Russian Journal of Cardiology 2023;28(S1):5337
doi:10.15829/1560-4071-2023-5337
https://russjcardiol.elpub.ru

LITERATURE REVIEWS
ISSN 1560-4071 (print)
ISSN 2618-7620 (online)
ISSN 2782-2257 (online)

Practical aspects of managing patients with cardiogenic shock

Novosadov M. M.[1], Novosadov V. M.[2], Dzhioeva O. N.[1,3], Drapkina O. M.[1]

[1]National Medical Research Center for Therapy and Preventive Medicine, Moscow; [2]V. V. Veresaev City Clinical Hospital, Moscow; [3]A. I. Yevdokimov Moscow State University of Medicine and Dentistry, Moscow, Russia.

Novosadov M. M.* ORCID: 0000-0002-7080-7438, Novosadov V. M. ORCID: 0000-0003-3753-9328, Dzhioeva O. N. ORCID: 0000-0002-5384-3795, Drapkina O. M. ORCID: 0000-0002-4453-8430.

*Corresponding author:
pegasustimi@gmail.com

Cardiogenic shock is the leading cause of death among patients with acute coronary syndrome. This pathology is characterized by high rates of inhospital and annual mortality. In Russian literature, data on the prevalence, diagnosis and treatment of patients with cardiogenic shock are limited. Therefore, the main aim of this publication is to increase the awareness of specialists about modern approaches to the diagnosis and treatment of this condition. This review discusses in detail the main causes of cardiogenic shock, aspects of pathophysiology, modern classification, diagnosis, and algorithms for pharmacological and non-drug therapy in patients with cardiogenic shock.

Keywords: cardiogenic shock, myocardial infarction, acute heart failure, revascularization, inotropic support, mechanical support.

Relationships and Activities: none.

Received: 19.01.2023
Revision Received: 26.01.2023
Accepted: 10.02.2023

For citation: Novosadov M. M., Novosadov V. M., Dzhioeva O. N., Drapkina O. M. Practical aspects of managing patients with cardiogenic shock. *Russian Journal of Cardiology*. 2023;28(1S):5337. doi:10.15829/1560-4071-2023-5337. EDN CEEORE

Key messages

- Cardiogenic shock remains the leading cause of death despite advances in therapy.
- The review suggests the creation of a registry of patients with cardiogenic shock in the Russian Federation in order to further optimize treatment protocols.

Cardiovascular diseases in the 21st century retain dominance in the structure of mortality in developed countries [1]. Over 17,3 million people die each year due to cardiovascular disease. Atherosclerotic cardiovascular diseases remain one of the most complex and unresolved problems of modern cardiology, since acute coronary artery disease (CAD) are the cause of cardiogenic shock (CS) in 82% of cases [2, 3].

CS is the most severe and unfavorable complication of acute CAD. The true prevalence of CS is unknown, but the 2019 European Society of Cardiology consensus [4] provides data that 3-5% of all hospitalizations for acute heart failure (AHF) occur in patients with true CS. In-hospital mortality, even with modern therapeutic methods, is in the range of 30-60%, with most deaths occurring within 24 hours of admission. The annual mortality of patients after CS is 50-60%, and most of the deaths occur in the first 30-60 days after hospital discharge. CS rate in patients with acute coronary syndrome (ACS) is 30-40% [5]. Interestingly, a decade ago, medical community believed that CS occurs mainly

in ACS. However, large US registry on CS problems revealed natural decrease in the number of patients with CS associated with myocardial infarction (MI), from 65,3% to 45,6% between 2005 and 2014 [6]. A similar trend was shown in the Canadian intensive care registry as followed: only a third of patients with MI had shock at admission, while ~18% of patients were admitted with decompensated heart failure (HF) against the background of ischemic cardiomyopathy without acute MI, 28% had non-ischemic cardiomyopathy and other causes (recurrent ventricular tachycardia, severe valvular heart disease) [7]. The aim of this review was to draw the attention of specialists to this urgent problem, encourage the formation of interdisciplinary teams of cardiologists and intensivists, as well as to assess the potential of creating a unified registry of CS patients in our country.

Definition, classification and epidemiology of CS

The most severe form of CAD is ACS, which is classified into 2 main forms: ST segment elevation MI (STEMI) and non-ST segment elevation MI (NSTEMI), which also includes unstable angina [8-12]. STEMI is a less favorable form of acute CAD due to the high incidence of complications [13], among which are arrhythmias, right ventricular (RV) involvement, AHF and mechanical complications: left ventricular (LV) free wall rupture, interventricular septal rupture, mitral valve papillary muscle rupture. AHF continues to be the most common complication of STEMI and appears to be one of the most important unfavorable prognostic factors [14]. The leading mechanism for AHF is LV contractile dysfunction caused by a large necrosis. There are following other causes of AHF: arrhythmias, mechanical complications, comorbidity factors. There are following unfavorable factors of AHF:

1. Severe manifestations of systemic congestion, characterized by pulmonary edema (Killip III).

2. Hypotension is a decrease in blood pressure (BP) <90 mm Hg. The causes can be both RV and LV dysfunction, arrhythmias, and mechanical complications. Long-term hypotension >30 min leads to acute kidney injury and other systemic complications.

