization in AMICS, the optimal timing of its performance, or specific interventions based on invasive hemodynamic profiles. Key parameters to assess and monitor include central venous pressure, pulmonary capillary wedge pressure, cardiac output, cardiac power output, pulmonary artery pulsatility index, and mixed venous oxygen saturation. Cardiac power output (Watts) is calculated as follows: cardiac output×mean arterial pressure÷451.[28] Pulmonary artery pulsatility index is calculated with the following equation: (pulmonary artery systolic pressure–pulmonary artery diastolic pressure)/right atrial pressure.[29] Right ventricular stroke work index is calculated as follows: (mean pulmonary artery pressure–central venous pressure)×stroke volume index. Invasive measures, including central venous pressure >10 mm Hg, central venous pressure/pulmonary capillary wedge pressure >0.63 mm Hg, pulmonary artery pulsatility index <2.0, and right ventricular stroke work index <450 g·m/m^2, may help identify right ventricular dysfunction complicating AMICS, a common phenomenon identified in 38% and 37% of patients in the SHOCK trial and registry, respectively.[30] For patients with early shock, invasive measurements can help to further delineate those patients who are hypotensive but normally perfused and those who are normotensive but hypoperfused.[31] Of note, right-sided heart catheterization is not required to diagnose shock. In cases of AMICS in which performance of right-sided heart catheterization would cause an undue delay in timely reperfusion therapy, consideration should be given to deferring its performance until completion of PCI.

CONTEMPORARY MCS TRIALS

Patients with AMICS with persistent hemodynamic compromise despite initial stabilization may benefit from

immediate MCS. The rationale for initiation of MCS early in AMICS is to reduce ventricular workload (unloading), increase systemic perfusion, enhance myocardial perfusion, and provide hemodynamic support during PCI.

Persistent clinical hypoperfusion, hypotension, vasopressor requirement, or cardiac power output <0.6 W despite adequate filling pressures may indicate a role for MCS as an adjunct to stabilization before coronary revascularization. For patients with predominant LV failure, MCS options include intra-aortic balloon counterpulsation (IABP), a transvalvular axial flow pump (Impella LP/CP/5.0/5.5), and the TandemHeart percutaneous LV assist device. Venoarterial (VA) extracorporeal membrane oxygenation (ECMO) may be considered to provide systemic circulatory support, but close monitoring for LV distension and worsening pulmonary edema is required. In these cases, VA-ECMO may require an additional LV decompression or venting mechanism, options for which include an IABP, a left-sided Impella device, pulmonary artery cannulation, or surgical LV venting.[32,33] For patients with predominant right ventricular failure, MCS options include the transvalvular axial flow Impella RP pump and TandemHeart Protek-Duo percutaneous right ventricular assist device. Patients with biventricular failure may be supported with bilateral Impella pumps or VA-ECMO with a concomitant LV venting mechanism. Patients with concurrent refractory respiratory failure should be considered for VA-ECMO. In part, the protective mechanisms associated with MCS in AMI are supported by extensive preclinical data beginning in the late 1970s.[34] Observational studies of AMICS systems of care incorporating early MCS have reported improved survival compared with historical controls,[15,35,36] but no randomized controlled trial has provided evidence in support of routine use for any short-term MCS platform.

The IABP-Shock II trial (Intra-Aortic Balloon Pump in Cardiogenic Shock II) randomized 600 patients with AMICS to a strategy of routine IABP use or conservative care.[7] Among the 277 patients randomized to IABP who received urgent revascularization, 86.6% of patients received the IABP after revascularization. Compared with the group of patients assigned to conservative care, the use of an IABP was not associated with a reduction in 30-day all-cause mortality (39.7% versus. 41.3%; *P*=0.69). In addition, key secondary end points, including time to hemodynamic stabilization, intensive care unit length of stay, renal function, and serum lactate levels, did not differ between the 2 groups. Although this trial did not support the IABP as a specific MCS device for the treatment of AMICS, some have argued that the lack of benefits observed in this trial may have been influenced by the timing of device insertion (after revascularization in the majority of patients), variability of shock severity across the study population, or limited hemodynamic effects of IABP relative to other devices. Randomized studies comparing the IABP with other MCS devices have not shown improved survival with any MCS device, although these studies were small and not powered to evaluate hard end points.[18,37,38] These findings should not be extrapolated to other causes of CS beyond AMI. More prospective studies are required to understand the clinical utility of IABP in ischemic and nonischemic forms of CS.

