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MANAGEMENT OF ACUTE CORONARY SYNDROMES (H JNEID, SECTION EDITOR)

Update in the Management of Acute Coronary Syndrome Patients with Cardiogenic Shock

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Abstract

Purpose of Review We provide a concise update on the contemporary management of cardiogenic shock in the setting of acute coronary syndrome (ACS). Early shock recognition, optimal selection and initiation of mechanical circulatory support (MCS), early coronary revascularization, and a team-based, protocol-driven approach are the current pillars of management.

Recent Findings Cardiogenic shock complicates approximately 5–10% of ACS cases and continues to have high mortality. Early use of mechanical circulatory may prevent the downward spiral of shock and has significantly increased over time, supported mainly by registry data. In the CULPRIT-SHOCK trial, culprit-only revascularization was associated with a lower 30-day incidence of all-cause death or severe renal failure, compared with immediate multivessel PCI. Routine revascularization of non-infarct related artery lesion(s) during primary PCI for cardiogenic shock is, therefore, not recommended. The routine use of an intra-aortic balloon pump (IABP) was not associated with improved outcomes in the IABP-SHOCK II trial. A team-based and protocol-driven approach may further improve outcomes.

Summary Recent advances in coronary revascularization and use of MCS, implementation of shock teams and standardized protocols may improve outcomes of cardiogenic shock in ACS patients.

Keywords Cardiogenic shock · Acute coronary syndrome · Acute myocardial infarction · Mechanical circulatory support · Update

Abbreviations

ACS	Acute coronary syndrome
AMICS	Acute myocardial infarction complicated with cardiogenic shock
CAD	Coronary artery disease
CPO	Cardiac power output
CS	Cardiogenic shock
CTO	Chronic total occlusion
CULPRIT-SHOCK	Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock
cVAD	Catheter-based ventricular assist device
CVP	Central venous pressure
e-CPR	Extracorporeal cardiopulmonary resuscitation
IABP	Intra-aortic balloon pump
IABP-SHOCK II	Intra-aortic Balloon Pump in Cardiogenic Shock II
IMPRESS	Impella versus IABP Reduces mortality in STEMI patients treated with primary PCI in severe cardiogenic SHOCK
MCS	Mechanical circulatory support
AMI	Acute myocardial infarction
PAPi	Pulmonary Artery Pulsatility Index
RIFLE-STEACS	Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome

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RV	Right ventricular
SBP	Systolic blood pressure
SHOCK	Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock
STEMI	ST segment elevation acute myocardial infarction
VA-ECMO	Veno-arterial extracorporeal membrane oxygenation

Introduction

Approximately 5–15% of acute coronary syndrome (ACS) patients develop cardiogenic shock (CS), and up to 80% of patients presenting with CS have underlying ACS [1, 2]. Typically, CS occurs when ≥ 40% of the myocardium is involved or in the presence of a mechanical complication of acute myocardial infarction (AMI), such as papillary muscle, ventricular septal, or free wall rupture. Multivessel coronary artery disease (CAD) is present in approximately 80% of patients with acute myocardial infarction complicated by cardiogenic shock (AMICS), and 25–30% have a chronic total occlusion (CTO) in the non-infarct related artery [3••, 4]. Presence of a CTO has been associated with higher 1-year mortality (HR 1.30 [1.02–1.67]; $p = 0.03$) [4]. Patients with non-ST-elevation myocardial infarction (NSTEMI) and CS have worse in-hospital outcomes compared with patients presenting with ST segment elevation MI (STEMI) and CS, likely due to the higher frequency of complex multivessel CAD in the former group, including CTOs and left main disease [5]. Another reason for this finding could be delays in revascularization in patients with NSTEMI compared with STEMI. In a study of 1853 STEMI patients, the majority of patients who had CS developed shock within 24 h (early shock) or after 24 h of admission (late shock) compared with shock present pre-admission. Late shock was associated with the highest mortality and was more common in patients older than 75 years [6].

The increasing incidence of CS may be associated with an aging population. In a Nationwide Inpatient Sample study, the incidence of AMICS increased from 6.5% in 2003 to 10.1% in 2010 ($p < 0.001$) with a greater increase among patients older than 75 years [7]. In-hospital mortality for AMICS declined from 44.6 to 33.8% during the same time period ($p < 0.001$), likely due to significant advances in revascularization and supportive care, such as use of mechanical circulatory support (MCS).

