Cardiogenic Shock in STEMI

Current trends in management and the use of mechanical circulatory support devices.

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Cardiogenic shock (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. The clinical presentation is typically characterized by persistent hypotension unresponsive to volume replacement and is accompanied by clinical features of end-organ hypoperfusion requiring intervention with pharmacologic or mechanical support. Acute myocardial infarction (AMI) is the most common cause of CS. Despite the widespread use of early revascularization, the mortality rate of patients with AMI complicated by CS remains high (approximately 50% at 30 days). Overall incidence of CS remained relatively stable throughout the last few decades, accounting for 5% to 8% of all AMIs. However, this could be increasingly higher in patients currently treated with primary percutaneous coronary intervention (PCI). In particular, among 21,270 patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI between 2005 and 2015, the London Heart Attack Group reported an increased incidence of CS from 7% in 2005 to 13% in 2015 with a consistently high mortality rate, ranging from 45% to 70%.

MANAGING CS

Pathophysiologic Profile

MI and the consequent depressed myocardial function lead to activation of several physiologic compensatory mechanisms, which can exacerbate the pathologic process in a cyclical self-generating (and degenerating) manner. These are initiated very early in CS and include sympathetic stimulation that increases heart rate, contractility, and renal fluid retention, which consequently increases the adverse left ventricular preload. The raised heart rate and contractility increase myocardial oxygen demand, further worsening myocardial ischemia. Fluid retention and impaired left ventricular diastolic filling caused by tachycardia and ischemia contribute to pulmonary venous congestion and hypoxemia. Sympathetic-mediated vasoconstriction to maintain systemic blood pressure increases myocardial afterload, which impairs cardiac performance by increasing the need for cardiac work. Increased myocardial oxygen demand with simultaneous inadequate myocardial perfusion worsens myocardial ischemia, initiating a vicious cycle that ultimately ends in death if uninterrupted.

Relief of ischemia by early reperfusion may have a beneficial impact on the potential downward spiral. In fact, revascularization has been the only treatment to result in a reduced mortality rate in patients with CS. The SHOCK trial enrolled 302 patients with AMI complicated by CS between April 1993 and November 1998. Patients randomized to early revascularization demonstrated a reduction in mortality at 6 months that was extended up to 6 years. The SHOCK trial laid the foundation for early revascularization in the context of CS. However, revascularization has to be restricted to the culprit lesion only according to the results of the CULPRIT-SHOCK trial—a multicenter, randomized, open-label trial that compared multivessel versus infarct-related artery-only PCI in patients presenting with AMI CS. PCI to only the culprit lesion resulted in lower mortality and need for renal replacement therapy at 30 days (primary endpoint), whereas mortality was not different at 12 months between both groups. Immediate multivessel PCI should be offered only when it is difficult to identify the infarct-related artery or there are multiple culprit lesions. Staged PCI to nonculprit lesions should be based on the risks and benefits associated with a new procedure.

Pharmacologic Therapy

Pharmacologic measures are aimed to ensure adequate oxygenation and ventilation and preserve an euvolemic state. Inotropes and vasopressors are used to maintain hemodynamic stability by improving cardiac output and tissue perfusion. Despite their widespread use, clinical evidence of their benefit in CS is scarce. Norepinephrine should be used as a first-line therapy because it has demonstrated benefit over dopamine in the subgroup of patients with CS from the randomized SOAP II trial. The dose of sympathomimetic agents should be kept to a minimum to avoid their deleterious effect at a cellular level that relates to an increase in mortality. β-Blockers and renin-angiotensin-aldosterone...
STEMI system antagonists are contraindicated in the initial phase of CS according to an analysis from the TRIUMPH trial.

MECHANICAL SUPPORT DEVICES

Over the last 2 decades, the use of several mechanical circulatory support (MCS) devices that offer hemodynamic support, independent of myocardial contractility, has been generalized in this clinical context. Current strategies related to the most commonly used MCS devices in CS secondary to AMI and the development of regional systems for the management of CS are discussed here.

Intra-Aortic Balloon Pump

Considered the mainstay treatment since its inception, intra-aortic balloon pumps (IABPs) augment coronary and peripheral perfusion and increase cardiac output by 0.5 L/min. IABPs are made of a polyurethane membrane mounted on a vascular 7- to 8-F catheter. The IABP should be placed in the descending thoracic aorta just distal to the left subclavian artery and should be timed to inflate and deflate in concert with the cardiac cycle, thereby increasing the diastolic blood pressure and reducing the systolic blood pressure. However, in the prospective, randomized, multicenter IABP-SHOCK II study, IABP use failed to demonstrate any benefit, including hemodynamic stabilization, length of stay in the intensive care unit, need for inotropic support, and, most importantly, mortality. Therefore, routine use of IABP counterpulsation in CS is not recommended; however, it may be considered for hemodynamic support in selected patients with mechanical complications (ie, severe mitral insufficiency or ventricular septal defect).

