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Review Article

CARDIOGENIC SHOCK FOLLOWING ACUTE MYOCARDIAL INFARCTION: WHAT'S NEW?

Martino Pepe,[*] Alessandro Santo Bortone,[†] Arturo Giordano,[‡§] Annagrazia Cecere,[*] Osvaldo Burattini,[*] Palma Luisa Nestola,[*] Giuseppe Patti,[¶||] Ottavio Di Cillo,[**] Nicola Signore,[††] Cinzia Forleo,[*] and Stefano Favale[*]

[*]Division of Cardiology, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy; [†]Division of Heart Surgery, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy; [‡]Invasive Cardiology Unit, "Pineta Grande" Hospital, Castel Volturno, Caserta, Italy; [§]Department of Invasive Cardiology, Casa di Salute "Santa Lucia", San Giuseppe Vesuviano, Napoli, Italy; [¶]Cardiology, University of L'Aquila, L'Aquila, Italy; [||]Campus Bio-Medico Hospital, Rome, Italy; [**]Chest Pain Unit, Cardiology Emergency, University of Bari, Bari, Italy; and [††]Division of Cardiology, Azienda Ospedaliero Universitaria Consorziale Policlinico di Bari, Bari, Italy

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ABSTRACT—Cardiogenic shock (CS) is a state of critical end-organ hypoperfusion primarily due to cardiac dysfunction. This condition is the most common cause of death in patients affected by acute myocardial infarction (AMI). Despite early revascularization, prompt optimal medical therapy, and up-to-date mechanical circulatory supports, mortality of patients with CS remains high. The objective of this review is to summarize epidemiology, pathophysiology, and treatment options of CS in light of the new European Society of Cardiology (ESC) recommendations. The latest European guidelines on myocardial revascularization have reviewed the previous guidelines with respect to early multivessel revascularization and routine use of intra-aortic balloon pump (IABP) in patients with AMI-related CS. Most of the current evidences come partly from randomized trials, but mostly from observational registries because of the difficulty to test different treatments in this life-threatening clinical setting. Some of the latest studies highlight the potential crucial benefit of newly introduced mechanical circulatory support devices, although evidences are not sufficient to definitely assess the benefit/risk ratio of the different systems. Many questions remain unanswered in this field, and further trials are advocated to better elucidate the best medical, reperfusion, and circulatory support approaches aimed to improve the poor prognosis of patients with CS after AMI.

KEYWORDS—Acute myocardial infarction, cardiogenic shock, IABP, mechanical circulatory support, multivessel revascularization, percutaneous coronary intervention

DEFINITION

Cardiogenic shock (CS) is a state of critical end-organ hypoperfusion primarily due to cardiac dysfunction, as described by the European Society of Cardiology (ESC) and the American Heart Association (AHA) (1, 2). Hypotension (defined as systolic blood pressure <90 mmHg or need for vasopressors to obtain a blood pressure ≥ 90 mmHg) and signs of impaired organs perfusion (central nervous system disturbances, loss of consciousness, oliguria, increased lactate >2 mmol/L) in a state of normovolemia or hypervolemia are the main diagnostic criteria for CS. Reduced cardiac index (CI <1.8 or <2.2 L/min/m^2 with cardiac support) or increased left ventricular filling pressure (pulmonary capillary wedge pressure >15 mmHg) has been recently proposed as additional hemodynamic criteria for CS diagnosis (3). The clinical severity of CS could range from mild hypoperfusion to the lack of arterial pulse (4). Within this spectrum, normotensive CS has also been described and is characterized by clinical evidence of left ventricle (LV) failure coupled with peripheral signs of hypoperfusion (cold extremities or oliguria) along with preserved or borderline blood pressure. In the "SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK" (SHOCK) trial, a group of 49 nonhypotensive shock patients with systolic blood pressure more than 90 mmHg in absence of vasopressor support presented significantly higher in-hospital mortality as compared with the remaining acute myocardial infarction (AMI) population (5). Refractory CS is defined as persisting shock despite the administration of fluids, inotropes, and vasoconstrictors, and is considered the most severe form of CS (3).

