CARDIOGENIC SHOCK – NOVELTY AND EMERGING THERAPEUTIC CONCEPTS

I. Petrov, Z. Stankov, S. Vasilev

Department of Cardiology and Angiology, UMHAT Acibadem City Clinic – Cardiovascular Center, Sofia University – Sofia

Abstract. The cardiogenic shock is a state of low cardiac output, primarily due to cardiac dysfunction, which leads to severe organ hypoperfusion with tissue hypoxia and increased lactate levels. It presents a severe complication with a prevalence of around 15% of all forms of shock and 2-5% of the cardiogenic shock is a complications of acute heart failure. Despite the diverse etiology of the cardiogenic shock, up to 80% of the cases are due to acute myocardial infarction. The ischemia, leads to dysfunction of the myocardium cells, which causes a decline in the blood pressure and subsequent tissue hypoperfusion. The most important part is to start the treatment regime as soon as possible in the pre-shock stage. The treatment of refractory cardiogenic shock is complex, as it contains an intravenous therapy with inotropes/vasopressors and mechanical circulatory support (MCS). The MCS devices are supposed to reduce the workload of the heart and the oxygen need of the myocardial cells and in the same time to maintain an adequate coronary and systemic perfusion. There are different MCS devices like IABP, Impella, Tandem Heart, V-A ECMO. The aim of this review article is to present the new trends in the treatment approach to cardiogenic shock and to bring clarity in the treatment regimes, based on the latest studies and guidelines.

Key words: cardiogenic shock, Impella, IABP, inotropes, vasopressors, complications, safety

Address for correspondence: Strahil Vasilev, Acibadem City Clinic, Cardiovascular Center, Sofia University, Sofia, Bulgaria, „Okolovrysten pъt” № 127, 1700 Sofia, Bulgaria, tel. number: +359 885879040, e-mail: strahilvasilevhealth@gmail.com
Въведение

Кардиогенният шок (КШ) е тежко усложнение с висока смъртност (до 50%), която остава не променена през последните 10 години, въпреки медикаментозни и технологични нововъведения. Независимо, че вътреболничната смъртност се е подобрила, дългосрочната смъртност при пациентите с КШ остава висока. Честотата на КШ е около 15%, като 2-5% са случаите на КШ, възникнал като усложнение на остра сърдечна недостатъчност. Общата честота на остър миокарден инфаркт (ОМИ) и КШ е 5 до 10% с по-висока честота при ОМИ със ST-елевация в сравнение с ОМИ без ST-елевация. Според информацията от последните публикувани регистри, лекуваните пациенти с КШ в САЩ са 40 000-50 000, а в Европа 60 000-70 000 годишно. Поради честотата и високия процент смъртност, КШ представлява сериозно предизвикателство пред медицинските специалисти [1].

Според клиничното ръководство на Европейското дружество по кардиология, КШ е състояние на нисък сърдечен дебит, поради сърдечна дисфункция, което води до тежка органна хипоперфузия с тъканна хипоксия и повишен серумен лактат [1]. Клинично, това се изразява в рефрактерна хипотония (систолно налягане < 90 mm Hg) с данни за органна хипоперфузия, налагаща медикаментозна терапия или механична поддръжка на хемодинамиката (MCS). Тази дефиниция на КШ е базирана на SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) и IABP-SHOCK II (Intra-aortic Balloon Pump in Cardiogenic Shock II) проучванията [2] (табл. 1).

Етиологията на КШ е разнообразна, като до 80% от случаите на КШ възникват като усложнение на остър миокарден инфаркт. Други причини могат да бъдат екзакзербирана хронична сърдечна недостатъчност (до 30%), клапни пороци (6%), кардиомиопатия или остър миокардит [2, 3]. Важно е да се отбележи, че КШ е водеща причина за смъртност при миокарден инфаркт [2]. Клиничните проучвания доказват, че до 80% от леталните случаи на КШ са в рамките на първите 30 до 60 дни от началото на шоковото състояние, а също така и половината от леталните случаи в болница са в първите 24 часа. Следователно е важно да се отбележи, че рискът от смърт при КШ е време-зависим [1].
Патофизиология и стадиране на кардиогенния шок

