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Advances and challenges in mechanical support for cardiogenic shock complicating acute myocardial infarct: a comprehensive review of the latest data

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Cardiogenic Shock represents a life-threatening condition characterized by high mortality and a spectrum of clinical presentations, complicating ~5%–10% of patients presenting with Acute Coronary Syndromes. Despite advances in interventional cardiology and emergency medicine, mortality rates remain extremely high and evidence concerning its management is scarce. Consequently, the decision making relies heavily on a single operator's experience. This comprehensive review aims to provide a thorough update on the latest proof regarding mechanical circulatory support devices of the left ventricle and examines the role of the classification scores on the selection of the appropriate patient and timing for the initiation of the device. The five necessary steps to a successful mechanical circulatory support device's insertion. The picture was made by Pixlr AI Image Generator.

KEYWORDS

cardiogenic shock, mechanical circulation support, CS, Impella, VA-ECMO

1 Introduction

Cardiogenic shock (CS) is a medical emergency with high mortality and morbidity, which consists of a wide spectrum of clinical presentations, ranging from an early hemodynamic compromise, shock to even full-blown multi-organ failure (1).

Despite the state-of-the-art advances in the field of cardiology and emergency medicine, its mortality rate as a complication of acute myocardial infraction (AMI) remains extremely high (2), complicating about 5%–10% of ST-elevation and non-ST elevation myocardial infarction cases.

Apart from the urgent revascularization of the culprit lesion, key components of CS management, are pharmacotherapeutic regimens concerning volume management, inotropes, vasopressors and the use of Mechanical Circulation Support (MCS) devices, if necessary. The current ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure recommend the use of MCS for patients with cardiogenic shock as

a bridge to bridge, a bridge to recovery or a bridge to decision (IIa), including treatment of the cause, long-term support, or transplantation (3, 4).

Although the timely introduction of the optimal device is of utmost importance, due to the emergent nature of this medical entity, the inherent difficulty in patient allocation and ethical issues surrounding the type of the scientific hypothesis, there is a lack of Randomized Control Trials (RCTs) increasing the definitive evidence. For this reason, the decision of whether, when and which circulatory support device to use is based mainly on observational data from specialized centers with conflicting results (5).

Herein, we aim to summarize the existing evidence regarding the use of MCS devices during AMICS in the literature and their current role in contemporary clinical practice.

2 Mechanical circulation support devices in cardiogenic shock

The temporary circulatory support devices are mainly introduced as a bridge to the heart's recovery and to limit the patient's dependency on inotropes and/or vasopressors. The utilization of these medications, apart from a beneficial role in improving the cardiac output and the vascular tone, could be possibly connected with severe adverse events. In more detail, due to their effect on the left ventricle's afterload, increased oxygen demand from the myocardium and arrhythmias could be provoked (6, 7). On the other hand, the temporary MCS devices unload the left ventricle, thereby intracardiac filling pressures are reduced, which contributes to a decline in myocardial stress and oxygen consumption; however, they are also connected to vascular and non-vascular adverse events (8).

Currently, the percutaneous devices that are mainly used to support the failing left ventricle are the Intra-aortic Balloon Pump (IABP), the Impella pumps (Abiomed Europe GmbH, Aachen, Germany), the Tandem Heart (LivaNova, London, United Kingdom) and the Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO). However, sufficient randomized data regarding them is still limited (Tables 1, 2).

2.1 Intra-aortic balloon pump

The IABP has undergone extensive utilization and research over the past decades. Nevertheless, recent guidelines have diminished its recommended use, with a significant rise in the critical application of supplementary percutaneous devices in the latest years, prompted by findings from the IABP SHOCK II Trial (9). This study aimed to examine the impact of initiating IABP in patients experiencing cardiogenic shock complicating acute myocardial infarction on 30-day mortality (39.7 vs. 41.3%; RR 0.96; 95% CI 0.79–1.17; $p = 0.69$). Furthermore, the long-term follow-up of the trial reaffirmed the absence of superiority in IABP usage concerning long-term mortality (66.3 vs. 67.0%; RR 0.99; 95% CI 0.88–1.11; $p = 0.98$) (10).

2.2 Veno-arterial extracorporeal membrane oxygenation

The VA-ECMO or extracorporeal life support (ECLS) exhibits the dual ability to initiate both circulatory and respiratory support, traits that make it appropriate for patients suffering concomitantly from cardiac and respiratory failure.