INCIDENCE AND MORTALITY OF CARDIOGENIC SHOCK FOLLOWING AMI

CS complicates approximately 5% to 10% of acute coronary syndromes (ACS) and represents a powerful determinant of mortality (6, 7). The SHOCK trial registry reported that the most common cause of CS during AMI is LV failure (78.5%), followed by severe mitral regurgitation (6.9%), ventricular septal rupture (3.9%), right ventricle failure (2.8%), and cardiac tamponade (1.4%) (8). The complex pathophysiology of CS after AMI has been elucidated over the past 2 decades. A severe

Address reprint requests to Osvaldo Burattini, MD, Azienda Ospedaliero Universitaria Consorziale Policlinico di Bari, Piazza G. Cesare 11, Bari, Italy. E-mail: osvaldoburattini@gmail.com

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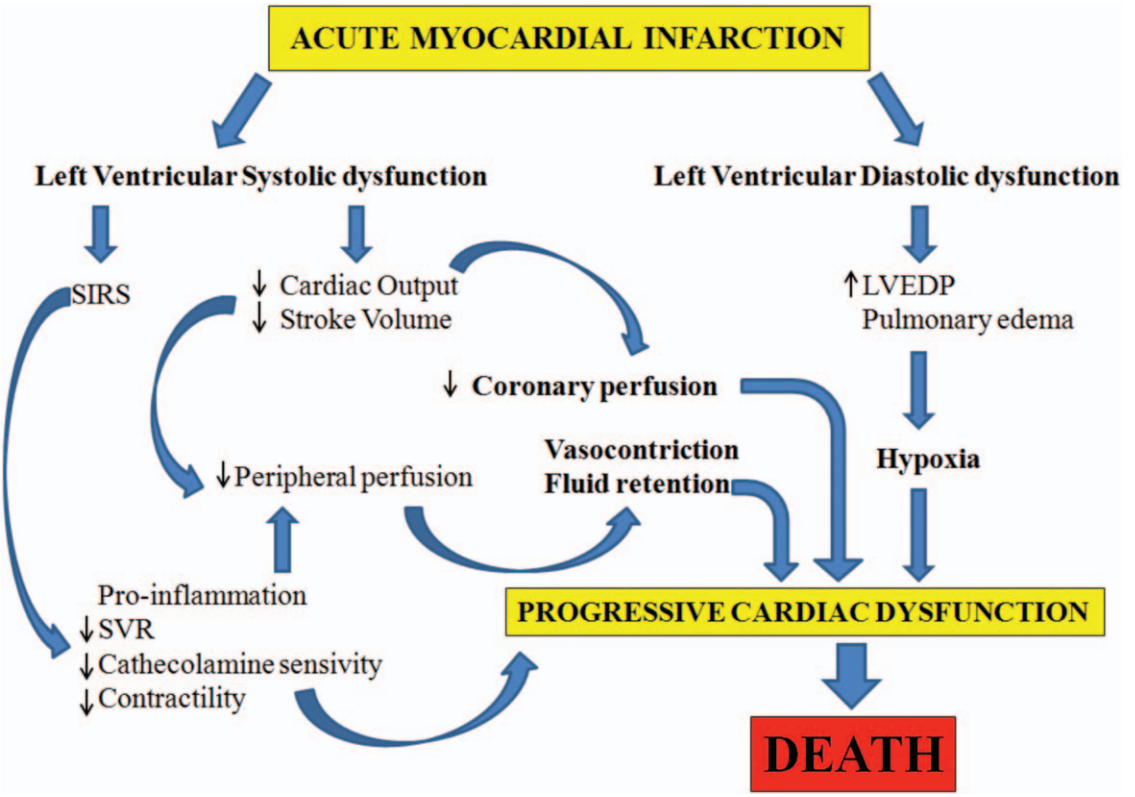

Fig. 1. **Pathophysiology of cardiogenic shock following acute myocardial infarction (Adapted from Diepen 2017).** LVEDP: left ventricular end-diastolic pressure; SIRS: systemic inflammatory response syndrome; SVR: systemic vascular resistance.

depression of myocardial contractility is responsible for LV systolic dysfunction leading to reduced cardiac output, hypotension, and resulting coronary hypoperfusion. From this starting point, vicious circles are sequentially triggered: (1) coronary ischemia further decreases myocardial contractility, and (2) the compensatory pathway to systemic hypoperfusion includes vasoconstriction and augmented serum arterial lactate levels, LV afterload, and cardiac oxygen consumption, contributing to myocardial dysfunction (Fig. 1) (2). The initial compensatory vasoconstriction is partly counteracted by the pathological vasodilation induced by capillary leakage and microcirculation impairment that is provoked by systemic inflammation (4). The composite of systolic and diastolic dysfunction increases the LV end-diastolic pressure and predisposes to pulmonary edema.