Патофизиологията на кардиогенния шок е комплексна, като най-важното е, че исхемията води до депресия на миокардния контрактилитет, което от своя страна води до порочен кръг на редуциран сърдечен индекс и ниско артериално налягане, до кръвопотекащо усилване на коронарната исхемия. Всичко това причинява тежка тъканна хипоперфузия и смърт [3]. Класическият патогенетичен механизъм за развитие на КШ представлява загуба на миокардна тъкан след ОМИ и вторично възникване на шока. В допълнение на загубата на миокард, развитието на механични усложнения (руптура на септума и свободната стена на ЛК, ЛК аневризма, руптура на папиларен мускул, остра митрална регургитация, остра настъпил перикарден излив с тампонада) често водят до тежка лява и дясна камерна дисфункция. Като следствие на нарушената камерна функция ударният обем (УО) намалява и води до остра редукция на артериалното налягане (АН) и повишаване на теледиастолния обем в ЛК. В опит да се компенсират ниските АН се наблюдава компенсаторна вазоконстрикция (което включва веновеноконстрикция, водеща към повишена венозна възпрепятстване на съдовете, като тяхното пропускливост, както и усилване на коронарната перфузия). Критерийт за диагноза на кардиогенен шок са клинични признаки на хипотрахическая, олигурия, ментални нарушения, ниско пулмонално налягане, повишен лактат, повишен креатинин и метаболитна ацидоза [1]. Многоетапно се използва биомаркери в допълнение към забележките, които могат да бъдат индикатори за прогресия на КШ. Нарушеният баланс между ангиопоиетин-1 и ангиопоиетин-2 показва нарушиена микроциркулация и повишен пропускливост на съдовете, като тяхното

<table>
<thead>
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<th>Таблица 1. Дефиниция за КШ според проучванията / Table 1. CS definition according to studies</th>
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<tbody>
<tr>
<td><strong>SHOCK [6]</strong></td>
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<tr>
<td>SBP &lt; 90 mm Hg za &gt; 30 min or the need of support in order to achieve SBP &gt; 90 mm Hg</td>
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<tr>
<td>Organ hypoperfusion (urine output &lt; 30 ml/h or cool extremities and heart rate &gt; 60 b.p.m.)</td>
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<td>Haemodynamic criteria:</td>
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<tr>
<td>CI of &lt; 2.2 l/min/m² and PCWP &gt; 15 mm Hg</td>
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**Pathophysiology and staging of cardiogenic shock**

The pathophysiology of cardiogenic shock is complex. Most importantly, ischemia leads to depression of the myocardial contractility, which in turn leads to a vicious cycle of reduced cardiac index and low arterial pressure, further amplifying coronary ischemia. All of this, causes severe tissue hypoperfusion and death [3]. The classic pathogenic mechanism for the development of CS, is the loss of myocardial tissue after AMI and the secondary occurrence of shock. In addition to myocardial loss, the development of mechanical complications (septal and LV free wall rupture, LV aneurysm, papillary muscle rupture, acute mitral regurgitation, acute onset pericardial effusion with tamponade) often leads to severe left and right ventricular dysfunction. As a consequence of impaired ventricular function, the stroke volume (SV) decreases and leads to an acute reduction in arterial pressure (BP) and an increase in LV end-diastolic volume. In an attempt to compensate for the low BP, compensatory vasoconstriction (involving constriction of the veins, which in turn leads to increased pulmonary pressure) occurs. The criteria for the diagnosis of cardiogenic shock are clinical signs of hypoperfusion, oliguria, mental disorders, low pulse pressure, elevated lactate, elevated creatinine, and metabolic acidosis [1]. Multiple other biomarkers, in addition to serum lactate, may be indicators of the progression of CS. The disturbed balance between angiopoietin-1 and angiopoietin-2 indicates impaired microcirculation and increased vascular permeability,
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10 проследяване в хода на КШ е показало проспективна връзка със смъртността [3]. Микроциркулаторните промени при КШ могат да бъдат измерени и със сублингвални образни тестове, но клиничната стойност на тези нови биомаркери и образни тестове не е напълно доказана [3].