3. Decrease in the cardiac index (CI) <2,2 l/min/m^2, leading to tissue hypoperfusion and cardiorenal syndrome followed by oligoanuria.

CS still remains the most severe complication of AHF, as well as the most common cause of death in patients in the cardiac intensive care unit [15]. The definition of CS reflects that this is a state of critical hypoperfusion and tissue dysoxia: a decrease in tissue oxygen saturation due to heart disease. In routine clinical practice, the diagnosis of CS is based on clinical criteria such as persistent hypotension <90 mm Hg without an adequate response to volemic load and accompanied by clinical signs of organ hypoperfusion: cold extremities, oligoanuria <20 ml/h and mental changes. In addition, there are following biological markers of tissue dysoxia: an increase in blood lactate level >2 mmol/l [16].

According to modern classification [17], CS has 3 stages:

1. Pre-CS: Patients with systolic BP (SBP) >90 mm Hg but with hypoperfusion signs: cold extremities, oligoanuria <20 ml/h, and altered mental status.

2. True CS with SBP <90 mm Hg for >30 min, need for pharmacologic or intraaortic balloon pump support, decreased CI <2,2 l/min/m^2, elevated filling pressures of the left, right, or both ventricles (increased pulmonary capillary wedge pressure (PCWP) and central venous pressure).

3. Refractory CS, which does not differ from stage 2 in hemodynamic characteristics, but there is no adequate response to ongoing therapy.

The e American College of Cardiology, the American Heart Association, the Society of Critical Care Medicine, and the Society of Thoracic Surgeons [18] proposed an extended version of A-E classification of CS (Figure 1). Stage A is a patient who is at risk of CS. Usually, there are no signs or symptoms of true CS. In such patients, there are no significant clinical and paraclinical abnormalities, but there is a risk of its development. Most often, these are patients with STEMI, as well as patients with decompensated HF, regardless of the LV ejection fraction (EF). Such patients require continuous round-the-clock monitoring of vital parameters in the intensive care unit.

Stage B: "Beginning" CS (pre-shock/compensated shock) describes a patient who has clinical evidence of relative hypotension or tachycardia without hypoperfusion. At this stage, there may be a mild volume overload, while lactate levels are normal.

Stage C: "Classic" CS, at this stage patients have signs of hypoperfusion and require pressor and inotropic support, often mechanical support or extracorporeal membrane oxygenation (ECMO) is often used. These patients have mean BP <60 mm Hg and SBP <90 mm Hg along with hypoperfusion. Laboratory findings may include signs of impaired renal function, elevated levels of lactate, natriuretic peptide, and liver enzymes. Invasive hemodynamics demonstrates a decrease in CI <2,2 l/min/m^2.

Stage D: "Deteriorating" CS describes a patient who has failed to stabilize despite intense initial efforts and further escalation is required. In addition, at least 30 minutes have elapsed but the patient has not responded with resolution of hypotension or end-organ hypoperfusion. Escalation consists in increasing the degree of vasopressor and inotropic

Figure 1. CS classification ([18], courtesy of Wiley).
Abbreviations: CS — cardiogenic shock, CPR — cardiopulmonary resuscitation, ECMO — extracorporeal membrane oxygenation.
Stage A — At risk. A patient who is not currently experiencing signs or symptoms of CS, but is at risk for its development. These patients may include those with large acute myocardial infarction or prior infarction acute and/or acute on chronic heart failure symptoms.
Stage B — Beginning CS. A patient who has clinical evidence of relative hypotension or tachycardia without hypoperfusion.
Stage C–Classic CS. A patient that manifests with hypoperfusion that requires intervention (inotrope, pressor or mechanical support, including ECMO) beyond volume resuscitation to restore perfusion. These patients typically present with relative hypotension.
Stage D — Deteriorating. A patient that is similar to category C but are getting worse. They have failure to respond to initial interventions.
Stage E — Extremis. A patient with circulatory collapse, frequently (but not always) in refractory cardiac arrest with ongoing cardiopulmonary resuscitation (CPR) or are being supported by multiple simultaneous acute interventions including ECMO-facilitated CPR. These are patients with multiple clinicians at bedside laboring to address multiple simultaneous issues related to the lack of clinical stability of the patient.

support to eliminate hypoperfusion and often the addition of mechanical circulatory support after the initial observation period. Colleagues from City Clinical Hospital № 52 in Moscow show that ECMO is actively used in refractory true CABG and in circulatory arrest, as a therapy for critical conditions [19].

Stage E: "Extremis" CS is the patient with circulatory collapse (refractory to treatment hypotension). Often (but not always), there is a circulatory arrest with ongoing cardiopulmonary resuscitation (CPR) or life support is provided by multiple simultaneous acute interventions, including ECMO-facilitated CPR. These are patients treated by a multidisciplinary team with doctors of various specialties, ranging from an intensive cardiologist to a cardiac surgeon. All of their work at the bedside is geared towards addressing multiple simultaneous issues related to the lack of clinical stability of the patient. Again, Russian specialists concluded that a cardiac intensivist is ideally suited to work in the cardiology unit, since he is equally competent in both clinical cardiology and intensive care [20].