The real incidence of AMI-related CS is still unclear and controversial: some evidences suggest an increase of CS over the last decades, whereas other studies report a reduction (7, 9, 10). Radovanovic, in the "Acute Myocardial Infarction in Switzerland" (AMIS) Plus Registry, identified a remarkable association between the reduction of AMI-related CS and the broader performance of percutaneous coronary interventions (PCI) (11). Moreover, with the advent of primary PCI, mortality from CS is declining; in this field, some evidences suggest that the early timing of reperfusion could play a key role, even more than the type of revascularization (9, 12, 13).

Short-term mortality in CS after AMI is estimated to be 40% to 60%, but it could even reach 80% in cases of ventricular septal rupture (8). Despite the absolute severity of prognosis, some scores have been proposed to discriminate the mortality risk of CS patients—for example, the Sleeper score (derived from the SHOCK trial), the CardShock risk score, and the "IntraAortic Balloon Pump in Cardiogenic Shock II" (IABP-SHOCK II) risk score (14, 15, 16). The Sleeper score obtained from the SHOCK trial cohort provides one of two scores that are different on the basis of the availability of invasive data from pulmonary artery catheterization (Table 1). The score uses eight variables for patients when invasive monitoring is not available (age, shock on admission, clinical evidence of end-organ-hypoperfusion, anoxic brain damage, systolic blood

Table 1. **The sleeper risk score**

Sleeper (2010)	
Scoring system without invasive hemodynamics	Scoring system for invasive hemodynamic cohort
Age	Age
Shock on admission	—
End-organ hypoperfusion	End-organ hypoperfusion
Anoxic brain damage	Anoxic brain damage
—	Stroke work
Systolic blood pressure	—
Prior CABG	—
Non-inferior MI	—
Creatinine ≥1.9 mg/dL	—
—	LVEF <28%

LVEF indicates left ventricle ejection fraction; MI, myocardial infarction.

Table 2. **The CardShock risk score**

CardShock (2015)	
Variable	Points
Age >75 y	1
Confusion at presentation	1
Previous MI or CABG	1
ACS aetiology	1
LVEF <40%	1
Blood lactate	0 point if <2 mmol/L 1 point if 2–4 mmol/L 2 points if >4 mmol/L
$eGFR_{CKD-EPI}$	0 point if >60 mL/min/1.73 m^2 1 point if 30–60 min/mL/1.73 m^2 2 points if <30 mL/min/1.73 m^2
Maximum	9

ACS indicates acute coronary syndrome; CABG, coronary artery bypass grafting; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration Formula; eGFR, estimated glomerular filtration rate; LVEF, left ventricle ejection fraction; MI, acute myocardial infarction.

pressure, prior coronary artery bypass grafting [CABG], non-inferior myocardial infarction, and creatinine $\geq$1.9 mg/dL) or five variables for patients when right heart catheterization data are accessible (age, end-organ hypoperfusion, anoxic brain damage, LV ejection fraction (EF) <28%, and stroke work). The CardShock includes only clinical and laboratory data: age, confusion at presentation, previous cardiac revascularization, ACS aetiology, LV systolic dysfunction, blood lactate, and estimated glomerular filtration rate (eGFR) (15) (Table 2). The most recent IABP-SHOCK II risk score demonstrated strong correlation with short-term prognosis and includes six variables proven to be independent predictors of 30-day mortality: age, prior stroke, Thrombolysis in Myocardial Infarction (TIMI) flow grade less than 3 after PCI, and admission levels of glucose, creatinine and arterial blood lactate (Table 3). From the score, three risk categories can be obtained: low (0–2), intermediate (3 or 4), and high (5–9) risk. The different risk profiles showed to be associated with a stepwise increase in short-term mortality rates: 20% to 30%, 40% to 60%, and 70% to 90%, respectively (16).

Table 3. **The IABP-SHOCK II risk score**

IABP-SHOCK II (2017)	
Variable	Points
Age >73 y	1
History of stroke	2
Glucose at admission >10.6 mmol/L (191 mg/dL)	1
Creatinine at admission >132.6 μmol/L (1.5 mg/dL)	1
Arterial lactate >5 mmol/L	2
TIMI flow grade <3 after PCI	2
Maximum	9
Risk category	
Category	Points
Low	0–2
Intermediate	3–4
High	5–9

PCI indicates percutaneous coronary intervention; TIMI, thrombolysis in myocardial intervention.