В клиничната практика КШ обхваща няколко етапа на развитие – от прешок до екстремен шок, при който пациентът е в сърдечен арест дори и при налична кардиопулмонална ресусцитация и MCS (фиг. 1).

Разпознаването на КШ в неговия прешок е важно, тъй като е свързано с по-ниска смъртност и възможност да се предотврати прогресията до крайните стадии на шока, при адекватно лечение [1, 2, 3]. Най-добрата скорова система, която се използва е ORBI (Observatoire Regional Breton sur l’Infarctus) скорът, чрез който се оценява рискът от развитие на КШ. Той се базира на 11 клинични показатели налични в катетеризационната лаборатория, като позволява да бъде независим предиктор за развитието на КШ по време и след първична PCI (нисък риск 0-7 точки, нисък към умерен риск 8-10 точки, среден към висок риск 11-12 точки висок риск > 13 точки). Както вече споменахме, най-честата причина за кардиогенен шок е остър миокарден инфаркт, по-често при миокарден инфаркт с ST-елевация. Такива пациенти имат необратима загуба на

Фиг. 1. Петте категории според пирамидата на КШ. Етап A – пациенти, при които има риск от развитие на КШ, но в момента на оценка нямат симптоми на шок. Етап B – пациенти с клинични данни за хипотония и/или тахикардия, без наличие на хипоперфузия. Етап C – пациенти в етап на класически КШ, придружен от органна хипоперфузия. Етап D – рефрактерен КШ с данни за влошаване и лош отговор към лечението. Етап E – пациенти, които са в сърдечен арест, дори и при извършването на CPR и MCS

Fig. 1. The five categories according to the CS pyramid. Stage A – patients who are at risk of developing CS, but have no symptoms of shock at the time of assessment. Stage B – patients with clinical evidence of hypotension and/or tachycardia without the presence of hypoperfusion. Stage C – patients in the classic CS stage, accompanied by organ hypoperfusion. Stage D – refractory CS, with evidence of worsening and poor response to treatment. Stage E – patients who are in cardiac arrest, even with CPR and MCS performed
миокардна тъкан, което трябва да бъдат лекувани в специализирани центрове с налична катетеризация, лаборатория, операционни зали, интензивно отделение и възможност за селекция на устройствата за MCS [5]. Ранната идентификация и лечение на причината за шоковото състояние е свързана с по-добро прогноза. [1] Според SHOCK проучването, най-важното в лечебната стратегия при пациенти с кардиогенен шок и миокарден инфаркт е ранната реваскуларизация [6]. Проучването не констатира разлика в 30 дневната смъртност между пациентите, при които е приложена ранна реваскуларизация и тези, при които е използвана само медикаментозна терапия. Независимо от това, SHOCK проучването и редица други регистри, показват статистически значимо понижаване на смъртността на 6ти месец и 1 година при пациенти подложени на ранна реваскуларизация [7]. Кардиохирургическото лечение с имплантиране на аортокоронален байпас има много малко приложение в случаите на кардиогенен шок и според проучвания, то е използвано при под 5% от случаите [7]. Според последните препоръки на Европейското дружество по кардиология първичната перкутана интервенция (pPCI) при едноклонова коронарна болест е клас I, препоръка C [8]. Повечето пациенти с миокарден инфаркт, усложнен с кардиогенен шок са с две или триклонова коронарна болест. В тези случаи Европейското дружество по кардиология препоръчва да се извършва ранна реваскуларизация на водещата лезия и последваща планирана (в кратки срокове, включително в рамките на същата хоспитализация) реваскуларизация на другите лезии [3, 7].

