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Management of Cardiogenic Shock: Present and Future

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Introduction

The prevalence of cardiogenic shock (CS) is high and involves approximately 1 in every 6 patients admitted to the cardiac intensive care unit. Despite the introduction of acute mechanical circulatory support (AMCS) and the institution of "shock teams," in-hospital mortality for patients with CS remains between 30% and 40%.[1] A striking paradox in the management of this critically ill population is that restoration of a more normal hemodynamic profile by means of mechanical circulatory support (MCS) has not been demonstrated to improve outcomes. This observation suggests that CS is a complex, systemic condition with poorly understood pathobiology that involves multiple interacting organ systems.

Current Limitations

Previous efforts to identify therapeutic interventions for CS have been limited in retrospective studies and clinical registries. The enrollment of patients with CS in prospective randomized clinical trials has been challenging because of the acuity of the presentation and the difficulty of obtaining informed consent in a timely manner. Another limitation is that the population enrolled in the clinical trials is not representative of the general CS population. Specifically, most of the clinical trials have enrolled patients with CS secondary to acute myocardial infarction (AMI-CS). Although AMI has been the prevalent etiology among patients with CS, recent studies have shown that the pathophysiology and outcomes of AMI-CS differ from those of CS caused by chronic heart failure exacerbation.[2]

Recent Developments

Current management options for CS fall into 4 categories: (1) coronary revascularization, (2) treatment with inotropes and vasopressors, (3) AMCS, and (4) institution of multidisciplinary shock teams. Among these interventions, early coronary revascularization and the institution of shock teams for the management of CS are the only interventions that have been shown to improve outcomes.[3-6] In the seminal SHOCK trial, Hochman et al[5] demonstrated that early coronary revascularization for AMI shock led to improved 6-month survival compared with that with medical therapy. Approximately 2 decades later, a study by Thiele et al[3] showed that in patients with multivessel coronary artery disease presenting with AMI shock, culprit lesion revascularization decreased the 30-day risk of death and kidney failure compared with multivessel revascularization. Following the development of revascularization strategies and the establishment of circulatory support devices, the need for standardized management of CS in this population increased, leading to the idea of a multidisciplinary team of heart failure cardiologists, interventional cardiologists, cardiothoracic surgeons, and cardiac intensivists who would streamline the process of evaluation,

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monitoring, and treatment of CS. Data from 2 independent observational trials showed that a team-based approach to managing CS resulted in an increased 30-day survival rate.[4,6]

Inotropes and the vasopressors remain the cornerstone of the medical therapy for CS, especially in its early stages. In the DOREMI trial, no significant difference was found between dobutamine and milrinone in the composite primary outcome, which included in-hospital death from any cause, resuscitated cardiac arrest, receipt of a heart transplant or MCS, nonfatal MI, transient ischemic attack, stroke diagnosed by a neurologist, or initiation of kidney replacement.[7] In another multicenter trial, patients presenting with CS who were randomized to receive intravenous dopamine experienced a higher incidence of arrhythmias than did patients who received norepinephrine.[8] Interestingly, the subgroup of patients who presented with shock of cardiac etiology and were treated with norepinephrine had lower rates of death than those treated with dopamine.[8] Along the same lines, patients with CS treated with norepinephrine had better hemodynamic and metabolic profiles than did those treated with epinephrine, suggesting that norepinephrine is the vasopressor of choice in patients with CS.[9]

Although inotropes and vasopressors remain important early therapeutic options, prolonged or escalating doses could result in adverse hemodynamic and metabolic effects. The adverse effects of inotropic support have led to a dramatic increase in the use of percutaneous circulatory support devices, which offer acute cardiac unloading and improve end-organ perfusion without the deleterious hemometabolic effects of prolonged inotropic support. Thus, AMCS can be used as bridge to decision, bridge to recovery, or bridge to more durable treatment (durable left ventricular assist device or transplantation). Despite this theoretical benefit of AMCS, randomized clinical trials have failed to demonstrate a survival benefit that would support their routine use in patient with CS. For example, use of an intra-aortic balloon pump (IABP) in patients with AMI-CS did not reduce the 30-day mortality in the IABP-SHOCK II trial.[10] Similarly, randomized trials comparing transvalvular or transeptal circulatory support devices with an IABP failed to demonstrate a survival benefit.[11]

The lack of randomized clinical data on AMCS led the American Heart Association to release a scientific statement providing a framework for implantation, escalation, and deescalation of percutaneous support devices.[12]

Abbreviations and Acronyms

AMCS	acute mechanical circulatory support
AMI-CS	cardiogenic shock secondary to acute myocardial infarction
CS	cardiogenic shock
IABP	intra-aortic balloon pump

Implantation and management of AMCS should be carried out by a multidisciplinary team, and decisions on AMCS use should be guided by invasive hemodynamic data (Table I).[12]

Future Directions

Patients with CS are a heterogenous and understudied population. They represent a closely monitored cohort that could serve as a unique research platform for clinical, hemodynamic, and echocardiographic data collection. Ongoing randomized clinical trials are trying to establish appropriate use criteria for AMCS support.[13] At The Texas Heart Institute, we are moving a step further by initiating a prospective study of the phenotypic characterization of the CS population supported by AMCS (Fig. 1). We will prospectively and serially collect echocardiographic, hemodynamic, genetic, and proteomic data to identify clinical and molecular predictors of CS recovery. This project has the potential to change medical practice by introducing novel biomarkers of CS recovery and identifying potential adjuvant therapeutic targets for the improvement of CS outcomes.