All of these scores only predict short-term mortality. Singh reported for CS patients who survived 30 days after an ST-elevation myocardial infarction (STEMI), an annual mortality rate that approximates the remaining STEMI population (17). This was in accordance with a previous evidence of good functional status in CS hospital survivors at 1-year follow-up. As a consequence, CS should be considered a life-threatening complication of AMI that mainly impacts on early outcome (18).

REPERFUSION THERAPY

Early revascularization

The keystones of CS treatment are early coronary reperfusion, hemodynamic support, and treatment of end-organ dysfunction. CS may complicate both STEMI and non-ST elevation myocardial infarction (NSTEMI) with a rate, as reported by a recent registry, of 12% and 4%, respectively (19). Anderson et al. revealed a higher adjusted mortality in NSTEMI patients as compared with the STEMI population; the worse prognosis can be explained by a greater burden of comorbidities and longer time delays to reperfusion (19).

Current ESC Guidelines encourage early revascularization in clinical practice for both NSTEMI and STEMI patients, and numerous registries have confirmed benefits from precocious reperfusion treatments and supporting medical therapy (1, 20). Data from real-world settings revealed that revascularization rates in CS have raised over the last decade (up to 70% in a recent Swiss registry) in keeping with the evidence that coronary reperfusion is the only therapy proven to carry survival benefit (10, 21, 22, 23, 24, 25). The SHOCK trial represents a cornerstone in the field: patients with AMI-related CS due to acute LV failure were randomly assigned to initial medical stabilization or emergency revascularization, accomplished by either CABG or PCI. Despite the limits carried by the ''enrolment era'' (only balloon angioplasty for the majority of patients undergoing PCI and two-thirds of patients receiving thrombolytic therapy in the medical stabilization group), the SHOCK trial demonstrated that emergency revascularization significantly improved 6-month survival, despite the fact that 30 days mortality did not differ between the two different approaches. At the time, the authors concluded that early revascularization should thus be strongly recommended (26). The coeval ''Swiss Multicentre trial of Angioplasty for SHock'' (SMASH) trial failed to confirm this evidence because it was prematurely stopped because of slow enrolment. Nevertheless, a few years later, Hochman and the SHOCK group confirmed a long-term (6 years) mortality advantage for patients undergoing early revascularization (27, 28).

Multivessel coronary artery disease

Multivessel coronary artery disease is reported in about 70% to 75% of CS patients and identifies a subgroup of patients at higher mortality risk according to the National Cardiovascular Data Registry (NCDR) and Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With The Guidelines (ACTION Registry–GWTG) (19, 29). In multivessel disease patients, the optimal management of additional

nonculprit lesions remains nowadays unclear and debated. Alternative approaches are an ''aggressive'', early, multivessel revascularization of all angiographically significant stenoses or the immediate PCI of the culprit lesion, followed by a staged evaluation and/or revascularization of the other stenoses.

The theoretical advantages of an early multivessel percutaneous revascularization are a better perfusion of the peri-infarct area and the prevention of recurrent ischemia in nonculprit sites. Conversely, early multivessel PCI could increase the risk of distal embolization, acute nonculprit vessel occlusion, loss of side-branches, and contrast-induced nephropathy. Further considerations appear mandatory: angiographic significance of epicardial coronary stenoses does not necessarily determine real flow limitation, and coronary spasm during AMI can cause overestimation of the lesions severity; nescience of these conditions could potentially lead to redundant procedures without resultant clinical benefits.

In the general STEMI population, several evidences demonstrated that multivessel PCI was not encumbered by higher risk of stroke, contrast-induced nephropathy, or major bleeding (30, 31, 32). Nevertheless, in the presence of CS, results are still controversial: Cavender reported that multivessel percutaneous revascularization was associated with a greater rate of in-hospital mortality, whereas in the registry by Bauer, after adjusting for confounding factors, a negative impact of multivessel PCI on early mortality was conversely excluded (33, 34). In a real-world cohort, Park described a decrease in in-hospital mortality, recurrent AMI, and need for repeat revascularization in patients with CS after STEMI treated with multivessel revascularization (35). On the basis of these evidences, the 2017 ESC Guidelines on STEMI stated a IIa/C recommendation for complete revascularization during the index procedure in patients with CS (1).