**MEDICAL THERAPY**

Intravenous infusion of fluids, vasopressors, and inotropes is key in initiating hospital treatment of patients with CS. Although one-third of patients in shock are euvolemic, they respond with an increase in stroke volume when fluids are infused. Vasopressors adequately maintain mean arterial pressure, thereby achieving adequate tissue blood supply in refractory hypotension. [1, 7] In the absence of evidence of stasis, intravenous infusion of sodium chloride 0.9% or Ringer 250 ml for a period of 15 to 30 minutes is the

### Treatment

Patients with CSH should be treated in specialized centers with an available catheterization laboratory, operating rooms, an intensive care unit, and the ability to select devices for MCS [5]. Early identification and treatment of the cause of shock is associated with a better prognosis. According to the SHOCK study, [1] the most important treatment strategy for patients with cardiogenic shock and myocardial infarction is early revascularization [6]. The study found no difference in 30-day mortality between patients who received early revascularization and those who received medical therapy alone. Nevertheless, the SHOCK trial and a number of other registries have shown statistically significant reductions in mortality at 6 months and 1 year in patients undergoing early revascularization [7]. Cardiac surgery with implantation of an aortocoronary bypass graft has very little use in cases of cardiogenic shock and, according to studies, it has been used in less than 5% of cases [7]. According to the latest recommendations of the European Society of Cardiology, primary percutaneous intervention (pPCI) for single-vessel coronary artery disease is class I, recommendation C [8]. Most patients with myocardial infarction complicated by cardiogenic shock have two- or three-vessel coronary artery disease. In these cases, the European Society of Cardiology recommends early revascularization of the leading lesion and subsequent planned (within a short time frame, including during the same hospitalization) revascularization of the other lesions [3, 7].
in is the first choice of therapy, and this infusion also plays the role of a therapeutic test, i.e., it gives us information whether, it is hypovolemic shock or the result of severe LV dysfunction. Although a large proportion of patients with CS require therapy with vasopressors and/or inotropes, it is generally recommended to use them in minimal doses and to avoid them in the presence of adequate tissue perfusion. They improve hemodynamics, but at the expense of increased myocardial oxygen demand and high arrhythmogenicity [1]. Inotropes are a class of drugs that improve cardiac contractile function and can be divided into 3 main groups – adrenergic agonists, phosphodiesterase III inhibitors and calcium sensitizers. Adrenergic agonists exert their positive inotropic effect by binding to beta-adrenergic receptors. They increase the HR, BP and EF of the heart. Dopamine, dobutamine, norepinephrine, and epinephrine are members of this group, and they can be further classified based on their systemic vascular effect (inopressors or inodilators) [5, 7]. According to the European recommendations, dopamine administration is class IIA and norepinephrine is class IIb, whereas other studies in patients with cardiogenic shock have shown that norepinephrine is associated with fewer arrhythmogenic effects and better survival, making it a suitable first choice in patients with low arterial pressure [3]. Dobutamine acts on 4 receptors, dopaminergic type 1 and type 2 receptors and adrenergic alpha 1 and beta 1 receptors. In low doses (< 2.5 μg/kg/min) it leads to vasodilation of coronary, renal and splanchnic arteries. In medium doses (3-5 μg/kg/min) it leads to significant inotropic and chronotropic effects, acting on beta-1 receptors of cardiomyocytes. At high doses (> 5 μg/kg/min), it leads to vasoconstriction, acting on alpha 1 adrenergic receptors, which can lead to severe hypertension and induce tachyarrhythmias. Dobutamine is a beta-adrenergic agonist with strong effects on beta 1 receptors and weaker effects on beta 2 and alpha 1 adrenergic receptors. The half-life of dobutamine is 2 min, eliminating the need for dose adjustment in patients with renal failure. In low doses (< 5 μg/kg/min), it increases OA and decreases afterload by vasodilating peripheral vessels. At doses (> 5 μg/kg/min), causes vasoconstriction by its action on alpha 1 adrenoceptors. From the group of phosphodiesterase III inhibitors is the drug – Milrinone. Phosphodiesterase III enzyme is responsible for the degradation of cyclic adenosine monophos-
Mechanical circulatory support (MCS) is used to improve hemodynamics, reduce the need for catecholamine administration, and improve the prognosis of patients with CS. The main goal is to reduce cardiac work and myocardial oxygen demand while maintaining adequate systemic and coronary perfusion. Percutaneous mechanical circulatory support devices can be classified as follows: left ventricle to aorta (IABP) configuration devices, left atrium to systemic circulation (Tandem Heart) configurations.
The most widely used device for mechanical support of hemodynamics is the intra-aortic balloon pump (IABP), popularly known as the balloon counterpulsator, which was first introduced in the early 1960s. Its configuration is left ventricle-aorta. For years, the IABP was used in patients with CS without evidence from randomized trials of its potential benefits. This has changed since the publication of the Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial, which randomized 600 patients with CS occurring as a complication of myocardial infarction and treated by early revascularization with or without IABP [7]. According to IABP-SHOCK II, there was no difference in mortality between the IABP group and the group without it. This was demonstrated at patient follow-up at day 30, 6 months, and 12 months [2, 11]. The European Society’s clinical guidelines issued a class IIIB recommendation for the use of passive devices for mechanical hemodynamic support after the only adequate, randomized trial failed to demonstrate the benefits of IABP use. Following the neutral results of IABP-SHOCK II and the new recommendations of the European Society of Cardiology, the use of IABPs, in recent years, has fallen by up to 30% in the US, 25% in England and by up to 18% in Germany, at the expense of the increased use of active mechanical circulatory support devices, such as V-A ECMO and Impella/TandemHeart [7].