Observational studies examining outcomes with MCS devices used for AMICS have reported variable results. The Detroit Cardiogenic Shock Initiative encouraged an aggressive protocol of early MCS in the management of patients with AMICS.[15] Among a cohort of 41 patients admitted to 4 hospitals in Detroit, MI, with AMICS who were treated with an Impella, 93% of patients were on vasopressors or inotropes before device implantation, and an additional 17% were receiving active cardiopulmonary resuscitation during Impella placement. The majority of patients (66%) received an Impella before revascularization. In this report, 85% of patients survived to device explantation. This number was notably higher than the 51% observed survival to device explantation reported for patients with AMICS in the metro Detroit area before implementation of this protocol. These findings have been further studied in the prospective single-arm National Cardiogenic Shock Registry.[36] Systematic exclusion of cardiac arrest and selection bias prompt caution in the interpretation and generalization of the favorable outcomes observed in these studies compared with historical controls.

In the RETROSHOCK registry of patients with AMICS admitted to 2 hospitals in Denmark,[39] patients treated with early Impella use (n=40) had a significantly lower rate of death compared with a matched group of patients receiving no therapy (40% versus 77.5%; *P*<0.001). On the other hand, the mortality rate of patients treated with IABP (n=40) was similar to that of a matched group of patients receiving no therapy (27.5% versus 37.5%; *P*=0.35). These data contrast with those reported in a European multinational registry of patients with AMICS,[40] in which 237 patients treated with an Impella were matched to 237 patients enrolled in the IABP-Shock II trial. Among the 237 patients selected from the multinational registry, 38.1% were treated with an Impella before revascularization. Use of an Impella was associated with no difference in 30-day all-cause mortality compared with the matched patients from the IABP-Shock II trial (48.5% versus 46.4%; *P*=0.64). Severe or life-threatening bleeding was higher in the Impella group (8.5% versus 3.0%; *P*<0.01), as were vascular complications (9.8% versus 3.8%; *P*=0.01) and sepsis (35.3% versus 19.4%; *P*<0.01). Subgroup analysis did not show an interaction between timing of insertion and outcomes. In addition, there were no differences in mortality when analysis was limited to a comparison of registry patients with an