Diagnosis and Risk Stratification

CS is defined as a state in which ineffective cardiac output, caused by a primary cardiac disorder, results in both clinical and biochemical manifestations of inadequate tissue perfusion [8••]. The SHOCK trial defined CS based on clinical and hemodynamic criteria [9]. Clinical criteria include systolic blood pressure (SBP) < 90 mmHg for ≥ 30 min or need for pharmacologic or intra-aortic balloon pump (IABP) support to maintain SBP > 90 mmHg, combined with end-organ hypoperfusion (urine output < 30 mL/h, cool extremities, altered mental status, elevated lactate). Hemodynamic criteria include a cardiac index (CI) ≤ 2.2 L/min/m^2, combined with pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg. However, some patients with CS may not have hypotension. The severity of CS can range from pre-shock with clinical evidence of hypoperfusion, despite SBP > 90 mmHg, to refractory shock, in which there is ongoing hypoperfusion despite ≥ 2 vasopressors and treatment of the underlying cause. The cardiac power output (CPO) in watts (W), calculated as CO × MAP/451, was the most important determinant of outcome in the SHOCK trial. CPO ≤ 0.53 W was associated with 58% in-hospital mortality [10].

In the Catheter-based Ventricular Assist Device (cVAD) registry, increasing age, anoxic brain injury, mechanical ventilation, and presence of CS prior to admission were independently associated with higher mortality [11••]. In the Impella versus IABP reduces mortality in STEMI patients treated with primary PCI in severe cardiogenic SHOCK (IMPRESS) trial, return of spontaneous circulation post-arrest in < 20 vs. > 20 min (19% vs. 70% mortality; HR 5.50 [1.82–16.58]; $p = 0.001$), and admission serum lactate level < 7.5 vs. ≥ 7.5 mmol/L (29 vs. 60% mortality; HR 3.09 [1.09–8.74]; $p = 0.04$) were associated with lower 30-day mortality [12••]. Similarly, age > 65 years and admission lactate levels > 3.8 mmol/L were associated with higher 30-day mortality in the EUROSHOCK registry [13]. A risk score was recently derived from the IABP-SHOCK II trial [14]. Six variables (age > 73 years, lactate > 5 mmol/L, creatinine > 1.5 mg/dL, glucose > 191 mg/dL, prior stroke, and TIMI flow grade < 3 after PCI) were included (with 1 or 2 points given to each variable), with 30-day mortality ranging from 20 to 30%, 40 to 60%, and 70 to 90%, in the low, intermediate, and high risk categories, respectively.

Coronary Revascularization

Timing of Revascularization

The pivotal SHOCK trial randomized 302 patients, who developed CS within 36 h of MI onset to early revascularization (within 6 h of randomization) with percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) versus initial medical stabilization (fibrinolytic therapy in 63%, followed by PCI or CABG after ≥ 54 h) [9]. The primary outcome of the trial, 30-day mortality, was similar in the two study groups. However, the early revascularization group had a significant 13% absolute reduction in 1-year mortality, which was sustained during 3-year and 6-year follow-up

(HR 0.74 [0.57–0.97]; $p = 0.03$), as well as at 11-year follow-up (number needed to treat = 8) [15]. While the original SHOCK trial demonstrated no benefit of early revascularization in patients older than 75 years at 1-year, this analysis was underpowered due to the small number of older patients (only 56 patients out of a total of 302 patients were older than 75 years). Long-term survival analysis showed that there was no interaction of treatment assignment with multiple patient factors, including age > 75 years. A benefit of early revascularization in > 75-year-old patients was also observed in the SHOCK registry [16]. In addition, a meta-analysis, which included observational data and sub-studies of randomized studies, demonstrated lower short and intermediate-term mortality in appropriately selected elderly patients treated with early revascularization compared with initial medical therapy or selective revascularization [17]. As a result, the current ACC/AHA STEMI guidelines recommend the immediate transfer of AMICS patients to a PCI-capable hospital, irrespective of the time delay from MI onset [18]. Despite these recommendations, early revascularization was performed in only 51% of cases in the National Inpatient Sample in 2010, with even lower rates among women and > 75-year-old patients [7].