Compared to IABP, VA-ECMO in a metanalysis of observational studies demonstrated a 33% higher 30-day survival rate (95% CI, 14%−52%; $p < 0.001$). In contrast, no significance was observed when comparing it with Tandem Heart/Impella (−3%; 95% CI −21% to 14%; $p = 0.70$) (11). Nevertheless, this 30-day mortality benefit was contradicted in the recently published EURO-SHOCK (12), ECMO CS (13), and ECLS-SHOCK (14) trials.

More specifically, in the EURO-SHOCK trial, which was held during the COVID-19 period and consequently the recruitment was limited, a superiority of the VA-ECMO group in terms of 30-day all-cause mortality (43.8 vs. 61.1%; HR 0.56, 95% CI 0.21–1.45; $p = 0.22$) and 1-year mortality (51.8 vs. 81.5%; HR 0.52, 95% CI 0.21–1.26; $p = 0.14$) was reported. At the same time, an increase of vascular (21.4 vs. 0%) and bleeding complications (35.7 vs. 5.6%) was documented. Due to the power failure, this trial could not provide sufficient data to draw definite conclusions. Moreover, the ECMO CS investigated its immediate implementation in patients with rapidly deteriorating or severe cardiogenic shock in comparison to early conservative pharmacological therapy. In that trial, even though greater clinical outcomes with the use of VA-ECMO were not depicted (63.8% early VA-ECMO vs. 71.2% no VA-ECMO; HR 0.72, 95% CI 0.46–1.12; $p = 0.21$), the cross-over rate from the conservative arm to ECLS or other pMCS device was notably high (39%), because of the rapidly deteriorating clinical situation of these patients. Additionally, the ECLS trial, a multicenter trial that included 420 patients proved that not only was there no decrease in 30-day mortality with early VA-ECMO introduction (47.8 vs. 49%; RR 0.98; 95% CI 0.80–1.19; $p = 0.81$), but there was also an increase in the complications (23.4 vs. 9.6%; RR 2.44; 95% CI, 1.50–3.95).

One notable limitation of employing the VA-ECMO is the resultant increase in left ventricular afterload due to the retrograde aortic flow. This, in the context of cardiogenic shock could potentially lead to myocardial ischemia, delayed ventricular recovery, ventricular arrhythmias, pulmonary edema, thrombotic events, and multiorgan dysfunction. Therefore, venting VA-ECMO with an IABP or other percutaneous ventricular assist device (pVAD) may be considered to address this challenge (15). This subject was recently approached in a meta-analysis of observational studies that included almost 4,000 patients (16). The venting technique seemed to provide lower mortality rate (54%) in comparison to (65%) the use of VA-ECMO without unloading (RR: 0.79; 95% CI: 0.72–0.87; $p < 0.00001$). On top of that, apart from a higher hemolysis rate, the double technique did not cause more adverse events. Nevertheless, in the absence of prospective randomized data, the consideration of left ventricular unloading may be appropriate for patients undergoing VA-ECMO support, provided they are carefully selected.

TABLE 1 Implantation characteristics, hemodynamic effects and adverse events of the temporary mechanical circulation support devices.

	IABP	Impella	VA-ECMO	Tandem-Heart
Mechanism of action	Left ventricle to aorta	Left ventricle to aorta	Right atrium to aorta	Left atrium to aorta
Pump mechanism	Pneumatic	Axial flow	Centrifugal	Centrifugal
Insertion cite	Femoral/axial artery	Femoral/axial artery	Femoral vein and Femoral artery	Femoral vein and femoral artery
Hemodynamic support (L/min)	0.8–1	2.5–5	>4.5	≤5
Cannula size	8 Fr	12–21 Fr	18–21 and 15–22 Fr	21 and 15–17 Fr
Ease of implantation	+++	+++	++	+
Afterload	↓	–	↑	↑
MAP	↑	↑	↑	↑
LVEDP	↓	↓	↑	↓
PCWP	↓	↓	↓	↓
Preload	–	↓	↓	↓
Coronary perfusion	↓	↑	–	–
Myocardial O_2 consumption	↑	↓	↑	↓
Peripheral tissue perfusion	↑	↑	↑	↑
Hemolysis	+	++	++	++
Risk of limb ischemia	+	++	+++	+++

+, positive answer; –, no effect; ↑, increase; ↓, decrease; ++, greater value than +; + + +, greater value than ++.

TABLE 2 Contraindications of each temporary circulatory support device.