A new horizon in the treatment of CS was opened with the advent of new percutaneous mechanical hemodynamic support devices, such as the Impel-
The Impella device is an axial pump that is percutaneously introduced through the femoral artery, passes retrogradely through the aortic valve into the left ventricle, where it takes blood and ejects it into the ascending aorta. The Impella-2.5 can maintain a stroke volume of 2.5-4 liters per minute. There is also a larger diameter, higher flow device, the Impella-5.0, which can maintain a stroke volume of 5 liters, but requires a 22-french introducer for its implantation [2]. These dives replace the function of the left ventricle by mechanically emptying it, potentially relieving the strain and aiding myocardial recovery [2, 12]. Prolonged emptying of the left ventricle, independent of cardiac function, results in the loss of normal isovolumetric periods, which is clearly shown in the pressure-volume curve (Figure 2). The curve changes its morphology from trapezoidal to triangular. The mechanism of Impella is precisely such that it acts independently of cardiac function, and as the rate of blood pumping increases, the maximum left ventricular pressure is reduced and a decrease in the area of the curve and myocardial oxygen demand is observed. At the same time, aortic pressure increases, resulting in a greater dissociation between aortic pressure (Ao) and left ventricular pressure (LV-Ao dissociation). These effects lead to a decrease in left atrial and pulmonary pressures, so Impella devices are contraindicated in patients with high-grade aortic stenosis or aortic insufficiency, mechanical aortic valve disease, and severe peripheral arterial disease [2]. The effect of Impella has been demonstrated in several trials, which have demonstrated the efficacy and safety of Impella-2.5 in high-risk percutaneous coronary interventions and in hemodynamically unstable ST-elevation myocardial infarction patients [13-15]. According to a pilot, non-randomized study, Impella-2.5 implantation is safe and results in an increase in stroke volume and a decrease in end-diastolic pressure. Furthermore, a marked recovery in left ventricular function was observed, suggesting a possible positive effect on left ventricular remodeling after myocardial infarction. Impella-2.5 has been shown to be associated with improved intracoronary perfusion pressure, coronary reserve and microvascular resistance [16]. According to the multicenter Impella-EUROSHOCK registry, Impella-2.5 implantation in CS patients is a feasible and safe method that results in a reduction of lactate levels, which in turn, suggests better organ perfusion. Impella device implantation represents a rapid method for establishing hemodynamic support, and it can be used in...
The Tandem Heart is a device connecting the left atrium to the arterial system. It cannulates the femoral vein, then passes through the atrial septum to reach oxygenated blood in the left atrium, which is aspirated and pumped into one or both femoral arteries at a rate of 4.0 liters/min. The effect is to lower pulmonary pressure multiplied by stroke volume (normal CPO values are between 4-8 L/min) [18]. One of the large studies, PROTECT II, proved that Impella leads to very good periprocedural hemodynamic stability with improvement in mean arterial pressure and CPO. Considering the key place of CPO in the hemodynamic evaluation and prognosis of patients with CS and the hemodynamic performance of Impella, at this stage, this device represents the most optimal choice for percutaneous mechanical support. The American Heart Association gives a class IIB recommendation for the use of Impella devices [2, 19]. Another retrospective analysis compared 237 patients in the CS treated with Impella and 237 patients from the IABP-SHOCK II registry. This analysis, failed to demonstrate a lower mortality rate in patients with Impella devices, and even showed that these patients had significantly more complications. [20] Despite the widespread use of percutaneous devices for mechanical hemodynamic support, a number of studies have shown a high mortality rate of ≈50%, in CS patients over the past 2 decades [11, 12, 18, 21]. The Detroit Cardiogenic Shock Initiative trial proposes a standardized protocol that emphasizes early implantation of Impella (‘prophylactically’), even before the incorporation of vasopressors/inotropes and before percutaneous coronary intervention. This approach has demonstrated a high success rate, low mortality, and 76% survival in patients with CS following myocardial infarction [22] (Table 2).