Arterial Access

Radial access is increasingly being used for cardiac catheterization in the USA and has been associated with lower risk for access site complications. There are, however, no randomized controlled trials comparing trans-radial and trans-femoral access in ACS patients presenting with CS. In RIFLE-STEACS, only 5% of patients in the radial arm had CS, and only 7.6% required IABP therapy. Cardiogenic shock at presentation was associated with crossover from radial to femoral access (HR 3.43 [1.7]; $p = 0.01$) [19]. A meta-analysis of five non-randomized, retrospective studies of CS patients showed lower rates of mortality, transfusion, and major bleeding with radial access [20]. However, patients undergoing trans-radial PCI were less sick compared with those in whom femoral access was used, suggesting the possibility of selection bias.

Revascularization: Multivessel Versus Culprit-Only

The debate on whether culprit lesion vs. multivessel revascularization should be performed was recently settled by the CULPRIT-SHOCK trial. CULPRIT-SHOCK randomized 706 CS patients with either STEMI (approximately 62%) or NSTEMI and multivessel CAD to either immediate multivessel PCI of culprit-only PCI [3••]. More than half of the patients had a prior cardiac arrest. A CTO was present in 22–24% of patients. Patients with onset of CS > 12 h before randomization and creatinine clearance < 30 mL/min were excluded. Complete revascularization was achieved in 81% of the multivessel PCI group. CTO PCI was also attempted in the multivessel PCI group as long as contrast volume did not exceed 300 mL. MCS was used in approximately 28% of patients. Compared with patients who underwent multivessel PCI, those who underwent culprit-only PCI had lower 30-day incidence of death or severe renal failure requiring renal replacement therapy (55.5 vs. 45.9%, RR = 0.83 [0.71 to 0.96]; $p = 0.01$; number needed to treat = 10) and lower mortality (51.6 vs. 43.3%; RR, 0.84 [0.72 to 0.98]; $p = 0.03$). The most common cause of death was refractory CS. The worse outcomes with multivessel PCI might be due to a deleterious effect of higher contrast volume or due to ischemia caused by a prolonged PCI procedure. During the 1-year follow-up, there was no difference in mortality or reinfarction between the two groups. Repeat revascularization (32.3 vs 9.4%, RR 3.44) and rehospitalization for heart failure (5.2 vs. 1.2%, RR 4.46), however, were less frequently required in the multivessel PCI group [21].

The CULPRIT-SHOCK results resulted in a change in the 2018 ESC/EACTS coronary revascularization guidelines, in which routine revascularization of non-infarct related artery lesions during primary PCI in patients with CS is not recommended (class III, level of evidence B) (Table 1) [22••].

Hemodynamic Support

Inotropic Support

Studies comparing inotropes and vasopressors are limited by small sample size and potential bias. At present, there is limited data to support preferential use of a specific agent, although norepinephrine may be preferred in patients with fast heart rate or arrhythmias and dopamine in patients with slow heart rate [7]. In a trial comparing dopamine and norepinephrine for shock, dopamine was associated with higher mortality in the subgroup with cardiogenic shock. However, the validity of this finding is limited by methodological and clinical concerns [7, 23].

Trends in Mechanical Circulatory Support

Use of MCS for AMICS has been increasing. In an analysis from the Nationwide Inpatient Sample, MCS use increased by 1151% between 2007 and 2011, with a concomitant decline in hospital costs and mortality (from 51.6 to 43.1%) [24].

A potential benefit of MCS is that it allows a reduction in the need for multiple inotropes and vasopressors. In an analysis from the cVAD registry, survival was lower in patients requiring a higher number of inotropes/vasopressors; 0 drug, 68%; 1 drug, 45%; 2–3 drugs, 35%; and 4 drugs, 26% (odds ratio 2.3 [0.99–5.32; $p = 0.05$) [11••]. Rapid weaning of these agents after institution of MCS has been emphasized in contemporary CS protocols.