Mechanism of CS development

The underlying mechanism for CS development is most often an acute decrease in LV contractility due to ischemia, which primarily causes a pronounced decrease in myocardial contractility, which first of all triggers a vicious circle of decreased CI, which further leads to the hypotension, which collectively worsen SI, and this further exacerbates coronary hypoperfusion [21]. RV contractile dysfunction and microcirculatory impairment can also contribute to the onset and worsening of CS course. A decrease in cardiac output (CO) affects coronary perfusion, which leads to impaired myocardial contractility and progression of CS. Impaired microcirculation in patients with decompensated HF and CS was already noted in the work [22], which showed that the proportion of perfused small (20 μm) vessels was lower in patients with HF and CS than in HF patients without CS (63% [46-65%] and 49% [38-64%] vs 92% [90-93%], p=0,001). Therefore, microcirculation disorders are quite common in patients with CS and are associated with a poor prognosis. The presence of obstructive CAD can further aggravate the decrease in coronary perfusion.

In the position statement of the European Society of Cardiology [4], much attention in the CS development and its pathophysiology is paid to microcirculation and multiorgan dysfunction (Figure 2). This is primarily due to the fact that the microcirculation is

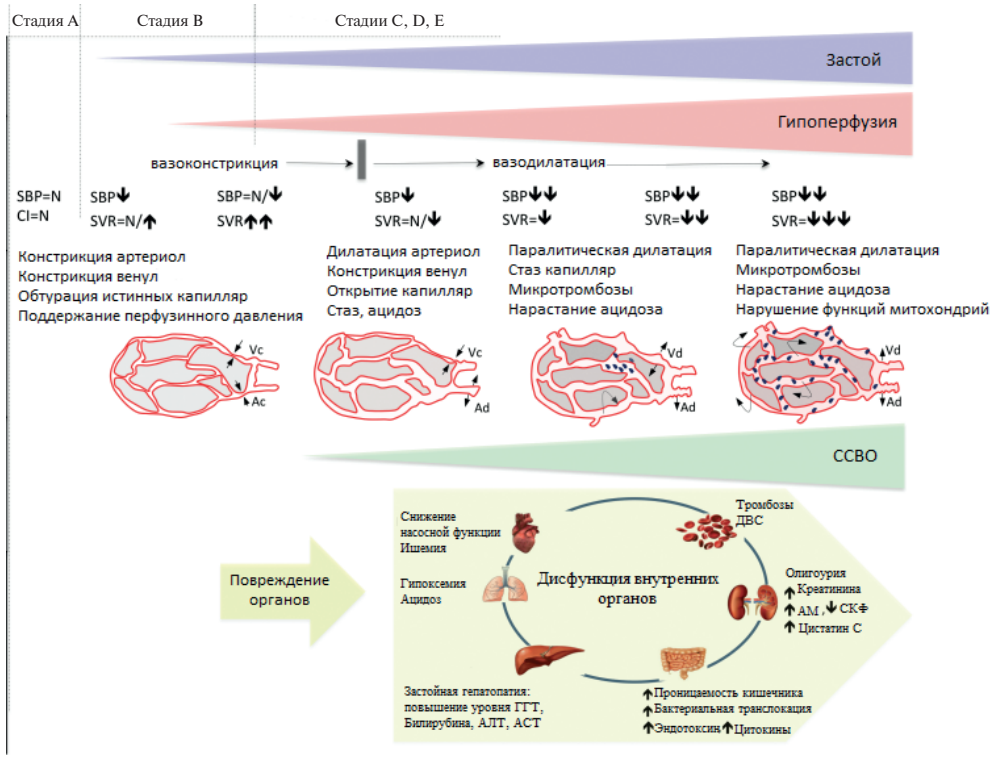

Figure 2. Organ dysfunction in CS ([4], courtesy of Wiley).
Abbreviations: ALT — alanine aminotransferase, AM — urea nitrogen, AST — aspartate aminotransferase, GGT — gamma-glutamyl transferase, DIC — disseminated intravascular coagulation, GFR — glomerular filtration rate, SIRS — systemic inflammatory response syndrome, Ac — arteriolar constriction, Ad — arteriolar dilatation, CI — cardiac index, SBP — systolic blood pressure, SVR — systemic vascular resistance, Vc — venular constriction, Vd — venular dilatation.