This position was overturned only 1 year later: in the latest 2018 ESC Guidelines on myocardial revascularization, the routine treatment of nonculprit lesions is not recommended during primary or immediate PCI in STEMI and NSTEMI patients with CS (class III/B). The indication for the nonculprit lesions revascularization before hospital discharge remained instead unchanged (class IIa/A) (36). The rapid change in international guidelines emphasizes the actuality of the topic and the difficulty to reach definite responses because of the hindrance to have randomized data from large studies. The new indications derive from the recent CULPRIT-SHOCK study, an international, multicenter, randomized, open-label trial that compared the culprit lesion only PCI (possibly followed by a staged nonculprit revascularization) with immediate multivessel PCI in patients with AMI-related CS (37). The primary end-point of the study was a composite of 30-day mortality and onset of severe renal failure needing renal replacement therapy: the rate of the primary endpoint was lower in the culprit-lesion-only PCI group in addition to mortality (38). The incidence of severe renal failure alone was also lower in the culprit-lesion-only group, despite the threshold for statistical significance was not reached. Besides the negative repercussion on renal function, the greater dose of contrast medium used in the multivessel PCI group was also hypothesized to be responsible for acute LV volume overload, bringing a consequent negative impact on myocardial contractility. The recently published data regarding the 1-year follow-up conversely highlighted a higher rate of repeat revascularization and rehospitalization for heart failure in the culprit-lesion-only PCI patients, which was partly explained as a consequence of higher occurrence of complete revascularization in the immediate multivessel PCI group (39). Similar results were also reported by de Waha in a recent large metanalysis of 10 cohort studies including more than 6,000 patients: aggressive early multivessel PCI was burdened with increased short-term mortality, whereas in the long-term, the two approaches did not differ in terms of mortality, stroke, renal failure, and bleeding (29). Despite the broad study population, it should be recognized that the observational nature of the analysis makes the results prone to bias. It is fair to hypothesize that early multivessel PCI was reserved by operators to patients with more severe coronary lesions and/or hemodynamic conditions as well as, on the contrary, to younger patients with lower prevalence of comorbidities. A recent real-world study, limited to STEMI patients, also failed to demonstrate clinical advantages from an early single-stage multivessel percutaneous revascularization (40).

A retrospective analysis of the IABP-SHOCK II trial further supports the lack of benefit in terms of 30-day and 12-month mortality in patients treated with early multivessel PCI versus culprit lesion only PCI (41). These evidences led to the above-mentioned 2018 ESC Guidelines that discourage the routine and immediate revascularization of nonculprit lesions; nevertheless, further divergent results by Lee generate the impression that the subject remains inconclusive (42).

PCI or CABG for early revascularization in CS following AMI?

As previously reported, since the SHOCK trial publication, early reperfusion therapy has been considered the best approach in terms of timing. Over the last years, a key unanswered question has conversely regarded the role of PCI and/or CABG in the setting of emergent revascularization of patients with CS. Data from the literature are indeed limited, come from nonrandomized trials, and are affected by the strong association of CS itself with adverse clinical outcome that attenuates the potential benefits of any therapeutic strategy (43, 44).

In the SHOCK trial, the reperfusion strategy was not randomized; CABG was advocated in patients with left main coronary stenosis of $\geq$50%, $\geq$2 total/subtotal occlusions, stenoses more than 90% in two nonculprit coronary arteries, stenoses unsuitable for PCI, or PCI unsuccessful. The decision was nevertheless left to the cardiologists, and thus many patients with three-vessel disease underwent PCI (26). Taking into the account the potential biases, White et al., in their subanalysis of the study, revealed a similar 30-day, 1-year, and 6-year mortality for patients treated with either of the two types of reperfusion, despite a longer time from symptom onset to revascularization and a greater prevalence of comorbidities (i.e., diabetes mellitus) and diffused coronary disease (i.e., left main and three-vessel disease) among patients undergoing CABG (45). Despite being 15 to 20 years old, the above-mentioned trials are the only two papers cited in the latest ESC Guidelines on myocardial revascularization as a demonstration

of the scarceness of data on the topic (36). Evidences in this field mostly come from observational reports. For example, a meta-analysis by Mehta comparing PCI versus CABG in patients with STEMI complicated by CS and multivessel disease showed similar mortality rate between the two treatment options (46). Despite coming from a small cohort, there is promising evidence that for multivessel patients, an hybrid approach of PCI followed by CABG is associated with lower 30-day mortality as compared with PCI alone (47).