Table 1 Summary of recommendations on treatment strategies in AMICS from the 2013 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for the management of ST segment elevation myocardial infarction [18] and the 2018 European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) guidelines on myocardial revascularization [22••]

Treatment	2013 ACC/AHA guidelines	2018 ESC/EACTS guidelines
Non-culprit lesion PCI	In patients with CS due to pump failure, PCI of a severe stenosis in a large non-infarct artery might improve hemodynamic stability and should be considered during the primary procedure No specific class of recommendation	In cardiogenic shock, routine revascularization of non-infarct related artery lesions is not recommended during primary PCI. Class III, level of evidence B
IABP	The use of IABP can be useful for patients with CS after STEMI who do not quickly stabilize with pharmacological therapy Class IIa, level of evidence B	Routine use* of IABPs in patients with cardiogenic shock due to ACS is not recommended. Class III, level of evidence B
MCS	Alternative LV assist devices for circulatory support may be considered in patients with refractory CS Class IIb, level of evidence C	In selected patients with ACS and CS, short-term MCS may be considered, depending on patient age, comorbidities, neurological function, and the prospects for long-term survival and predicted quality of life. Class IIb, level of evidence C

* IABP for CS due to AMI mechanical complications was a class IIa, level of evidence C, recommendation in the 2014 ESC guidelines

IABP

The IABP was the main device used for left ventricular support of AMICS patients for many years. IABP lowers left ventricular systolic and end-diastolic pressures and total peripheral resistance, improves mean arterial pressure and coronary perfusion, and modestly improves cardiac output by 0.5–0.8 L/min.

Use of the IABP has decreased in recent years, in large part due to the IABP-SHOCK II trial that was conducted between 2009 and 2013. IABP-SHOCK II randomized 600 patients with AMICS to IABP vs. control [21]. Patients who required cardiopulmonary resuscitation (CPR) for > 30 min, or had shock onset > 12 h prior to presentation, mechanical causes of shock, severe anoxic brain injury, and contraindications to IABP were excluded; 45% of the patients had undergone CPR, 90% had required vasopressors, and 77% had multivessel CAD. In 55% of patients with available data, the median time from onset of shock to randomization was 2.17 h, but time from shock onset was not associated with survival. IABP was inserted after revascularization in most patients (88%), and 10% and 7.4% of the control group crossed over to IABP or received MCS, respectively. The incidence of peripheral vascular complications requiring intervention in the IABP group was low (4.3%). There was no difference in 30-day (39.7 vs. 41.3%, RR 0.96; 95% CI 0.79–1.17; $p = 0.69$) or 12-month (51·8 vs 51·4%, RR 1·01, 95% CI 0·86–1·18, $p = 0·91$) all-cause mortality between the IABP and control groups. Despite high rates of primary PCI (95%), TIMI 3 flow post-PCI (82%) and placement of an IABP, 30-day mortality was 40%. In a pre-specified subgroup analysis, IABP was beneficial in patients < 50 years old and those with a first MI. Shortcomings of IABP-SHOCK II include inclusion of patients with mild or moderate instead of severe CS, crossover from medical therapy to IABP, and lack of long-term follow-up [25••]. In addition, there was a low rate of IABP insertion pre-PCI (13.4%), although no benefit was noted in the subgroup which received IABP pre-PCI compared with those who received IABP post-PCI.

Based on the results of this trial, the 2018 European guidelines on myocardial revascularization do not recommend routine use of IABP in patients with CS due to ACS (class III, level of evidence B) [22••]. The 2013 ACC/AHA STEMI guidelines provide a class IIa recommendation, level of evidence B, for IABP in patients with STEMI who do not quickly stabilize with pharmacological therapy (Table 1) [18].

Impella

The data supporting Impella use for AMICS is largely derived from registries and is, therefore, subject to the limitations of observational studies. In a registry of 15,259 AMICS US patients who were supported with Impella between 2009 and 2016, 51% survived to explantation of the Impella device [26••]. Survival was lower in women compared with men and in patients > 80 years of age. Survival to explantation was significantly higher in patients who received Impella pre-PCI (as compared with those who received it after IABP failure), patients who received hemodynamic monitoring with a pulmonary artery catheter and at institutions with a higher volume of Impella use (> 4 AMICS cases per year). Impella-related complications include hemolysis, mitral valve injury, arrhythmias, dislodgement, bleeding, and limb ischemia.

Rates of access site bleeding requiring transfusion vary from 17 to 24% and hemolysis from 7.5–10% [13, 27].