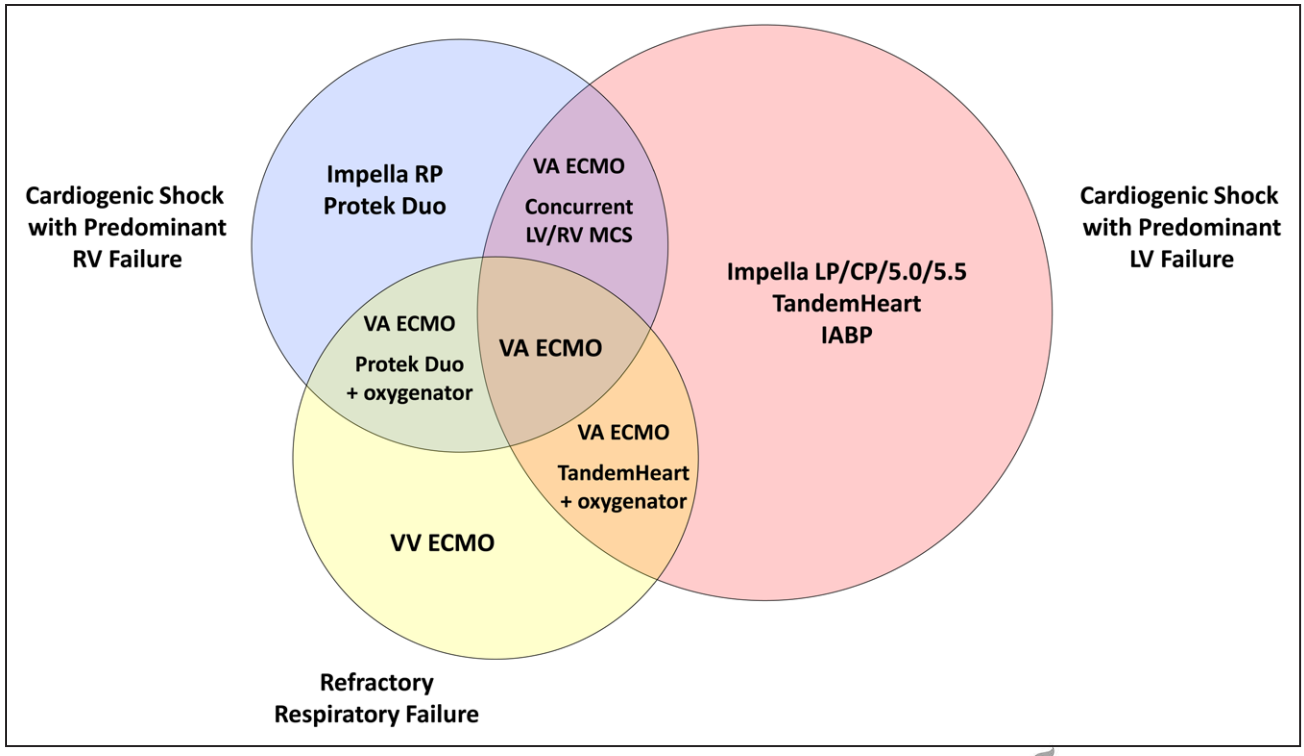

Figure 3. Matching of mechanical circulatory support (MCS) platforms with clinical presentations.
Cardiogenic shock complicating acute myocardial infarction may present with a variable and dynamic combination of left ventricular (LV) failure, right ventricular (RV) failure, and respiratory failure. Different MCS platforms support these 3 axes of organ dysfunction to different degrees. ECMO indicates extracorporeal membrane oxygenation; IABP, intra-aortic balloon counterpulsation; VA, venoarterial; and VV, veno-venous.

Impella and patients either in the treatment arm (IABP) or in the control arm of the IABP-Shock II trial.

The DanGer trial (Danish-German Cardiogenic Shock) is a prospective open-label multicenter trial that aims to randomize 360 patients with AMICS to the Impella CP or guideline-driven therapy.[41] Multiple randomized studies of VA-ECMO in AMICS are also ongoing, including EURO SHOCK (Testing the Value of Novel Strategy and Its Cost Efficacy in Order to Improve the Poor Outcomes in Cardiogenic Shock; URL: ClinicalTrials.gov. Unique identifier: NCT03813134), ECLS-SHOCK (Extracorporeal Life Support in Cardiogenic Shock; URL: ClinicalTrials.gov. Unique identifier: NCT03637205), ECMO-CS (Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock; URL: ClinicalTrials.gov. Unique identifier: NCT02301819), and ANCHOR (Assessment of ECMO in Acute Myocardial Infarction Cardiogenic Shock; URL: ClinicalTrials.gov. Unique identifier: NCT04184635). The results of these and other trials will further inform the management of patients with AMICS. In the meantime, there is cause for caution, with observational data illustrating heterogeneity in safety and outcomes of MCS use in the context of steadily growing use. Indeed, 2 recent registry studies demonstrated signals toward increased rates of major bleeding and in-hospital death among propensity-matched patients with AMICS treated with an Impella versus IABP.[42,43] It is important that we individualize care for our patients, considering the underlying mechanisms of shock, anticipated benefits and risks of MCS, and ideal timing for device insertion. MCS platforms differ substantially with respect to vascular access requirements, learning curve, and support provided, and limited data exist to inform allocation of specific MCS devices based on clinical or hemodynamic profile. Specific device selection requires the input of a multidisciplinary team with consideration of patient needs and device availability and familiarity (Figure 3).

Putative benefits of early MCS include support of systemic perfusion, reduced cardiac workload, enhanced coronary perfusion and decongestion, and, through these mechanisms, arrest of the progression of shock to end-organ injury and death.[44] Offsetting these benefits are variable, device-dependent risks of bleeding, hemolysis, vascular complications, and limb ischemia, as well as the additive complexity of postimplantation management.[45] In the context of STEMI, there is a theoretical concern that benefits of MCS may be further offset by increased delay to reperfusion therapy. The Door to Unload-STEMI pilot study, which did not include patients with CS, did not identify harm with a strategy of first unloading the LV for up to 30 minutes before reperfusion but also did not show benefit.[46] The STEMI-DTU pivotal trial (Primary Unloading and Delayed Reperfusion in ST-Elevation Myocardial Infarction) will test whether early MCS before reperfusion limits myocardial damage in patients with anterior