It is also fair to emphasize that in the current PCI era, emergency CABG in AMI-related CS is performed in less than 4% of patients and, also in presence of three-vessel coronary disease, CABG is performed in a proportion of cases ranging from 3.2% to 8.8% (6, 25). This is mainly due to both the logistical difficulties of organizing emergency surgical revascularization and the last decades of improvement in percutaneous reperfusion success that represents the most powerful predictor of clinical outcomes in CS patients as in the general AMI population (22). Over the last years, PCI has in fact demonstrated a comparable outcome to surgery in terms of hard endpoints also in settings traditionally considered a prerogative of cardiac surgeons such as multivessel and left main coronary disease (48, 49).

In the latest ESC Guidelines on myocardial revascularization, emergency PCI of the culprit lesion gained a class IB recommendation, whereas emergency CABG is advocated in patients with a coronary anatomy judged not amenable to PCI (36). In addition, the same guidelines strongly support the use of DES rather than BMS. Despite that in the setting of CS the differences driven by the stent choice appear difficult to be demonstrated, some evidences on the safety and clinical advantages of DES use are available (50). The radial access is also suggested as the best approach for PCI, mainly in emergency settings when the bleeding risk is higher. In a recent metanalysis, Pancholy highlighted that in patients with CS, radial access was associated with lower all-cause mortality and a reduced rate of major cardiac and cerebral events at 30 days (51). In hypotensive CS, an ultrasound guidance has been also proposed to overcome the difficulty to approach the radial artery (52).

MECHANICAL CIRCULATORY SUPPORT (MCS)

Despite being recently improved by early revascularization, mortality of AMI-related CS remains high. To address the organs hypoperfusion and consequent multiorgan failure, the mechanical circulatory support (MCS) appears to be a hopeful approach for all patients who remain unstable despite optimal medical therapy. MCS can be achieved by both temporary and durable devices and is aimed to improve cardiac output and/or resize the use of catecholamines reducing their cardiotoxicity (38, 53).

TEMPORARY MECHANICAL CIRCULATORY SUPPORT

The temporary devices are intended for hemodynamic stabilization and end-organ failure recovery, but they can also facilitate revascularization and durable left ventricular assisted device (LVAD) implantations. These temporary supports are indeed identified as ''bridge'' solutions and might represent a bridge to recovery, a bridge to transplantation, a bridge to decisions, or a bridge to-bridge in those patients in whom the implant of a durable MCS after initial cardiac stabilization has been already planned (2). Temporary MCS are classified into passive (Intra-aortic-balloon-pump, IABP) or active (Impella, TandemHeart, V-A ECMO) devices, which are described below.

Passive temporary device

Intra-aortic-balloon-pump (IABP)—In the last 5 decades, IABP has been the most used temporary MCS (54). Once percutaneously positioned into the thoracic aorta distally to the left subclavian artery, IABP inflates and deflates according to diastole and systole, respectively, to increase the diastolic blood pressure into the coronary and cerebral circulation. On the cardiac level, IABP improves coronary perfusion and reduces LV afterload. In absence of randomized trials, a 2009 metanalysis including nine observational cohort studies on IABP implantation in patients with CS after STEMI showed a significant decrease of 30-day overall mortality in patients treated with IABP support, besides thrombolysis (53, 55).

Nevertheless, in the current PCI era, as per the multivessel coronary disease management, these evidences have become a matter of debate. The IABP-SHOCK II trial is a recent prospective randomized trial that enrolled 600 patients with AMI-related CS demonstrating similar 30-day, 6-month, and 12-month mortality rates in patients treated with PCI with or without IABP (54). The recent Cochrane review also failed to demonstrate, despite the improvement of some hemodynamic parameters, a net survival benefit from IABP use in patients with AMI complicated by CS as compared with the standard medical and reperfusion treatment (56). As a consequence, the latest 2018 ESC Guidelines on myocardial revascularization do not indicate the routine use of IABP in patients with AMI-related CS (class III-B) (36).

When IABP is still a choice, the optimal timing also remains controversial. In the IABP-SHOCK II trial, no differences between patients in whom IABP was started before versus after revascularization were detected (54). Only one small single-centre retrospective registry reported a more favorable in-hospital outcome in patients in which IABP assistance was started before PCI (57). Conversely, a larger registry highlighted higher CPK peak levels, which is a sign of larger infarct size, in patients in whom IABP implantation preceded PCI, and the authors addressed the longer reperfusion delay as a plausible explanation (58).