The IMPRESS trial was an open-label multicenter, randomized controlled trial that compared IABP with Impella CP in 48 AMICS patients between 2012 and 2015 [12••]. Unlike prior studies, IABP therapy pre-randomization was an exclusion criterion. Patients were extremely sick, all were mechanically ventilated, 96% were receiving catecholamine, and 92% had suffered cardiac arrest with time to ROSC > 20 min in 48%. Therapeutic hypothermia was performed in 75%, with a median duration of support of 48 h. The timing of device placement and multivessel versus culprit-only PCI were at the discretion of the operator. In most cases, MCS was inserted after PCI and 20% underwent PCI of non-culprit vessels. Three of the 24 patients randomized to IABP crossed over to Impella, and 3 of the 24 patients randomized to Impella received no device or an alternate device (IABP or Impella 5.0). There was no difference in the 30-day all-cause mortality (IABP 50%, Impella 46%, HR (Impella) = 0.96 [0.42–2.18]; $p = 0.92$). The most frequent cause of death was anoxic brain damage followed by refractory CS, which is not surprising given the high percentage of patients with > 20 min required for return of spontaneous circulation. Higher rates of bleeding were noted in the Impella group. Due to the small sample size, IMPRESS was underpowered to detect a mortality difference but remains the largest trial comparing IABP and Impella CP in AMICS. The ongoing DANSHOCK trial is randomizing AMICS patients to Impella CP vs. conventional circulatory support for a minimum of 48 h with a primary endpoint of all-cause mortality after at least 6 months of follow-up (NCT01633502).

Early (pre-PCI) implantation of Impella has been shown to be independently associated with improved survival to discharge [26••]. More than 1.25-h delay in Impella implantation after the onset of shock was associated with higher mortality, despite use of IABP or inotropes [[11••] [27],]. Based on this data, systematic early (pre-PCI) implantation of Impella has been proposed as part of regional CS initiatives and has been associated with lower mortality compared with historical controls [28••]. The impact of pre-PCI Impella insertion in decreasing infarct size in STEMI patients was studied in the "Door to Unloading (DTU) with Impella CP System in Acute Myocardial Infarction to Reduce Infarct Size" prospective, multicenter trial. Fifty patients with STEMI without CS received an Impella device and were randomized to immediate vs delayed (by 30 min) reperfusion. Delayed reperfusion was associated with similar MACE and mean infarct size as immediate reperfusion [29].

TandemHeart

The TandemHeart (TandemLife, Pittsburgh, PA, USA) is a continuous flow centrifugal pump that provides left atrial-femoral bypass and delivers flow up to 4 L/min and achieves 80–90% unloading of the LV. A 21F trans-septal cannula withdraws blood from the left atrium and returns it to the femoral artery via a 15–17F cannula. A recently published case series reported outcomes in 56 patients who underwent TandemHeart placement for CS due to different causes [30]. Of these, 28% ($n = 16$) had AMICS, including four patients with post-MI ventricular septal defect. Survival to hospital discharge was highest in the group which underwent corrective surgery or placement of a durable ventricular assist device. It was very low (21.5%) in patients who had no definitive exit strategy. All four patients with post-MI ventricular septal defect, which historically is associated with a very high mortality rate, were bridged to surgery or percutaneous repair. Disadvantages of TandemHeart include high rates of bleeding requiring transfusions, disseminated intravascular coagulation, limb ischemia, embolic and hemorrhagic stroke, and risk for cannula dislodgement that can be fatal.

VA-ECMO

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) provides circulatory support (of both ventricles) and oxygenation. As a result, it is the preferred MCS modality for patients with refractory cardiogenic shock and those with cardiac arrest.

In a recently published study of 46 patients with refractory AMICS, VA-ECMO initiation pre-PCI was independently associated with improved survival compared with post-PCI initiation (14.7 vs. 58.3%, $p = 0.006$) [31]. In the setting of cardiac arrest due to ACS, rapid support and a high rate of PCI performed during cardiac arrest with VA-ECMO support resulted in return of spontaneous circulation in all patients, though 30-day survival with neurological recovery was only 24% [32]. Furthermore, in the setting of cardiac arrest due to AMI, early initiation of support (median 40 min, from time of arrest to ECMO initiation) was associated with better outcomes compared with delayed support. On multivariable analysis, > 12.5 min of CPR were independently associated with higher 30-day mortality (adjusted hazard ratio, 4.71; 95% CI, 1.30–17.406; $p = 0.018$) [33]. The availability of compact, portable devices in which the pump can be primed within minutes has led to increasing use of extracorporeal cardiopulmonary resuscitation (e-CPR), in which VA-ECMO is initiated for patients with out-of-hospital or in-hospital cardiac arrest. In a propensity score-based analysis, e-CPR was associated with improved survival to discharge and 1-year compared with conventional CPR in patients with in-hospital cardiac arrest [34]. An important limitation of VA-ECMO is the increased afterload on the LV resulting in increased LVEDP and dilatation which requires concomitant unloading with a device such as Impella.