flow-dependent. A decrease in CO with a compensatory vascular tone increase reduces the sensitivity of capillaries, which does not meet the requirements of cellular metabolism, and this primarily leads to cellular hypoxia. However, even under severe hypoxia, mitochondrial viability and function are maintained for several hours, and animal models suggest initial activation of the mitochondrial transport chain to maintain normal functioning to support metabolic demands [23]. Subanalysis of the CULPRIT-SHOCK study [24] showed an independent correlation between microcirculatory perfusion and the composite endpoint of 30-day mortality, renal replacement therapy, especially in patients with a hemodynamic imbalance between microcirculation and macrocirculation characteristics [25]. Systemic inflammation also plays an important role in CS development and is observed in 20-40% of patients with CS, and ultimately leads to a decrease in systemic vascular resistance [26]. Elevated levels of cytokines (interleukin-1β, 6, 7, 8, and 10) were found in patients shortly after the CS onset, which is a predictor of death [27]. The production of nitric oxide and other inflammatory mediators leads to vasodilation, which impairs macrocirculation. Infection complicates the course of approximately 20-30% of CS cases [28]. Infection risks include vascular access as well as gastrointestinal mucosal damage associated with hypoperfusion and consequent bacterial translocation. Multiple organ dysfunction is the result of macrohemodynamic abnormalities and is associated with poor prognosis. Despite the fact that LVEF is a marker of poor prognosis in CS patients, contrary to popular belief, LV contractility is not always sharply reduced, which was shown, for example, in the SHOCK study [29], where most patients had EF >30%. An important factor is the presence of not only contractile dysfunction in these patients, but diastolic dysfunction with a restrictive pattern, leading to an increase in filling pressure. Reynolds HR, et al. [30] described in detail the echocardiographic patterns of CS. The pattern of increased filling pressure was observed in 60,9% of examined patients. Patients with this pattern had a lower LVEF (31,1% vs 39,0%, p=0,02) and a higher LV wall motion score index (2,1 vs 1,8, p=0,05). Patients with severe diastolic dysfunction were more likely to receive counterpulsation during echocardiography (73,7% vs 43,5%, p=0,03). The restrictive pattern had a positive predictive value of 80% for elevated PCWP ⩾20 mm Hg. Thirty-day survival was 53,9% with restriction versus 68,0%

without restriction (p=0,31). Therefore, restrictive filling pattern is common in patients with CS and is associated with its unfavorable course. CS can also occur with RV involvement, but the percentage of such patients is much less, because most of them are found with primary LV failure. Studying the registry for patients with CS, some researchers [31] conclude that patients with RV infarction have outcomes comparable to those in patients with CS and LV failure. There are following mechanism of LV failure: RV dysfunction affects LV contractility, not only by reducing LV preload, but also due to the effect of interventricular septum prolapse on LV geometry, which leads to a decrease in its contractility. The investigators made the following conclusions: patients with predominant shock in RV involvement were younger, with a lower rate of prior MI (25,5 vs 40,1%, p=0,047), anterior MI and multivessel disease (34,8 vs 77,8%, p=0,001), there was also less time spent from the diagnosis of MI to CI (2,9 vs 6,2 h, p=0,003) compared with patients with shock due to LV involvement. Inhospital mortality was 53,1% compared with 60,8% (p=0,296) for patients with predominance of RV and LV shock, respectively, and the effect of revascularization on mortality did not differ between groups. Therefore, CI against the background of RV failure has the same unfavorable prognosis as true LV CS. Thus, we see that true CS leads to macro- and micro-organ dysfunction, often leading to death. The instability of hemodynamic parameters and the severity of such a cohort of patients suggests the idea of decision-making speed and the timeliness of providing competent care.

Treatment of CS

To answer the question of what is the basis of therapy for such severe patients with true CS, it is important to understand the mechanism of CS development in each specific case, and one should try to influence the entire chain of organ dysfunction. Perhaps the most important is to perform revascularization in such patients, i.e. emergency percutaneous coronary intervention (PCI) should be performed [32]. In another review [33], the authors show that patients with return of spontaneous circulation after successful CPR should be taken to a PCI center as soon as possible. Early emergency echocardiography and laboratory tests (acid-base balance, lactate levels) are important and can be performed in the operating room, but only with limited delay without delaying PCI. Triage, stabilization and diagnostic evaluation of such patients are essential before invasive treatment. Stable patients with risk factors for shock (Stage A) or in the case of pre-CS (Stage B) can usually have immediate coronary angiography followed by infarct-related artery revascularization, with ongoing clinical, laboratory and physical reevaluation of patients for progression of shock every 60 minutes. Patients with more severe CS (Stages C-E) may generally need to be stabilized initially based on BP, target organ perfusion status, oxygenation, and acid-base status. However, in cases of STEMI, any necessary stabilization efforts should be accelerated to minimize the delay in reperfusion therapy, because every 10-min delay results in 3 deaths per 100 patients undergoing PCI [34].

What are the options for stabilizing the patient condition at the present time? Intravenous inotropic and pressor agents have been and remain the mainstays in the emergency treatment of CS. These agents can increase ventricular and CO contractility, decrease filling pressure, and maintain target organ perfusion. Among the most commonly used drugs, dobutamine can be distinguished, which is a direct agonist of β2-adrenergic receptors with a positive inotropic effect, in addition to it, norepinephrine can also be noticed, stimulating both α and β-adrenergic receptors, but more precisely with a vasopressor effect and minimal inotropic, as well as milrinone and levosimendan [35]. Norepinephrine is a fairly strong and reliable vasopressor with a minimal inotropic effect, which is important given compensatory tachycardia in this category of patients, and norepinephrine is often used in combination with dobutamine. The use of vasopressor agents in severe true CS is justified by the fact that in many patients the effectiveness of target organ perfusion directly correlates with BP: namely, with SBP or, as it is often called, perfusion BP, the level <60 mm Hg of which increases inhospital mortality. Norepinephrine in this case not only can maintain the perfusion of internal organs at an adequate level, but also stimulates a BP increase without concomitant increase in heart rate (HR). Currently, there are no comparative studies of pure inotropic and vasodilatory agents in CS. In clinical practice [36], three drugs can be used: dobutamine, which is a pure inotrope, as well as levosimendan and phosphodiesterase (PDE) inhibitors, both of which are combined inodilators. Interestingly, these three drugs act in different ways. Dobutamine is predominantly a β-1-agonist with weak activity at β-2 and α-1 receptors. PDE inhibitors prevents the breakdown of cyclic adenosine monophosphate (cAMP). In the myocardium, increased cAMP levels activate protein kinase A, which in turn produces calcium channel phosphorylation, increasing calcium influx into the cardiomyocyte, which in turn increases contractility. In smooth muscle, elevated levels of cAMP inhibit myosin light chain kinase, which primarily causes arterial and venous vasodilation. Levosimendan interacts with Ca^{2+}-saturated troponin C (cTnC) and this underlies Ca^{2+}-sensitizing mechanism. The