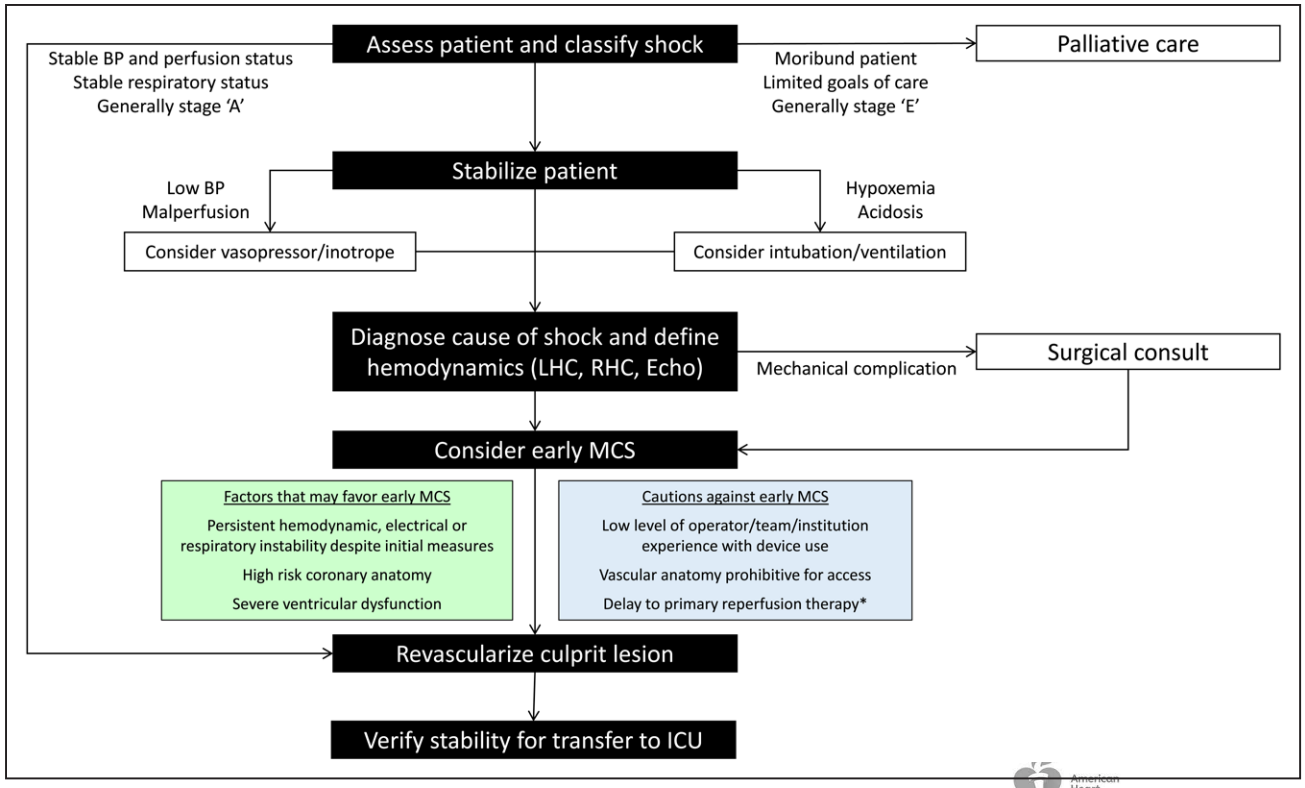

Figure 4. Algorithmic approach to the patient with acute myocardial infarction (AMI) complicated by cardiogenic shock (CS). Several centers have developed specific institutional protocols for triage and management of CS complicating AMI (Supplemental Figures). We here outline a general framework for triage, diagnosis, and management with considerations for early use of mechanical circulatory support (MCS). Stages refer to the Society for Cardiovascular Angiography and Intervention classification for CS.[8] BP indicates blood pressure; Echo, echocardiography; ICU, intensive care unit; LHC, left-sided heart catheterization; and RHC, right-sided heart catheterization. *Implications of time delay incurred during MCS initiation before primary reperfusion therapy are uncertain pending dedicated trials in the setting of CS complicating AMI.