The 2013 ACC/AHA guidelines recommend considering MCS for refractory CS, while the 2018 ESC/EACTS guidelines state that support may be considered depending on patient age, comorbidities, neurological function, and the prospects for long-term survival and predicted quality of life. Both guidelines give MCS a class IIb, level of evidence C recommendation [18, 22••].

Device Selection for MCS in CS

A practical algorithm for selecting the type of MCS was proposed by Atkinson et al. and is shown in Fig. 1 [35••]. IABP can be useful in patients with pre-shock. VA-ECMO is the device of choice for cardiac arrest patients and patients with severe shock who are hypoxemic or have biventricular heart failure. Impella or TandemHeart are preferred for patients who have isolated left ventricular failure. A summary of commonly used MCS devices is provided in Table 2. MCS devices should be modified and weaned based on continuous assessment of patient's clinical condition and measurement of hemodynamic parameters such as the CPO and the Pulmonary Artery Pulsatility index (PAPi, calculated as (systolic pulmonary artery pressure − diastolic pulmonary artery pressure)/right atrial pressure [28••].

Right Ventricular Shock

CS due to right ventricular (RV) infarction is less common than cardiogenic shock due to left ventricular failure, yet mortality is similar [36]. Similar to different categories of left ventricular failure, criteria for RV dysfunction, severe RV dysfunction, and