The Tandem Heart is a device connecting the left atrium to the arterial system. It cannulates the femoral vein, then passes through the atrial septum to reach oxygenated blood in the left atrium, which is aspirated and pumped into one or both femoral arteries at a rate of 4.0 liters/min. The effect is to lower pulmonary pressures and left ventricular preload, resulting in improved perfusion of peripheral tissues. The Tandem Heart is most commonly used for a short period of time, a few hours to a maximum of 14 days [23]. A randomized tri-
Fig. 2. The effects of mechanical assist devices on the pressure-volume curve: 1 – Normal pressure-volume curve under physiological conditions, 2 – IABP effect, 3 – Impella effect. MC – mitral valve, AC – aortic valve, IABP – intra-aortic balloon pump, IOP – stroke volume, LV – left ventricle.

Table 2. Data for the effects of the mechanical circulatory support

<table>
<thead>
<tr>
<th>Study/Register</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Randomized study (n = 600)</td>
<td>No difference in mortality at 30 days, 6 and 12 months</td>
</tr>
<tr>
<td>IABP versus Medical therapy</td>
<td></td>
</tr>
<tr>
<td>Protect II Trial (2012) [19]</td>
<td>IABP versus Impella</td>
</tr>
<tr>
<td>Randomized clinical investigation (n = 448)</td>
<td>Impella shows greater CPO</td>
</tr>
<tr>
<td>IMPRESS in severe shock (2021) [21]</td>
<td>IABP versus Impella</td>
</tr>
<tr>
<td>Randomized clinical investigation (n = 48)</td>
<td>Impella has fewer complications at the 90-th day of the follow-up</td>
</tr>
<tr>
<td>IMPRESS in severe shock (2021) [21]</td>
<td>No difference in the mortality rate for the 5-years follow-up</td>
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CPO – cardiac power output, IABP – intra-aortic balloon pump, IMPRESS – mechanical circulatory support
In 2005 showed that patients in the CS complicated by myocardial infarction showed improvement in CPO with Tandem Heart implantation. Tandem Heart patients also had an increase in MAP from 71 to 82 mm Hg, and a decreased mean pulmonary pressure from 27 to 17 mm Hg. Most studies made no mention of device dysfunction and severe complications. There have been no cases of hemolysis or device-associated thromboembolic events [24]. Tandem Heart implantation has some significant limitations in terms of its mass applicability, due to the need for specialized operator skills for transseptal puncture and the time from the time of onset of shock to insertion, which in this case would be longer [2].