interaction site for levosimendan on the cTnC molecule was located on the hydrophobic N-domain, in close proximity to so-called D/E linker. Levosimendan binding results in Ca^{2+}-saturated cTnC stabilization in the drug presence, thereby increasing the inotropic function of cardiomyocytes. This drug also has a vasodilation effect on vascular smooth muscle, mediated through the opening of adenosine triphosphate-sensitive potassium channels [37]. Despite the whole pool of favorable effects, levosimendan is usually considered as a second-line agent in CS therapy. Based on clinical experience, availability, and cost, dobutamine is generally recommended as a first-line drug. Dobutamine has been shown to significantly increase heart rate, CI, and mixed venous oxygen saturation (SvO_2) in CS, while decreasing both PCWP and lactate levels. Milrinone, a member of PDE inhibitors, was found not to significantly increase HR with a decrease in PCWP and an increase in CI, but no marked increase in SvO_2 or decrease in lactate was noted. In the end, both drugs were associated with arrhythmias and systemic hypotension. However, studies suggest that milrinone and dobutamine showed similar efficacy and safety profiles, but with little difference in side effects. The choice of milrinone or dobutamine as initial inotropic therapy in CS may depend more on the tolerability of adverse events [38]. Dopamine is an endogenous catecholamine, the cardiovascular effects of which are directly dependent on the dose. Small dose (2 μg/kg) cause vasodilation due to stimulation of dopamine D1 receptors of smooth muscles, which dominate in the endothelium of the celiac and renal arteries. In addition, stimulation of D1 receptors causes natriuresis due to inhibition of sodium-potassium ATPase, and due to the acceleration of renal blood flow during stimulation of renal artery receptors. In addition, a decrease in sodium reabsorption in the proximal tubule was also noted, which is especially important in patients with severe HF. At medium doses (2-5 μg/kg/min), dopamine stimulates cardiac β-receptors and vascular sympathetic receptors, causing an inotropic effect. At higher doses (5-15 μg/kg/min), alpha-adrenergic stimulation with peripheral arterial and venous constriction occurs. The effects of dopamine in CS include an increase in HR (+11%), CO (+40%), stroke volume (+30%) and PCWP (+2,4 mm Hg), but at high doses the drug increases systemic vascular resistance [39]. Therefore, dopamine is still better not to use in CS, despite all favorable effects. Dopamine has been shown to be associated with an increase in 28-day mortality compared to norepinephrine. The study [40] included 1679 patients, of which 858 received dopamine as the main line of pressor therapy and 821 — norepinephrine to restore and maintain perfusion pressure. There was no significant difference in mortality at 28 days (52,5% in the dopamine group and 48,5% in the norepinephrine group), but there were more life-threatening cardiac arrhythmias in the dopamine group (207 events (24,1%) vs 102 events (12,4%), p<0,001). A subanalysis showed that dopamine, compared with norepinephrine, was associated with increased mortality at day 28 among 280 patients with CS, but not among patients with septic shock or hypovolemic shock (p=0,03 for CS, p=0,19 for septic shock and p=0,84 for hypovolemic shock). Another meta-analysis on inotropic and pressor support showed [41] that norepinephrine was associated with a lower 28-day mortality rate, as well as a lower risk of arrhythmic events. This superiority of norepinephrine over dopamine is seen regardless of CS caused by CAD. As for vasopressin, it is not recommended for use due to lack of inotropic properties. Therefore, it does not improve the cardiac power index and CI, while norepinephrine increases CI. Therefore, norepinephrine is currently considered the best vasopressor agent, which has such a significant effect as an increase in systemic vascular resistance and maintenance of perfusion pressure at a target level, while dobutamine is the optimal inotropic agent. With regard to mechanical support methods, they should be used as early as possible when refractory to inodilator and vasopressor therapy. Available devices include a intra-aortic balloon counterpulsation (IABP), support devices Impella, Tandem Heart, and venoarterial ECMO (VA-ECMO) (Figure 3). According to a review on mechanical support devices [42], IABP is considered to be one of the best, most commonly used method. The device consists of an inflatable balloon, which is connected to a double-lumen catheter and a pump that helps with counterpulsation. The catheter is placed in the descending aorta, proximal to the renal arteries and distal to the left subclavian artery. The most used area is the femoral artery. IABP provides cardiac support by inflating during diastole with an increase in coronary perfusion with subsequent deflating during systole and creating a vacuum that greatly reduces aortic pressure and reduces LV afterload, synchronizing the device with the patient's electrocardiography. Despite the usability and availability, IABP is associated with a large number of vascular complications, often leading to patient immobilization. The Impella is a pump that unloads the LV by directing blood flow from the LV to the aorta and can provide flow up to >5 L/min, depending on the device used: Impella 2.5 and Impella CP can be rapidly implanted percutaneously in a catheterization laboratory, while the Impella 5.0 requires surgical implantation. Unlike IABP, Impella does not require electrocar-