Active temporary device

Impella (Abiomed)—An Impella device, which is an axial pump allocated across the aortic valve, aspirates from the LV and ejects blood into the ascending aorta reducing the end-diastolic wall stress and pulmonary capillary wedge pressure. The diverse available devices require different insertion approaches. For example, the Impella 2.5 and Impella CP are percutaneously inserted, whereas the Impella 5.0 needs a surgical cutdown of the femoral or axillary artery. The three

devices allow a flow rate up to 2.5, 4.0, and 5.0 L/min, respectively (6). The ISAR-SHOCK randomized trial firstly compared in a small cohort the hemodynamic support of Impella 2.5 and IABP; the Impella-supported patients showed higher cardiac output and mean arterial pressure as well as reduced serum lactate levels. Although the improvement was confined to the first hours after implantation, the opportunity to rapidly reverse the vicious circle triggered by CS appears promising (59). Nevertheless, the IMPRESS trial failed to demonstrate a 30-day mortality reduction in patients randomly assigned to Impella CP and compared with IABP support. A similar outcome has been also confirmed by Scharge in a recent retrospective study (60, 61).

Timing for the use of these devices is another object of debate. Only a retrospective analysis of the cVAD Registry reported an improvement of survival when Impella was implanted before PCI and before inotropes/vasopressors initiation, supporting the hypothesis of a potential collateral harm from these drugs administration that may aggravate the neurohormonal and molecular cascade triggered by CS (62).

Data on the different risk/benefit profiles of the three available devices are also limited: a retrospective single-center analysis compared the Impella 2.5 versus the 5.0 version in patients with AMI-related CS and reported a higher 30-day survival in the Impella 5.0 group (63). In parallel, the different devices appear burdened by diverse risk of complications, such as bleeding at vascular access site, pericardial tamponade, and hemolysis. The choice of the ''right size'' should be patient-tailored and take into consideration specific features such as peripheral vascular disease or severe calcification of the aortic valve. A recent registry evaluated the Impella 5.0 as a bridge-to-transplantation or to-LVAD and reported a survival rate to the next therapy of 75% with a risk of severe bleedings, hemolysis, and limb ischemia accounting for 28%, 8%, and 3%, respectively. (64).

TandemHeart (Cardiac Assist Inc)

The TandemHeart (TH) is a left atrial-to-femoral artery bypass system that consists of a trans-septal cannula, a 15 to 17 Fr arterial cannula, and a centrifugal blood pump able to deliver flow rates up to 4.0 L/min (Fig. 2). The oxygenated blood is aspirated from the left atrium and injected into the lower abdominal aorta via the femoral artery with the effect of increased cardiac output, augmented mean arterial pressure, and reduced left ventricular filling pressure (6). Ventricular sept defects and apical thrombus are contraindications to TH. Two different randomized trials comparing the use of TH and IABP in patients with AMI-driven CS reported a significant improvement of hemodynamic parameters in the TH group at the cost of more complications (65, 66). In a relatively large cohort of patients with severe CS refractory to IABP and vasopressors, the use of TH determined early hemodynamic improvement, though the short-to-mid term mortality remained high (67).

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) (Medtronic)

The percutaneous extracorporeal membrane oxygenation (ECMO) system is a simplified form of cardiopulmonary bypass consisting of a centrifugal pump that deviates the desaturated blood from the femoral vein through a membrane oxygenator and then, via an outflow cannula, reintroduces the oxygenated blood into the femoral artery. The system provides a full biventricular support that is capable of generating a continuous flow of 7.0 L/min (6). The main drawback of the device is the increased afterload generated by the retrograde flow through the peripheral cannulation that produces an incomplete emptying of the LV, augments oxygen demand, and increases the risk of acute pulmonary edema (68).