VA-ECMO is another alternative for CS patients, and involves draining blood from the venous system, oxygenating it through an external oxygenator, and returning the already oxygenated blood to the arterial system via a centrifugal pump. Implantation of VA-ECMO, can be done centrally by cannulation of the right atrium and aorta or peripherally by cannulation of the femoral artery or vein. Although VA-ECMO lowers left ventricular preload, the device also results in increased ventricular wall stress due to retrograde blood flow through the femoral artery. Other potential complications include a high risk of bleeding, changes in blood coagulation with up to a 10% likelihood of stroke [23]. The advantages of VA-ECMO over other devices are its high flow rate that maintains all circulation, even during resuscitation, its ability to provide complete oxygenation of blood, and its combined support of both left and right ventricles. The indications for the use of VA-ECMO are varied, and the device can be implanted in both LV dysfunctions after cardiotomy and in severe CS. Studies and data on VA-ECMO are scarce. A recent meta-analysis including prospective and retrospective cohort studies showed a reduction in CV mortality in patients treated with VA-ECMO. In cases of cardiac arrest, there was a significant increase in 30-day survival, which may be due, precisely, to its advantages of whole-body circulatory support and complete blood oxygenation. The survival rate of patients in whom VA-ECMO was used was 39%, with European STEMI recommendations giving it a class IIb class in patients with refractory CS [25, 26].
Complications and their management

Complications associated with percutaneous mechanical hemodynamic support devices can be serious and life-threatening. They can be divided into complications related to the device, its implantation, organ function or anticoagulation. The complications that can occur are infections, hemolysis, ischemia or bleeding, which is the most common complication [9]. Despite the most common complications that are characteristic of all types of devices, there are also complications that are specific to each of them. For example, cases of hemolysis are most common with the Impella, while air embolism and cardiac tamponade are specific to and most common with the Tandem Heart [9]. According to the cited retrospective analysis comparing the Impella to patients from the IABP-SHOCK II registry, bleeding and peripheral vascular complications were seen more frequently with the Impella [20]. A 2014 retrospective study of 47 patients with an Impella device implanted showed complications in 14 of the patients, with the most common complication being a malfunctioning device due to kinking, and only 1 patient had upper gastrointestinal bleeding, which was resolved by endoscopic coagulation. Regardless of the complications present, they did not lead to lethal outcomes in any of the patients [27]. VA-ECMO results in retrograde return of blood to the aorta, leading to an increase in LV afterload and end-diastolic pressure. This effect can induce the development of pulmonary edema and myocardial ischemia. The combination of VA-ECMO and IABP (which ablates LV) leads to better outcomes and lower mortality.

Antithrombotic therapy

Since bleeding is a major complication of the use of devices for mechanical support of hemodynamics, refinement of anticoagulant therapy is a key point in treatment. The balance between bleeding complications and thrombosis complications is extremely challenging, which is closely related to mortality. Up to 80% of VA-ECMO patients have device-associated bleeding that requires blood transfusion and 16% develop intracranial hemorrhage. Anticoagulation therapy with unfractionated heparin is the classic approach because of its short half-life, rapid onset and end of effect, low cost, and widespread use [9, 28]. Monitoring therapy with unfractionated heparin is also a difficult task, with the preferred methods being the activated partial
termoblokirovanevo vreme (aPTT), koeto e shiroko
izpolzvano metod ili Xa-analiz, koeto predstavlya-
va zlaten standard za monitoriziranje na terapija,
no ne e shiroko raspredoston. Niskomolekulyarni-
te heparini i kumarinovite antikoagulanti ne trebva
da se prilagat v tizii salec za tehnii dalj
polozhitelny i renalna ekscrcija [9, 29]. V konteksta
na heparin-induzirana tromboiitiopleniya moje da
se pristxpli k druga strategiya s izpolzvaniem
na bivalirudin, fondaparinux ili argatroban. Go-
lya ixat ot patientite s divaisi za mehainica
poddrxka na xemodinamikata xe imat nuxda i ot
dvoina antagreganta terapiya, poradii proveden-
na perkutanna koronarna intervencija s implantaci-
a na stent. Pri tezi patientite niska doza Aspirin i
klopidogrel trebva da se pribyvat kum terapiyata s
heparin (tryna antitrombotichna terapiya) [9, 30].
Lipsvat randomizirani prouchniya ono dozo-
viva rikim na lechenie s heparin. Preporyuikite za
antikoagulaciya pri Impella dokazat, che izpol-
vaneoto na terapeutchii dazi pri vsicxi patienti,
pi ot koito ne e konstatirano kuvrene, sa dostatn-
zi, da bdyat protektiirani. Nezavisno ot na-
lchnata informacija za momenta naj-preporuqven
e individuализиранияt podhod.