STEMI without CS. It is not certain that findings in STEMI without shock can be extrapolated to AMICS. Among patients with AMICS, emerging observational data suggest that early MCS may improve, not worsen, outcomes in select patients.[15] Operator technique and judgment in vascular access, management of anticoagulation, surveillance and timely management of vascular complications, expertise in device positioning and management, and integration of device use within a global plan of care collectively have substantial potential to influence the net benefit of early MCS use for an individual patient. An array of trials are attempting to decipher this complex landscape. Until data become available from randomized clinical trials sufficiently powered to define risks and benefits of early MCS for patients with different stages of AMICS, we strongly encourage an individualized approach to care and participation in clinical research protocols to test the utility of MCS in AMICS. Early MCS placement before PCI may be considered for patients with AMICS who exhibit refractory hemodynamic instability despite aggressive medical therapy (Figure 4).

CORONARY REVASCULARIZATION

PCI of the infarct-related artery is the recommended method of reperfusion for patients with AMICS regardless of time delay.[5,47,48] The SHOCK trial established the clinical benefit of an early invasive strategy with intent for early revascularization in patients with AMICS, demonstrating a significant mortality reduction at 6 months and in long-term follow-up for individuals <75 years of age compared with initial medical stabilization.[6,49,50] To save 1 life, only 8 patients need to be treated according to this landmark trial. Of note, the SHOCK trial did not identify a difference in its primary end point, all-cause mortality at 30 days, with benefits of early revascularization becoming evident only with longer follow-up. This example underscores challenges in the design and interpretation of randomized trials in AMICS. With the progressive availability of early PCI, multiple registries have since shown a decrease in mortality from prior levels of 70% to 80% to 40% to 50%.[12,51–54] Early revascularization has become the most important strategy in the treatment of AMICS, with recent registries highlighting increased risks with revascularization delays.[21,22]

Modality of Revascularization

There is uncertainty about the optimal revascularization approach in AMICS because previous trials assessing the effect of revascularization on outcomes did not specify

the mode of reperfusion. PCI is the most widely available and most often performed revascularization therapy in AMICS, whereas coronary artery bypass graft surgery (CABG) is rarely performed. In the IABP-Shock II trial and registry, for example, only 4% of patients had immediate CABG.[7] In observational reports comparing PCI with CABG, mode of revascularization has not appeared to influence outcomes of patients with AMICS.[55,56] Factors influencing the possible selection of CABG include the suitability of coronary anatomy, including the caliber and quality of prospective distal anastomotic targets for bypass grafts; importance of the infarct-related artery; and surgical availability and experience. Given the very high mortality of patients with unsuccessful PCI, emergency CABG should be considered a rescue modality in such cases, as well as in cases in which AMI is complicated by myocardial rupture. A hybrid approach of culprit lesion PCI (with or without stent placement) followed by staged CABG has also been considered, in particular for patients with AMICS and multivessel disease with or without diabetes.

Because of its limited efficacy, fibrinolytic therapy is reserved for patients with ST-segment–elevation AMI when timely PCI is unavailable.[47,48] For those patients with AMICS who initially present to a non–PCI-capable facility, the question of safe transfer to a PCI-capable hospital arises.[4] Availability of a transfer network and early activation of an established AMICS communication pathway become important early measures. If immediate transfer cannot be arranged safely, evaluation for emergency fibrinolytic therapy and subsequent transfer should be considered, granting that many patients may possess contraindications to fibrinolytic therapy such as traumatic resuscitation efforts, cardiac arrest with unclear neurological prognosis, no clear ST-segment elevation on the initial ECG, coagulopathy, and advanced age.

Management of Multivessel Disease

Additional stenoses or occlusions beyond the infarct-related artery can be found in ≈70% to 80% of patients.[57] Patients with AMICS with multivessel disease have a higher mortality compared with patients with single-vessel disease.[58] Until recently and mainly on the basis of theoretical considerations, multivessel PCI of all critical lesions was encouraged in patients with AMICS.[47,48,59] This approach was not supported by pooled results of observational studies that demonstrated higher short-term mortality when multivessel PCI was performed in patients with AMICS.[60]

The CULPRIT-SHOCK trial (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock),[9] to date the largest randomized trial in CS, addressed the question of optimal revascularization therapy in patients with multivessel disease and AMICS. This study of 706 patients with AMI (66% with STEMI) showed a significant reduction in 30-day mortality or renal replacement therapy (primary end point) with a strategy of culprit lesion–only PCI (with an option for staged revascularization of additional lesions) compared with immediate multivessel PCI (45.9% versus 55.4%; relative risk, 0.83 [95% CI, 0.71–0.96]; P=0.01), driven primarily by an absolute 8.2% reduction in mortality.[9] These results were further supported by a sustained reduction in the same composite end point at the 1-year follow-up.[61] Results were consistent across all predefined subgroups, including patients with out-of-hospital cardiac arrest.