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TABLE I. Device Selection for Patients With Cardiogenic Shock

Cardiac failure	Hemodynamic indexes	*Percutaneous device*
Left ventricular	RA <15 mm Hg PCWP >18 mm Hg PAPi >0.9 RA/PCWP <0.63 mm Hg	Impella CP, 5.0, or 5.5 heart pump (ABIOMED) TandemHeart device (LivaNova) IABP
Right ventricular	RA >15 mm Hg PCWP <18 mm Hg PAPi ≤0.9 RA/PCWP >0.63 mm Hg	Impella RP (ABIOMED) TandemHeart RVAD with or without ProtekDuo kit (LivaNova) VA-ECMO
Biventricular	RA >15 mm Hg PCWP >18 mm Hg PAPi ≤0.9	VA-ECMO TandemHeart LVAD plus TandemHeart RVAD without or without the ProtekDuo kit BiPella (ABIOMED)

IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; RA, right atrium; RVAD, right ventricular assist device; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

Source: Geller BJ, Sinha SS, Kapur NK, et al. Escalating and De-escalating Temporary Mechanical Circulatory Support in Cardiogenic Shock: A Scientific Statement From the American Heart Association. *Circulation.* 2022;146(6):e50-e68.[12]

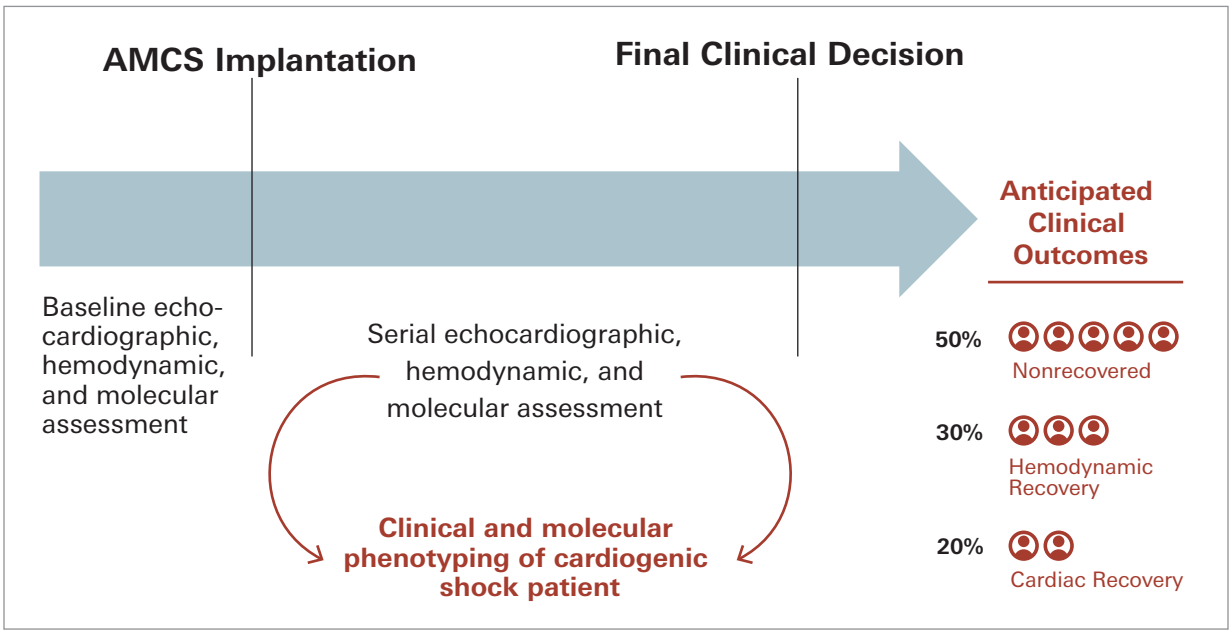

Fig. 1 The Texas Heart Institute protocol for clinical and molecular phenotyping of patients with CS. Our prospective study will include patients presenting with CS who require AMCS. Blood samples as well as echocardiographic and hemodynamic data will be obtained before device implantation and during circulatory support at serial time points. The integration of hemodynamic, echocardiographic, and molecular data will enable us to introduce biomarkers for the early diagnosis of hemodynamic and cardiac recovery and identify potential adjuvant therapeutic targets for the improvement of CS-related outcomes.

AMCS, acute mechanical circulatory support; CS, cardiogenic shock.

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