IABP	Impella	VA-ECMO	Tandem-Heart
Absolute			
Aortic aneurism	Prosthetic aortic valve	Irreversible organ failure	Vascular septal defect
Severe aortic regurgitation	Left ventricle thrombus	Unwitnessed asystole	End stage refractory heart failure- no transplant/VAD option
Aortic dissection	Ventricular septal defect	End stage refractory heart failure- no transplant/VAD option	
	Severe peripheral artery disease		
Relative			
Peripheral arterial disease	Aortic stenosis	No candidate for transplantation/VAD	Coagulopathy
Mild aortic regurgitation	Aortic regurgitation	Severe aortic regurgitation	Severe aortic regurgitation
Bleeding		Aortic dissection	Aortic dissection
Sustained tachyarrhythmias		Coagulopathy	Severe aortic aneurism
		Peripheral arterial disease	Peripheral arterial disease

VAD, ventricular assist device.

2.3 Impella devices

As far as the Impella pumps are concerned, their mechanism of action relies on pulling blood from the left ventricle and consequently delivering it to the systematic circulation through the aorta. Thus, the cardiac output is increased, while the myocardial oxygen consumption and the pulmonary capillary wedge pressure are diminished. Based on the type of the pump, the Impella can provide a contribution to the circulation of 2.5–5.5 L/min. In some RCTs (17, 18), which included a small number of patients, the Impella 2.5 device, in comparison to the IABP exhibited superior hemodynamic support (19, 20). Nonetheless, in the IMPRESS study (21), a multicenter trial which evaluated the use of Impella CP vs. IABP in 48 patients, the investigators reported similar results concerning the circulatory support of the two devices and the mortality, both on the short-term (50 vs. 46% at 30 days; HR 0.96; 95% CI 0.42–2.18; $p = 0.92$) and the long-term (50 vs. 63% at 5 years; RR 0.87, 95% CI 0.47–1.59, $p = 0.65$) follow-up (22).

Of note, this came at the cost of increased vascular and bleeding complications for the Impella cohort, with the authors commenting on its wider sheath size (14 vs. 7.5 Fr).

The results of the ongoing STEMI-DTU (23) and DanGer shock (24) trials may shed light to whether the use of Impella CP could improve survival in Acute Myocardial Infarct complicated by Cardiogenic Shock (AMICS).

2.4 Tandem Heart

With the Tandem Heart's assistance, the left ventricle is unloaded by redirecting blood from the left atrium to systemic circulation, therefore is the preload reduced and systematic perfusion with a maximal flow of 5 L/min is achieved. Interestingly, this device functions by creating a left atrium to femoral artery bypass. This is succeeded by access through the femoral vein with a 21 Fr cannula and a septostomy, which offers entrance to the left atrium. In this way, oxygenated blood is withdrawn from the left atrium and is reinstated in the femoral artery via a 15 or 17 Fr cannula. The requirement for a transseptal puncture may pose a challenge for operators, who are not proficient in this technique. Additionally, the limited adoption of this approach may be attributed to its intricate nature and the considerable amount of time that its placement requires.

In early reports, a mean flow of 3.2 ± 0.6 L/min, an improvement to the cardiac index of 0.7 ± 0.3 L/min and to the mean blood pressure of averagely 17 mmHg were documented. Furthermore, the pulmonary capillary wedge pressure, central venous pressure, and pulmonary artery pressure were reduced in average by 7, 5, and 8 mmHg respectively. Finally, the 30-day mortality rate was reported to be 44% (25).

Even though the initiation of the TandemHeart in comparison to the IABP showed promising data concerning hemodynamic and metabolic variables, contemporary outcomes remain scarce and until recently have not been reported (26). Lately, a retrospective analysis of the THEME registry, a multicenter, prospective, observational cohort (27), reported a significant amelioration in cardiac index 1.0 (0.5–2.25 L/min/m^2) and lactate clearance −2.3 (−5.0 to −0.7 mmol/L). Furthermore, it is important to note that the 30- and 180-day survival were 74% (95% confidence interval: 60%−85%) and 66% (95% confidence interval: 51%−79%), respectively.

3 Mechanical circulation support devices in out-of-hospital cardiac arrest

The use of MCS devices has also been investigated and may be beneficial in the case of refractory out-of-hospital cardiac arrest. Currently, continued conventional cardiopulmonary resuscitation (CCPR) and defibrillation constitute the standard of care for such patients. However, a significant number of patients fail to achieve return of spontaneous circulation (ROSC), restraining physicians to implement necessary intervention measures (28).