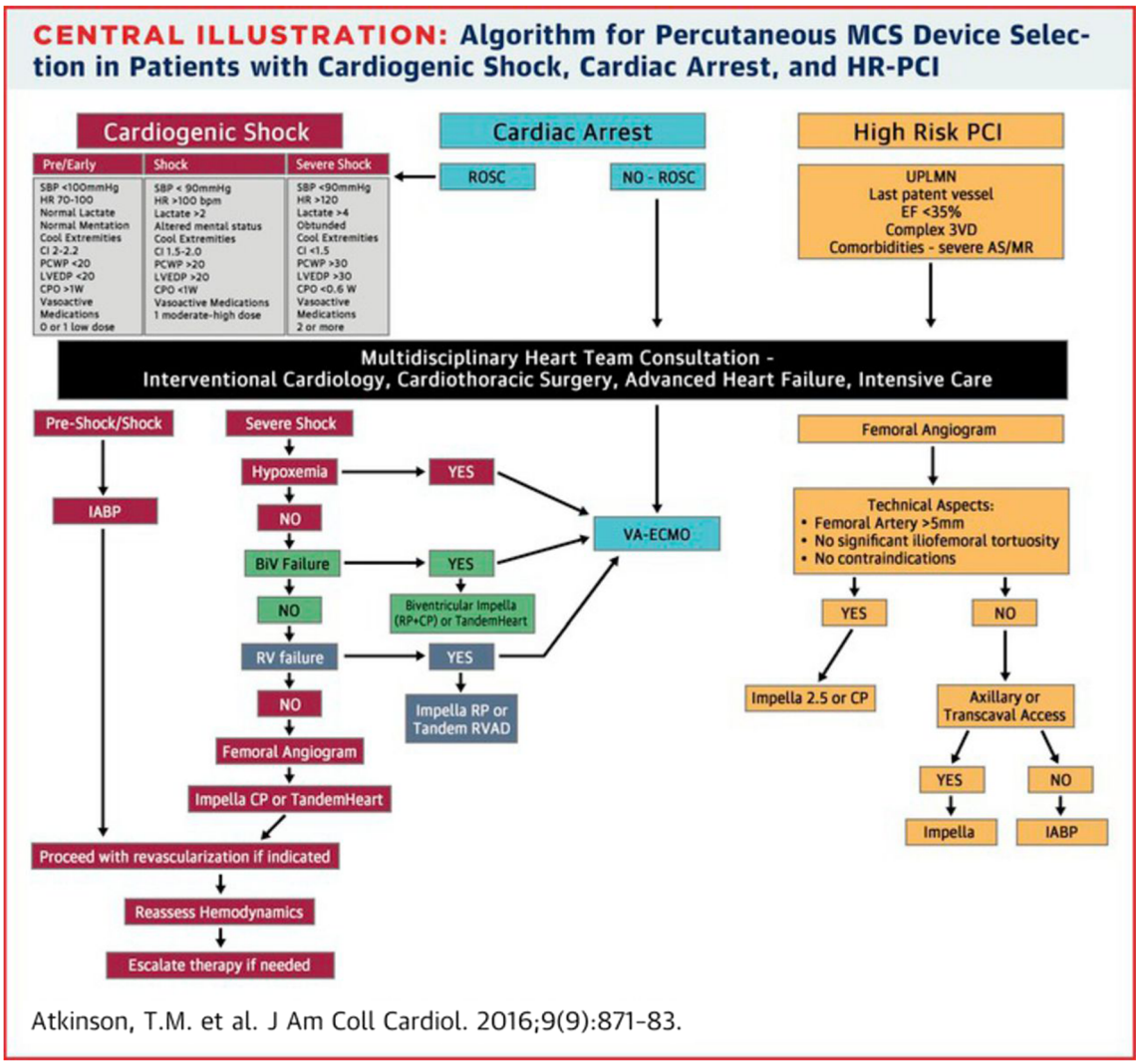

Fig. 1 Algorithm for percutaneous mechanical circulatory support (MCS) device selection in patients with cardiogenic shock. *ROSC,* return of spontaneous circulation; *UPLMN,* unprotected left main; *AS,* aortic stenosis; *MR,* mitral regurgitation; *BiV,* biventricular; *RVAD,* right ventricular assist device; *IABP,* intra-aortic balloon pump. (Reprinted from Atkinson et al. JACC Cardiovasc Interv 2016;9(9):871–83. https://doi.org/10.1016/j.jcin.2016.02.046, with permission from Elsevier) [35••]

Table 2 Summary of mechanical circulatory support devices

	IABP	Impella	TandemHeart	VA-ECMO
Feasibility				
Availability	+++	++	+	+
Arterial access size required	7–8 Fr	12 Fr (Impella 2.5) 14 Fr (Impella CP) 21 Fr (Impella 5.0)	15–17 Fr arterial 21 Fr venous	14–17 Fr arterial 18–21 Fr venous
Contraindications	• High bleeding risk • Severe aortic regurgitation • Thoracic or abdominal aorta aneurysm	• High bleeding risk • Severe aortic regurgitation • Severe PAD† • Left ventricular thrombus • Mechanical aortic valve • Ventricular septal defect	• High bleeding risk • Severe aortic regurgitation • Severe PAD†	• High bleeding risk • Severe aortic regurgitation • Severe PAD†
Efficacy				
Cardiac output increase (L/min)	0.3–0.5	≈ 2.5 (Impella 2.5) ≈ 4.0 (Impella CP) ≈ 5.0 (Impella 5.0)	4–5*	4–5*
Affected by arrhythmias	Yes	No	No	No
Requires adequate right ventricular function	Yes	Yes	Yes	No
Can correct respiratory failure	No	No	Yes‡	Yes
Complications				
Risk for lower limb ischemia	+	++	+++	+++
Trans-septal puncture required	No	No	Yes	No
Risk for bleeding	+	++	++	++
Risk for hemolysis	+	++	++	++

† transcaval access can be used for placing the arterial cannula in case of severe peripheral arterial disease