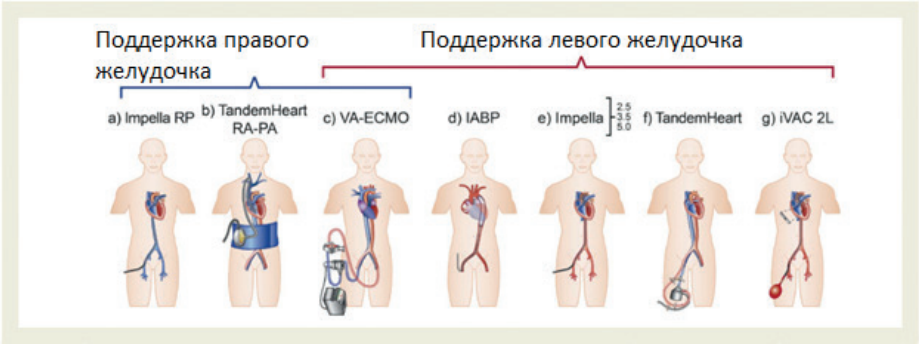

Figure 3. Devices for mechanical LV and RV support ([16], courtesy of the European Heart Journal).

diographic trigger, which contributes to stability even in the presence of tachyarrhythmias or electromechanical dissociation. Although it provides better hemodynamic support than IABP, there is no evidence of improved survival in CS, mainly due to vascular complications and bleeding [43]. VA-ECMO is a portable device that resembles a heart-lung machine. The device has a number of components including a membrane oxygenator, a controller, a heat exchanger, a centrifugal flow pump, a venous inflow cannula, and an arterial outflow cannula. During ECMO, deoxygenated blood from the right atrium (RA) is sent to a membrane oxygenator for oxygenation and then sent to a heat exchanger for warming and then to a controller for pumping back into the arterial system. In patients with RV failure, VA-ECMO can be cannulated from the RA into the pulmonary artery. The most commonly used is peripheral VA-ECMO, which increases left ventricular afterload directly affecting the elevated PCWP, which can ultimately increase pulmonary congestion. Decompression strategies for LV ventilation include additional procedures such as IABP, septostomy, and hybrid circuit. When cardiac recovery precedes lung recovery, an influx of deoxygenated blood into the ascending aorta results in upper body hypoxia, Harlequin syndrome, requiring CO reduction or reconfiguration of the apparatus until lung recovery. The use of VA-ECMO has a significant impact on the quality of life. The study [44] demonstrated that VA-ECMO was associated with a significant improvement in 30-day survival in both groups compared with IABP, and there was no difference in comparison with TandemHeart or Impella. It is worth noting that the idea of combining IABP and VA-ECMO is the best practice. IABP can neutralize the undesirable effects of VA-ECMO, such as a decrease in afterload, as well as an increase in coronary perfusion. With regard to mechanical ventilation, acute respiratory failure with or without the use of mechanical ventilation correlates with higher in-hospital mortality, and therefore a patient with CS should be intubated sooner. This is due to the fact that an additional energy consumption to maintain a high respiratory rate, which is not able to compensate for ventilation-perfusion mismatch with metabolic acidosis, can lead to CS progression. Particular care should be taken to ventilate the lungs under positive pressure in CS with RV dysfunction, since high levels of positive end-expiratory pressure may exacerbate RV failure [45]. Also, with the development of cardiorenal syndrome, renal replacement therapy should be performed. Continuous venovenous hemodiafiltration is recommended for severe acute kidney injury (creatinine $\geqslant$2 of the baseline and urine output <0,5 ml/kg/h for $\geqslant$12 h) or severe hypervolemia, electrolyte disbalance or pronounced acid-base balance changes [46].

Conclusion

CS is a complex multifactorial clinical syndrome with extremely high mortality, with rapid development of multiple organ failure and death. There are few clinical and registry studies in this area, the results of which remain not entirely satisfactory. Future multicenter trials should consider the timely therapy in an appropriately selected cohort of patients with CS [4]. Educational activities are also needed to increase the awareness of specialists about modern principles of therapy for patients with complicated coronary and non-coronary myocardial diseases.

Relationships and Activities: none.