Extracorporeal cardiopulmonary resuscitation (ECPR) presents a potential solution by restoring circulation. This approach could help minimize or even reverse organ damage, prevent re-arrest due to ischemia-induced myocardial dysfunction, and provide time for the identification and treatment of the underlying cause (29).

Several studies have indicated the feasibility and potential advantages of ECPR in terms of both survival rates and neurological outcomes compared to conventional methods (30). Recently, the INCEPTION and Prague OHCA trials randomized patients (31, 32) who experienced out-of-hospital cardiac arrest (OHCA) to receive either ECPR or CCPR, with the primary outcome being survival with a favorable neurological outcome at 30 and 180 days, respectively. Although both studies showed promising results and positive neurological outcomes with the initiation of ECPR, neither met the primary endpoint. Only in the ARREST trial (33) was it demonstrated that for patients with OHCA and refractory ventricular fibrillation, survival to hospital discharge and functional status were significantly improved with the use of extracorporeal life support (ECLS) compared with standard ACLS treatment. This finding not only has paved the way for multicenter phase 3 trials, but also underscores the importance of a well-organized and experienced emergency system.

4 Risk stratification

As it was stated earlier in this paper, the CS is a medical entity that could be presented with a wide variety of clinical presentations. Therefore, the immediate risk stratification and the correct patient selection for each therapy type is critical. The conflicting results of the up to this point published trials, have been attributed to the high complication rates of the pMCS devices but also non-personalized patient selection (34). Subsequently, the identification of the mortality predictors and the introduction of a unanimous risk assessment score may be beneficial to the treatment planning and the optimal patient enrollment in upcoming clinical trials.

4.1 Biomarker-based predictive scores

In the past few years, various biochemical factors were accused of predicting CS complicated AMI mortality. More specifically, cytokines such as INF-γ, TNF-α, MIP-1β, G-CSF, MCP-1β and IL6-10 have been accused of reflecting the inflammatory response that is initiated after an acute coronary syndrome (ACS) and consequently the CS triggered multiorgan dysfunction syndrome (MODS), which is combined with poor clinical outcome and high mortality rates (35, 36).

The CLIP score (37) is a biomarker-based predictive model that evaluates the levels of cystatin C, lactate, IL-6 and N-terminal pro-B-type natriuretic peptide (NT-proBNP), biomarkers that represent the neurohormonal stress and the inflammatory response of the cardiogenic shock. In the internal and external validation, it was proven to outperform the prediction of the 30-day mortality risk of previously established scores. Even so, it is argued that the mortality in cardiogenic shock is stronger connected to clinical factors than biomarkers reflecting its pathophysiology (38). In addition to

TABLE 3 Parameters used in the risk stratification score systems.

IABP shock II	CardShock	SCAI-CSWG	CSS	CLIP	BE-ALIVE
Age	Age	SBP	Age	Cystatin C	Age
Stroke	Confusion	MAP	Sex	Lactate	Lactate
TIMI flow <3	Previous MI	Lactate	AMI-CS	IL-6	Base excess
Lactate	Previous CABG	ALT	SBP	NT-proBNP	Intubation/ventilation
Previous stroke	ACS	Ph	HR		Ventricular impairment
	LVEF <40%	Vasoactive drugs	Ph		CPR
	Lactate	Inotropic drugs	Lactate		
	eGFR	MCS devices	Glucose		
			CPR		

TIMI, thrombolysis in myocardial infarction; MI, myocardial infarct; SBP, systolic blood pressure; MAP, mean arterial pressure; AMI-CS, acute myocardial infarction induced cardiogenic shock; HR, heart rate; LVEF, left ventricle ejection fraction; ACS, acute coronary syndrome; IL, interleukin; CPR, cardiopulmonary rescuscitation; GFR, glomerular filtration rate; MCS, mechanical circulatory support; CABG, coronary artery bypass graft; ALT, alanine aminotransferase.

that, its administration in the current clinical practice could be challenging, because even though it consists of four biochemical values, such parameters are not routinely obtained in acute settings.