In the vast majority of patients with AMICS, PCI should be limited to the culprit lesion with possible staged revascularization of other lesions. However, the role of multivessel PCI in AMICS remains under active investigation. Notably, few patients in the CULPRIT-SHOCK trial received MCS. Furthermore, recent data from the Korea Acute Myocardial Infarction National Health Registry showed that multivessel PCI was associated with a lower risk of all-cause death than culprit-artery–only PCI at 3 years, suggesting possible benefit of nonculprit lesion revascularization during the index hospitalization on long-term clinical outcomes.[62] Selected angiographic scenarios such as subtotal nonculprit lesions with reduced TIMI (Thrombolysis in Myocardial Infarction) grade flow or multiple possible culprit lesions may benefit from immediate multivessel PCI. Such decisions are complex and not addressed in practice guidelines, absent a robust clinical trial for each decision step, requiring individualized consideration on a patient and lesion basis.

Antiplatelet Therapy

CS is a potent predictor of stent thrombosis.[63] Potential factors contributing to this association may include AMICS-associated abnormalities in coronary perfusion, thrombus burden, microvascular occlusion and dysfunction, platelet activation, PCI quality, and limited bioavailability related to absorption (in particular in the setting of morphine or fentanyl) and pharmacodynamics of antithrombotic therapies. In this context, a strategy of more potent and more consistent antiplatelet therapy may be desired for AMICS,[64] although no adequately powered randomized trial specific to AMICS has tested this to date. Avenues to increase potency, consistency, and rapidity of antiplatelet therapy in AMICS may include preferential use of third-generation oral $P2Y_{12}$ inhibitors instead of clopidogrel,[64,65] administration of crushed ticagrelor via gastric tube,[66] and parenteral administration of cangrelor,[67] alone or in combination with ticagrelor.[68] Platelet reactivity may be further reduced with adjunctive use of glycoprotein IIb/IIIa inhibitors,[69] but the safety of these agents in the context of AMICS is not well established, particularly in the

setting of large-caliber access for MCS devices. Rapid reversibility of cangrelor despite bowel, liver, and kidney dysfunction might improve safety.

Transition From Laboratory to Cardiac Intensive Care Unit

After completion of PCI, attention turns to preparation for patient transfer to the cardiac intensive care unit. This transition may be aided by a checklist. Critical elements of a general survey of stability include hemostasis at all access sites; electric stability, noting evidence of ongoing bradyarrhythmia or tachyarrhythmia; hemodynamic stability, including verifying optimal positioning, securing, performance, and adequate distal limb perfusion with any MCS devices; respiratory stability, including adequate oxygenation and control of acid-base status; sufficient vascular access; and consideration of an indwelling pulmonary artery catheter.

CARDIAC INTENSIVE CARE

Comprehensive critical care after acute invasive management comprises prevention, diagnosis, and management of multiorgan system failure complicating AMICS; continuous reassessment of hemodynamics and perfusion status with clinical and invasive measures; ongoing and relentless titration of therapies based on evolving data; anticipation and management of complications of acute invasive management; collaboration and shared decision making by a multidisciplinary shock team, including consideration of timing and approach to escalation or de-escalation of MCS; and close communication with family to provide regular updates and reassessment of prognosis and goals of care. Areas of consensus, controversy, and uncertainty are considered in detail elsewhere.[4]

SPECIAL CONSIDERATIONS

Cardiac Arrest

Cardiac arrest is common among patients with AMICS and confers an increased risk of mortality that is independent of shock stage.[8,19] Outcomes are exponentially complicated by a variable degree of hypoxic-ischemic encephalopathy, with a subset of patients at risk for severe neurological disability or brain death regardless of a positive cardiac outcome. Proceeding with a complex cardiac evaluation and treatment plan while neurological status is unknown for up to several days poses unique difficulties in care delivery and ethics.