* Depending on arterial cannula size

RV failure in CS have been proposed. Even in the absence of RV infarction, RV dysfunction is common in patients with AMICS. In an analysis of 394 patients with available hemodynamic data from the 1491 patients in the SHOCK trial and registry, RV dysfunction (defined as central venous pressure or CVP > 10 mmHg, CVP/PCWP > 0.63, pulmonary artery (PA) systolic pressure–PA diastolic pressure/CVP, or Pulmonary Artery Pulsatility index- PAP_i < 2 and RV stroke work index-RVSWI < 450 g m/m^2) was present in 38% [37]. Severe RV dysfunction (CVP > 15, CVP/PCWP > 0.8, PAP_i < 1.5, RVSWI < 300 g m/m^2) was present in 15%. The high incidence of RV dysfunction in CS, regardless of the culprit, could be explained by the unique characteristics of the RV. The RV responds poorly to sudden increases in afterload, dilatation, septal dysfunction and ischemia and 40% of its contractile force depends on the interventricular septum. Due to its thin walls, it fails rapidly in these situations. Right ventricular shock occurs approximately 3 h earlier than left ventricular shock. Fortunately, the RV uniformly recovers once the acute insult resolves. Identification of predominant RV shock is more difficult than diagnosis of left ventricular shock and depends mainly on hemodynamic criteria as outlined above. The focus should, therefore, be on early recognition, correction of the underlying cause of RV failure and, if needed, early consideration for RV mechanical support that can be achieved using the Protek Duo cannula and pump (TandemLife, Pittsburgh, PA) or the Impella RP catheter (Abiomed, Danvers, MA). The Protek Duo contains 2 lumens within one 29F or 31F cannula. One lumen serves as an inflow cannula from the right atrium (RA) and encompasses a series of inflow vents positioned across the superior vena cava. The second lumen has a multi-fenestrated distal tip to deliver blood into the main PA. The inflow cannula drains blood from the RA into an extracorporeal centrifugal pump, which delivers the blood back to the PA [38••] The Impella RP is a 22F 3-dimensional catheter-based micro-axial pump mounted on an 11F catheter inserted via the femoral vein through a 23F peel-away sheath. It aspirates blood from the inferior vena cava (IVC) and delivers it to the PA at a rate of up to 4 L/min at 33,000 rpm. In a pilot study of 30 patients with refractory RV failure (five of whom had AMICS) treated with the Impella RP, hemodynamics rapidly improved after device insertion, with 73% 6-month survival [39].

Team-Based Management and Regional Systems of Care

A team-based approach including interventional cardiologists, cardiac surgeons, heart failure specialists, cardiac intensivists, and perfusionists is also used in many centers that treat AMICS patients [40]. Early involvement of advanced heart failure teams facilitate initiation of MCS and allows evaluation for advanced treatment options, such as durable left ventricular assist devices or cardiac transplantation that provide an "exit" strategy for patients who receive MCS but do not improve. Cardiac intensivists also have an important role on the team. In a historical control study, care by a cardiac intensivist was associated with significantly lower mortality (adjusted odds ratio [aOR] 0.44 [0.25–0.75]; $p < 0.001$), which was also true for patients on VA-ECMO (in-hospital mortality 29.4 vs. 57.6%, aOR 0.28 [0.10–0.81]; $p = 0.02$) [41]. Development of dedicated protocols for the assessment and management of AMICS patients can help expedite and optimize care. An example of such a protocol is the Detroit Cardiogenic Shock Initiative. Initial application of this protocol in 41 AMICS patients was associated with a remarkable 76% survival to hospital discharge without the need for permanent left ventricular assist device or cardiac transplantation [28••].

Challenges, Unanswered Questions, and Future Directions

Despite advances in management, mortality in AMICS remains high, highlighting the need for additional research and innovative approaches to the care of these patients. Those approaches should focus on prevention (with prompt coronary revascularization), early recognition, and aggressive supportive care including MCS. Although coronary revascularization should be performed as soon as possible, the optimal timing for MCS requires further evaluation. Expansion of AMICS teams and protocol-based treatment also hold great promise for standardizing outcomes and optimizing care. The high incidence of readmission in patients who survive AMICS is also a challenge. Almost one in five patients is readmitted within 30 days mostly due to cardiac reasons. Many of these patients develop chronic heart failure which is associated with continued high mortality and treatment costs [42].

Conclusions

Recent updates in the management of AMICS include early recognition and risk stratification with hemodynamic parameters derived during right heart catheterization, avoidance of non-culprit lesion PCI during primary PCI, expeditious implantation of MCS in patients with severe shock, and a team-based approach. Despite these advancements, prognosis AMICS patients remains poor, highlighting the need for additional developments and innovations.

Compliance with Ethical Standards

Conflict of Interest Jayant Bagai declares no conflict of interest.

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Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

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3.•• Thiele H, Akin I, Sandri M, et al. CULPRIT-SHOCK Investigators. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. N Engl J Med. 2017;377(25):2419–32 **Definitive RCT comparing outcomes with multivessel vs. culprit-only PCI in AMICS.**
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