References

1. Laslett L, Alagona P, Clark B, et al. The worldwide environment of cardiovascular disease: Prevalence, diagnosis, therapy, and policy issues. Journal of the American College of Cardiology. 2012;60(25):1-49. doi:10.1016/j.jacc.2012.11.002.
2. Bauersachs R, Zeymer U, Brière J, et al. Burden of Coronary Artery Disease and Peripheral Artery Disease: A Literature Review. Cardiovasc Therapy. 2019;2019:26:e8295054. doi:10.1155/2019/8295054.
3. Malakar A, Choudhury D, Halder B, et al. A review on coronary artery disease, its risk factors, and therapeutics. Journal of Cellular Physiology. 2019;234(10):16812-23. doi:10.1002/jcp.28350.
4. Chioncel O, Parissis J, Mebazaa A, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock — a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2020;22(8):1315-41. doi:10.1002/ejhf.1922.
5. Babaev A, Frederick PD, Pasta DJ, et al. Trends in Management and Outcomes of Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock. JAMA. 2005;294(4):448-54. doi:10.1001/jama.294.4.448.
6. Shah M, Patnaik S, Patel B, et al. Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. Clinical Research in Cardiology. 2018;107(4):287-303. doi:10.1007/s00392-017-1182-2.
7. Berg D, Bohula E, Diepen S, et al. Epidemiology of Shock in Contemporary Cardiac Intensive Care Units: Data from the Critical Care Cardiology Trials Network Registry. Circ Cardiovasc Qual Outcomes. 2019;12(3):e005618. doi:10.1161/CIRCOUTCOMES.119.005618.
8. Wan M, Qian S, Huang Y, et al. Drug Discovery for Coronary Artery Disease. In: Wang, M. (eds) Coronary Artery Disease: Therapeutics and Drug Discovery. Advances in Experimental Medicine and Biology. 2020;1177:297-339; Springer, Singapore. doi:10.1007/978-981-15-2517-9_8.
9. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: Epidemiological update. Eur Heart J. 2014;35(42):2950-9. doi:10.1093/eurheartj/ehu299.
10. Drapkina OM, Shalnova SA, Kutsenko VA, et al. Myocardial infarction in the population of some Russian regions and its prognostic value. Russian Journal of Cardiology. 2022;27(6):4952. (In Russ.) doi:10.15829/1560-4071-2022-4952.
11. Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. The Lancet. 2017;389(10065):197-210. doi:10.1016/S0140-6736(16)30677-8.
12. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. European Heart Journal. 2019;40(3):237-69. doi:10.1093/eurheartj/ehy462.
13. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal. 2018;39(2):119-77. doi:10.1093/eurheartj/ehx393.
14. Velagaleti RS, Pencina MJ, Murabito JM. Long-term trends in the incidence of heart failure after myocardial infarction. Circulation. 2008;118(20):2057-62. doi:10.1161/CIRCULATIONAHA.108.784215.
15. Boytsov SA, Akchurin RS, Pevzner DV, et al. Cardiogenic shock — the current state of the problem. Russian Journal of Cardiology. 2019;(10):126-36. (In Russ.) doi:10.15829/1560-4071-2019-10-126-136.
16. Thiele H, Ohman EM, de Waha-Thiele S, et al. Management of cardiogenic shock complicating myocardial infarction: An update 2019. European Heart Journal. 2019;40(32):2671-83. doi:10.1093/eurheartj/ehz363.
17. Furer A, Wessler J, Burkhoff D. Hemodynamics of Cardiogenic Shock. Interventional Cardiology Clinics. 2017;6(3):359-71. doi:10.1016/j.iccl.2017.03.006.
18. Baran D, Grines L, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheterization and Cardiovascular Interventions. 2019;94(1):29-37. doi:10.1002/ccd.28329.
19. Lysenko MA, Ketskalo MV. Moscow health care system in the prism of global leadership: Collection of reports of the II scientific and methodological forum of health care organizers with international participation, Moscow, December 10-11, 2020. Moscow: State Budgetary Institution of the City of Moscow "Research Institute of Health Organization and Medical Management of the Department of Health of the City of Moscow", 2020. p. 146. (In Russ.) ISBN: 978-5-907404-04-5.
20. Arbolishvili GN, Lysenko MA, Lysenko SV. Cardiac care unit department. History, evolution, innovations, new challenges. Moscow medicine. 2020;3(37):54-66. (In Russ.) EDN BASZWJ.
21. Thiele H, Ohman E, Desch S, et al. Management of cardiogenic shock. European Heart Journal. 2015;36(20):1223-30. doi:10.1093/eurheartj/ehv051.
22. De Backer D, Creteur J, Dubois M, et al. Microvascular alterations in patients with acute severe heart failure and cardiogenic shock. American Heart Journal. 2004;147(1):91-9. doi:10.1016/j.ahj.2003.07.006.
23. Stenberg T, Kildal, Sanden E, et al. The acute phase of experimental cardiogenic shock is counteracted by microcirculatory and mitochondrial adaptations. PLoS One. 2014;9(9):e105213. doi:10.1371/journal.pone.0105213.
24. Thiele H, Ibrahim A, Sandri M, et al. PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock. New England Journal of Medicine. 2017;377(25):2419-32. doi:10.1056/nejmoa1710261.
25. Jung C. Assessment of microcirculation in cardiogenic shock. Current Opinion in Critical Care. 2019;25(4):410-6. doi:10.1097/MCC.0000000000000630.
26. Kohsaka S, Menon V, Lowe A, et al. Systemic Inflammatory Response Syndrome After Acute Myocardial Infarction Complicated by Cardiogenic Shock. Arch Intern Med. 2005;165(14):1643-50. doi:10.1001/archinte.165.14.1643.
27. Prondzinsky R, Unverzagt S, Lemm H, et al. Interleukin-6, -7, -8 and -10 predict outcome in acute myocardial infarction complicated by cardiogenic shock. Clinical Research in Cardiology. 2012;101(5):375-84. doi:10.1007/s00392-011-0403-3.
28. Parenica J, Jarkovsky J, Malaska J, et al. Infectious complications and immune/inflammatory response in cardiogenic shock patients: A prospective observational study. Shock. 2017;47(2):165-74. doi:10.1097/SHK.0000000000000756.
29. Hochman JS, Sleeper LA, Godfrey E, et al. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock: An international randomized trial of emergency PTCA/CABG-trial design. American Heart Journal. 1999;137(2):313-21. doi:10.1053/hj.1999.v137.95352.
30. Reynolds HR, Anand SK, Fox JM, et al. Restrictive physiology in cardiogenic shock: Observations from echocardiography. American Heart Journal. 2006;151(4):890.e9-890.e15. doi:10.1016/j.ahj.2005.08.020.
31. Jacobs AK, Leopold JA, Bates E, et al. Cardiogenic shock caused by right ventricular infarction: A report from the SHOCK registry. Journal American College Cardiology. 2003;41(8):1273-9. doi:10.1016/S0735-1097(03)00120-7.
32. Collet JP, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021;42(14):1289-367. doi:10.1093/eurheartj/ehaa575.
33. Henry TD, Tomey MI, Tamis-Holland JE, et al. Invasive Management of Acute Myocardial Infarction Complicated by Cardiogenic Shock A Scientific Statement From the American Heart Association. Circulation. 2021;143(15):e815-e829. doi:10.1161/CIR.0000000000000959.