In general, patients successfully resuscitated from cardiac arrest with return of spontaneous circulation and neurological function (Glasgow Coma Scale score ≥8) and a diagnosis of AMICS should be triaged to the cardiac catheterization laboratory as soon as possible for complete assessment. Vigil is required during transport and in the laboratory for recurrent arrest. Patients with AMICS and resuscitated cardiac arrest who remain comatose (Glasgow Coma Scale score <8) or unable to follow simple commands should be treated with targeted temperature management as soon as possible.[70–72] Early invasive therapy in comatose patients with out-of-hospital cardiac arrest should be individualized and based on the absence of unfavorable prognostic features, which may include unwitnessed arrest, an initial nonshockable rhythm, lack of bystander cardiopulmonary resuscitation, >30 minutes to return of spontaneous circulation or ongoing cardiopulmonary resuscitation, pH <7.2, lactate >7 mmol/L, age >85 years, end-stage renal disease, and noncardiac cause of arrest.[73] In the absence of multiple unfavorable prognostic features, patients with AMICS with or without ST-segment elevations should be considered for emergency triage to the cardiac catheterization laboratory.[74] Although a recent randomized study found no penalty in terms of 90-day mortality with a strategy of delayed versus immediate angiography in cardiac arrest without ST-segment elevations, it should be noted that this trial systematically excluded patients with shock.[75]

Patients with AMICS and ongoing cardiac arrest without return of spontaneous circulation represent the highest-risk group in whom multiorgan failure is uniform and mortality is common. Successful invasive management has been reported with the use of automated cardiopulmonary resuscitation and ECMO in carefully selected patients by experienced multidisciplinary teams at tertiary centers.[76] A majority of such patients stabilized with ECMO who undergo coronary angiography have obstructive coronary artery disease with indication for PCI.[77] Further research is required to guide patient selection, define feasibility, and organize delivery of this resource-intensive approach on a broader scale. Also requiring further research are the role and optimal modality of LV venting when ECMO is used to support AMICS, noting benefit in meta-analysis of observational studies and variable use and multiple tools in practice.[42,43] Results of ongoing trials are anticipated.

Futility

A subset of patients with AMICS will die regardless of invasive management. Risk predictive models developed for patients with shock[1,78,79] and patients treated with ECMO[80] may provide useful adjuncts to clinical assessment to identify patients at highest risk for mortality, but it is unclear that such scores should be used to determine eligibility for invasive management because of potential risk-treatment paradox. Assessment of the utility of invasive therapy is complex and

requires ascertainment of patient and family values and wishes and the clinical judgment of a multidisciplinary shock team.

CONCLUSIONS AND FUTURE DIRECTIONS

AMICS is a complex clinical entity that remains prevalent and the major cause of death after AMI. Treatment decisions made in the early invasive management of AMICS can have significant ramifications for the progression of shock, patient survival, and outcomes of AMICS at large. Optimization of care requires a multidisciplinary team effort to coordinate early assessment and triage (including possible interhospital transfer), noninvasive and invasive diagnostics, coronary revascularization, and expert ongoing intensive care management, including a sophisticated understanding of the evolving pathophysiology and hemodynamics of AMICS.[81] Advances in systematic recognition and classification of AMICS are expected to allow a new wave of clinical investigation into this highly morbid and mortal disease and its invasive management.

Essential avenues for future research in invasive management of AMICS include but are not limited to the following:

- System-level approaches to expediting identification of AMICS and activation of established multidisciplinary shock teams, including at shock centers, non–shock center PCI-capable hospitals, and non–PCI-capable hospitals;
- Applications of SCAI shock classification to therapeutic critical pathways, including consideration of early MCS, use of invasive hemodynamic monitoring, and selection for invasive management;
- Selection of vasoactive drug therapies to support hemodynamics in the presence or absence of MCS devices, including guidance of selection and titration of drug therapies with invasive hemodynamic measures and consideration of specific inotrope and vasopressor agents alone and in combination;
- Strategies for allocation of MCS, before or after coronary revascularization, including appropriate initial selection of specific MCS devices; criteria for allocation of secondary MCS devices, including use of adjunctive LV venting for patients on ECMO; and criteria for weaning and discontinuing support;
- Approaches to multivessel coronary artery disease, including criteria for selected application and timing of multivessel PCI and consideration of CABG;
- Choice of pharmacotherapy to support PCI, including antiplatelet therapy and reversal/bridging considerations;
- Management and safety of MCS devices in the cardiac intensive care unit, including strategies to reduce bleeding and vascular complications, anticoagulation management, parameters for monitoring device function and necessity, and interplay with vasoactive drug therapies; and
- Application of targeted temperature management in patients with AMICS and resuscitated cardiac arrest, including optimal target temperature and cooling modality.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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*Modest.

†Significant.

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