Impella

Impella (Abiomed, Inc.) is a catheter-mounted, microaxial flow pump that is designed to be positioned across the aortic valve to actively pump blood from the left ventricle into the aorta (ie, to unload the left ventricle). The Impella family includes devices capable of augmenting circulatory support by 2.5, 3.5, and 5 L/min. The Impella 2.5 has a 12-F pump motor size and can be inserted through a 13-F sheath. The Impella CP, which offers circulatory support up to 4 L/min, can be inserted through a 14-F sheath; the Impella 5.0 requires surgical cutdown. Despite this improvement in hemodynamic support as compared with IABP, no benefit in mortality has been demonstrated in clinical practice. Additionally, Impella may pose an increased risk of vascular complications. The IMPRESS in Severe Shock study was the first randomized pilot trial to compare the efficacy and safety of the Impella CP versus IABP in patients with AMI-CS. However, this small trial (N = 48) did not show a survival benefit of Impella CP. Similarly, a meta-analysis that included 95 patients also found a neutral outcome for Impella compared with IABP. A retrospective analysis matched patients treated with Impella at several European centers (n = 237) with patients included in the IABP-SHOCK II trial (n = 237). Again, Impella use showed no benefit in mortality at 30 days and showed an increased risk of bleeding and vascular complications as compared with IABP.

Against this background, the DANSHOOK (NCT01633502) trial has been designed to demonstrate...
whether left ventricular MCS with Impella CP will improve all-cause mortality at 6 months (primary endpoint) as compared with conventional guideline-driven treatment. In the experimental arm, the Impella device should be implanted before revascularization. Patients who experience cardiac arrest outside of the hospital and remain comatose after return of spontaneous circulation are excluded from the study. A total of 360 patients will be included. The flowchart of the study is presented in Figure 1.\textsuperscript{19}

**Venoarterial Extracorporeal Membrane Oxygenation**

Used in the clinical setting for nearly 50 years,\textsuperscript{20} venoarterial extracorporeal membrane oxygenation (VA-ECMO) provides blood flow support and extracorporeal gas exchange at the same time.\textsuperscript{19} The blood from the venous system is drained through a cannula and becomes oxygenated, decarboxylated, and warmed in an extracorporeal gas exchange unit. Then, blood is returned through another cannula into the arterial system. The standard technique uses peripheral cannulation of the femoral vessels, usually with 21- to 25-F draining and 15- to 19-F returning cannulas (Figure 2). With arterial cannulation, placement of a dedicated sheath for antegrade perfusion of the cannulated leg is recommended to prevent leg ischemia. VA-ECMO reduces preload and increases aortic flow and end-organ perfusion. VA-ECMO usually offers flow rates of 3 to 4 L/min. However, it may also increase left ventricular afterload, resulting in increased left ventricle filling pressures, wall stress, and severe pulmonary congestion. In these cases, combining VA-ECMO with IABP, Impella, or other venting maneuvers may help achieve more complete left ventricular unloading.\textsuperscript{22,23} Potential complications of VA-ECMO include distal limb ischemia, thromboembolism, stroke, bleeding, hemolysis, infection, and aortic valve insufficiency.

Clinical evidence for other MCS devices in the context of AMI complicated by CS is scarce. The ongoing EUROSHOCK (NCT03813134; Figure 3) and ANCHOR trials (NCT04184635) have been designed to evaluate the efficacy of VA-ECMO in CS.

The different types of MCS are not mutually exclusive. Rather, they may be complementary. In a recent
study, the combination of Impella and VA-ECMO was able to stabilize and rescue patients with refractory CS, an otherwise ominous prognosis. Another key issue is the timing of the MCS device insertion; the earlier they can be placed, the more efficacious they may be. In this regard, the DANSHOCK trial is studying the efficacy of Impella even before revascularization (Figure 1). Similarly, the EUROSHOCK trial is evaluating the early initiation of ECMO (< 6 hours after the onset of CS) (Figure 3).

CS NETWORK

Patients with CS should be managed by fully trained multidisciplinary professionals in tertiary medical centers with level 1 cardiac intensive care units, as outlined by international scientific statements. CS centers should have the on-site monitoring, medical services, and therapeutic technologies to coordinate and deliver care for all causes of CS, from the resuscitation phase to recovery, durable supportive therapy, or palliation. A closed-unit model with care led by a dual-trained cardiologist-intensivist may improve outcomes. A well-coordinated network becomes crucial to provide the best treatment in a timely fashion. A model for CS regional care proposed by the American Heart Association is depicted in Figure 4. This model is based on the implementation of hub-and-spoke CS systems of care. Hub centers would be required to create mobile multidisciplinary CS teams available 24/7 for on- or off-site consultation, referral, and ECMO/MCS insertion. Local logistics and geographic variables should be taken into account to adapt the model to every region.

CONCLUSION

The development of CS in the context of STEMI poses an ominous prognosis for the patient despite the performance of early revascularization. Standard pharmacologic therapy is usually insufficient to stabilize hemodynamics and improve outcomes. MCS devices may provide greater hemodynamic support, but they are not free of potential complications. Results of ongoing properly designed randomized trials will shed light on the benefit of these devices for this clinical condition. Future research on the combination of MCS is also warranted. Finally, the establishment of regional CS networks is crucial to deliver the best treatment in a timely manner before the development of the pathophysiologic downward spiral that leads to death if uninterrupted.


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