34. Wijns W, Naber CK. Reperfusion delay in patients with high-risk ST-segment elevation myocardial infarction: Every minute counts, much more than suspected. European Heart Journal. 2018;39(13):1075-7. doi:10.1093/eurheartj/ehy069.
35. Levy B, Buzon J, Kimmoun A. Inotropes and vasopressors use in cardiogenic shock: When, which and how much? Current Opinion in Critical Care. 2019;25(4):384-90. doi:10.1097/MCC.0000000000000632.
36. Nativi-Nicolau J, Selzman CH, Fang JC, Stehlik J. Pharmacologic therapies for acute cardiogenic shock. Current Opinion in Cardiology. 2014;29(3):250-7. doi:10.1097/HCO.0000000000000057.
37. Papp Z, Édes I, Fruhwald S, et al. Levosimendan: Molecular mechanisms and clinical implications: Consensus of experts on the mechanisms of action of levosimendan. International Journal of Cardiology. 2012;159(2):82-7. doi:10.1016/j.ijcard.2011.07.022.
38. Lewis TC, Aberle C, Altshuler D, et al. Comparative Effectiveness and Safety Between Milrinone or Dobutamine as Initial Inotrope Therapy in Cardiogenic Shock. Journal of Cardiovascular Pharmacology and Therapeutics. 2019;24(2):130-8. doi:10.1177/1074248418797357.
39. Westfall TC, Westfall DP. Adrenergic agonists and antagonists. In: Brunton L. L., & Chabner.B.A., & Knollmann B. C. Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 12e. McGraw Hill. ISBN 978-0-07-162442-8.
40. De Backer D, Biston P, Devriendt J, et al. SOAP II Investigators. Comparison of dopamine and norepinephrine in the treatment of shock. New England Journal of Medicine. 2010;362(9):779-89. doi:10.1056/NEJMoa0907118.
41. Karami M, Hemradj VV, Ouweneel DM, et al. Vasopressors and inotropes in acute myocardial infarction related cardiogenic shock: A systematic review and meta-analysis. Journal of Clinical Medicine. 2020;9(7):1-12. doi:10.3390/jcm9072051.
42. Ramteke H, Walke V. Management of advanced stage heart failures by mechanical circulatory supportive devices: current technologies and future perspectives. Life Research. 2022;5(3):2.
43. Schrage B, Ibrahim K, Loehn T, et al. Impella support for acute myocardial infarction complicated by cardiogenic shock: Matched-pair iabp-shock II trial 30-day mortality analysis. Circulation. 2019;139(10):1249-58. doi:10.1161/CIRCULATIONAHA.118.036614.
44. Ouweneel DM, Schotborgh JV, Limpens J. Extracorporeal life support during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis. Intensive Care Medicine. 2016;42(12):1922-34. doi:10.1007/s00134-016-4536-8.
45. Vallabhajosyula S, Kashani K, Dunlay SM. Acute respiratory failure and mechanical ventilation in cardiogenic shock complicating acute myocardial infarction in the USA, 2000-2014. Ann Intensive Care. 2019;9(1):96. doi:10.1186/s13613-019-0571-2.
46. Ronco C, Bellomo R. Dialysis in intensive care unit patients with acute kidney injury: Continuous therapy is superior. Clinical Journal of the American Society of Nephrology. 2007;2(3):597-600. doi:10.2215/CJN.00430107.