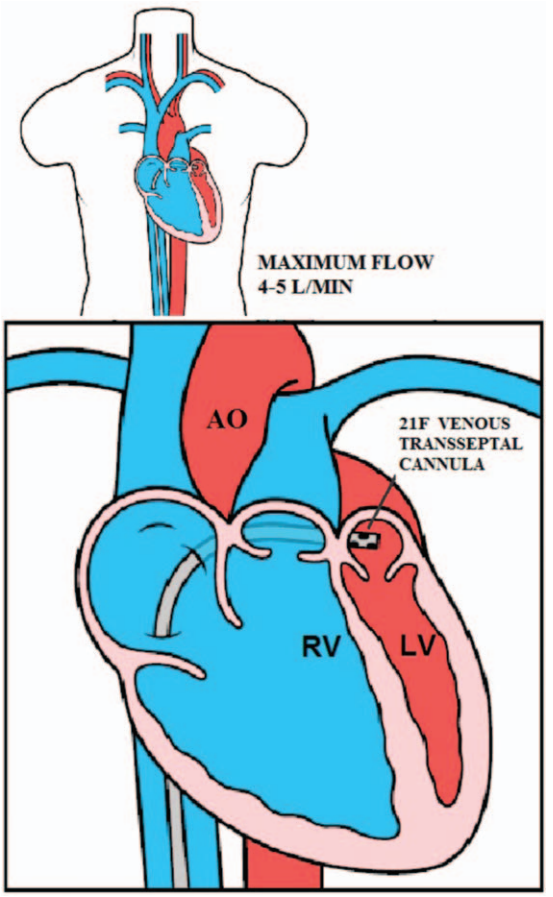

Fig. 2. **Tandem Heart.** AO: aorta; LV: left ventricle; RV: right ventricle.

In a small retrospective study on 27 patients with CS after AMI, ECMO support demonstrated improved survival rates, and early implantation of the device was correlated with better outcomes (68). Inotropic agents, as well as the insertion of IABP or Impella, may be also considered in order to favor ventricular unloading, despite that only few evidences exist on the conjunct use of IABP and ECMO (6). Limb ischemia, renal failure, infections, and bleedings at multiple sites are the most reported complications from ECMO use; cerebral hypoxemia can also occur mostly because the well-oxygenated blood is conveyed to the lower part of the body, whereas the blood coming from the LV preferentially supplies the cerebral and coronary circulation (6, 69, 70).

A retrospective trial reported improved 30-day and 1-year mortality rates in patients with AMI-related CS if ECMO was used as back-up support for CS refractory to IABP implantation

(71). A recent metanalysis of 13 observational studies including patients with both Cardiac Arrest and/or CS complicating AMI, demonstrated a better 30-day survival in the ECMO group as compared with IABP (72). Nevertheless, if VA-ECMO represents the gold standard ''bridge'' therapy for resuscitated patients, issues have been raised on the possible hamper driven by afterload increase in isolated LV dysfunction (73). A recent review confirms the effectiveness of ECMO in cardiac arrest, while in the setting of CS a retrospective analysis on 79 patients revealed no significant advantages from ECMO use in terms of in-hospital mortality and complications compared with Impella or TH (74).

Unsolved questions and current indications of active temporary device

After the technological progresses in the field of medical devices, the use of active MCS has been rapidly *broadened* in recent years. Nevertheless, their clinical benefit still remains a matter of debate. Thiele et al. conducted a relatively large meta-analysis on 148 patients with AMI-related CS and showed that short-term mortality was similar in patients treated with active MCS to those treated with IABP or with no mechanical support (38). In fact, though active MCS showed significant increase of mean arterial pressure and reduction of arterial lactate levels, bleeding and leg ischemia occurred more frequently in the active MCS group, encumbering the net clinical benefit (38). Data on the timing of active temporary MCS utilization are also limited. The USpella registry collected data from 154 patients affected by CS complicating AMI and treated with Impella 2.5, and early pre-PCI Impella implantation showed an overall better survival compared with post-PCI use (75).

The substantial lack of definite evidences is a consequence of the scarceness of data from randomized trials. As a result, short-term MCS deserved an IIb-C recommendation in the latest ESC Guidelines on myocardial revascularization. The same document also advocates a case-by-case careful evaluation based on patient age, comorbidities, neurological function, predicted survival, and quality of life (36). The choice of the device also requires a careful selection and should take into consideration multiple variables such as the centre experience, the costs, the contemporary presence of right heart failure, the degree of the support needed.

In the future, large randomized trials may give support to the current indications and answer the remaining open questions.

CONCLUSIONS

CS is a fearsome complication of AMI and deeply influences prognosis. Despite early revascularization, prompt optimal medical therapy, and state-of-the-art mechanical supports, the mortality rate of patients with CS remains high. The available literature is hardly conclusive because of the difficulty to randomize such very high-risk patients to comparative treatments. Moreover, data from the few and small randomized trials and from observational reports are often controversial.

The latest 2018 ESC Guidelines on myocardial revascularization have resized the role of early multivessel revascularization and of the routine use of IABP. The recently introduced mechanical support devices could potentially offer a crucial clinical benefit as ''bridge'' therapies. Nevertheless, the non-negligible complications rates due to the invasiveness of the techniques and the scarceness of clinical data make it difficult to reliably estimate the benefit/risk ratio of these innovative approaches.

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