4.2 Clinical classification scores

Several studies have proposed a practical risk classification score. Firstly, a risk stratification in three levels (low, intermediate, and high risk) of patients suffering from Cardiogenic Shock of all causes has been proposed by CardShock score. In this score, age, confusion, ACS as a cause, previous myocardial infract, Coronary Artery Bypass Graft, Left Ventricle Ejection Fraction, eGFR and lactate levels are estimated to allocate the patients to the appropriate treatment. In the same context, the IABP-SHOCK II score (39) applies only for ACS patients, incorporates age, history of stroke, TIMI flow after Percutaneous Coronary Intervention, glucose, creatinine, and lactate values at first presentation. Although these prediction models have been externally validated regarding the 30-day mortality prediction, in everyday clinical practice, their use remains limited owing to the acute nature of this clinical setting. Indeed, patient information regarding past medical history may even be impossible to retrieve, especially when the patient is intubated or in an impaired mental condition, and unaccompanied.

Recently, the Society for Cardiovascular Angiography and Interventions (SCAI) shock stage classification has been introduced (40). Since its publication, it has been widely cited, validated, and incorporated in multiple clinical studies (41, 42). Nevertheless, it is argued that it lacks uniform criteria defining each stage. For this reason, it was modified to the SCAI-CSWG Classification (43, 44) that was based on objective parameters estimated on admission and throughout hospitalization. More specifically, five stages (1–5) from hemodynamic stability to refractory shock, depending on the hypoperfusion, the hypotension and the treatment intensity have been established.

Another recently developed score system that tried to help pursue a targeted treatment approach in CS, irrespective of the underlying cause is the CSS (45). According to it, age, sex, acute myocardial infarction as a cause, cardiac arrest and the measurement of systolic blood pressure, heart rate, pH, lactate and glucose are the most important predictors of the CS induced mortality.

Finally, the BE-ALIVE Classification (46), is a newly developed score that includes parameters that are always available at the first contact with the patient. It assesses laboratory parameters like the base excess, lactate levels, as well as the patient's age, ventricular impairment by echocardiography, whether the patient is intubated and if the patient experienced a cardiac arrest (Table 3).

5 Discussion

Although hospitalizations attributed to CS have tripled between 2004 and 2018, in-hospital and short-term mortality due to CS has remained relatively same (47). On top of that, the lack of sufficiently powered randomized controlled trials in this emergent field leaves clinical decision-making largely reliant on the experience of medical practitioners.

Except for the treatment of the culprit lesion, the use of vasopressors, inotropes and temporary circulatory support devices is important. The use of such devices could be demanding, as the initial improvements in cardiac output may be counterbalanced by significant complications such as limb ischemia, bleeding, embolization of material, stroke, infection, and hemolysis (48).

One major limitation of the lack of robust data stemming from the available studies is the selection bias that was introduced since patients opted for circulatory support may be either in preliminary or in very advanced shock stages (49). In a recent editorial (50), the initiation of extracorporeal circulatory support was compared to parachute opening. Therefore, the incorporation of risk stratification tools may be a solution to guiding treatment decisions in a timely manner, as well as facilitate patient selection for enrolment to the new randomized control trials.

In addition, the miniaturization of the circulatory support systems could serve as a valuable aid for physicians, contributing to simplified insertion procedures and simultaneously reducing the risk of complications. In recent developments, a miniaturized catheter-mounted axial flow pump, which incorporates a self-expanding impeller and pump head has been introduced for providing mechanical circulatory support to the left ventricle.

This pioneering high- output, low-French size device, currently undergoing examination in the EFS study (51), aims to achieve mean flows exceeding 5 L/min through insertion via a 10 Fr arterial sheath, accessed from the femoral artery. Preliminary results of the study were presented at the TCT 2023 in San Fransisco and reported positive outcomes regarding the delivery of the device and the device-related adverse events.

Promising results could be also claimed through the combination of the percutaneous circulatory support devices. For example, the combination of VA-ECMO and Impella, referred as ECMELLA is currently widely used and has already showed improving clinical outcomes in selected VA-ECMO patients, which needs to be further validated (52, 53).

In conclusion, the role of temporary mechanical circulatory support devices is limited because of the conflicting results of the available data. However, the incorporation of prediction scores to provide a personalized treatment approach selection has recently been linked with encouraging results. Apart from that, the administration of such devices is important to be held by experienced staff and in a manner to prevent possible complications. Nonetheless, all these should be sufficiently investigated and validated by upcoming clinical trials.

Author contributions

AP: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. DC: Methodology, Resources, Supervision, Validation, Visualization, Writing – review & editing. AA: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. TM: Methodology, Supervision, Validation, Writing – review & editing. GT: Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

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