**Osvobozhavane Ot Mekhainichnata Poddrxka Na Xemodinamikata**

Indikatsiiite za osvobozhavane na patientita na
mekhainichnata poddrxka trebva da bdyat ocenivane
na vseki 24 do 48 chasa sled niciita na pod-
drjxkata. Naykolkol klinichni pokazateli mogut da
bdyat prediktori za uspevnovuetozstanovuvane na
patientita sled premakhvaneoto na mekhanichnata pod-
drjxka. Takiva prediktori sa: vsxraata na patient-
ti, pvrichnata etiologiya i lisata ili nalicixeto
na pulmonalna hipertoniia [9]. Ekoardiohragnitski
pokazateli, kata frakcija na izglaavanje, kaeen di-
astolen diametor na OK, naileyane na pulmonalna
arteriya, strxen na luvata camera i tkxanen dolpier,
sa shiroko izpolzvani prediktori za uspevnov ek-
plantiiranije na asistiraqti dixaisi. Pri patienti,
kioto sa v stabilno vostoyanie, bez dnikhi za be-
lodyoben otok ili hipoperfuziya, na niska koncen-
tracija vazopresori/inotropi, ekoardiohragnitski
dixani za podobraena OK funkciya (frakcija na izглас-
kevane na OK > 20-25%, pikova sistolna sotrost na
dvijenie na lateralnata chast na mitralnata anulus
> 6 cm/s) po vreme na namanalna poddrxka, bez spad
v srednata AH e prediktor za uspevnos osvobo-
davane ot MCS [31]. V prouchvanieto si Termuhlen et al.
izsledvati prediktori za uspevnov ekplantiiranije
na asistiraqti dixaisi pri patienti sled KSH. Spoi-

**Weaning from Mechanical Circulatory Support**

Indications for patient discharge from mecheni-
cal support should be assessed every 24 to 48 hours
after the initiation of the support. Several clinical indi-
cators may be predictors of successful patient recov-
ery after removal of the mechanical support. Such
predictors are the patient’s age, primary etiology, and
the absence or presence of pulmonary hypertension
[9]. Echocardiographic parameters such as ejection
fraction, LV end-diastolic diameter, pulmonary artery
depressor, left ventricular strain, and tissue Doppler
are widely used predictors of successful explanta-
tion of assisted devices. In patients who are stable,
without evidence of pulmonary edema or hypoper-
fusion, on low vasopressor/inotrope concentrations,
echocardiographic evidence of improved LV function
(LV ejection fraction > 20-25%, peak systolic lateral
mitral anulus velocity > 6 cm/s) during reduced main-
tenance without a drop in mean BP is a predictor of
successful discharge from MCS [31]. In their study,
Termuhlen et al, investigated predictors of success-
ful explantation of assisted devices in patients after
CS. According to them, daily monitoring of on-pump

thromboplastin time (aPTT) assay, which is a wide-
ly used method, or Xa-analysis, which represents
the gold standard for monitoring therapy but is not
widely used. Low-molecular-weight heparin and
coumarin anticoagulants should not be used in
these cases, because of their long half-lives and
renal excretion [9, 29]. In the context of heparin-in-
duced thrombocytopenia, another strategy using
bivalirudin, fondaparinux, or argatroban may be
pursued. A large proportion of patients with devices
for mechanical hemodynamic support will also need
dual antiplatelet therapy due to percutaneous cor-
nary intervention with stent implantation. In these
patients, low-dose aspirin and clopidogrel should
be added to heparin therapy (triple antithrombotic
therapy) [9, 30]. There are no randomized trials on
heparin dose regimens. Recommendations regarding
anticoagulation in Impella, demonstrate that the
use of therapeutic doses in all patients in whom
bleeding is not detected is sufficient to be prosthett-
ich. Regardless of the available information, an indi-
vidualized approach is most recommended for the
time being.
and off-pump cardiac function is a reliable predictor for the successful removal of mechanical support devices. Other very safe predictors are an increase in mixed venous saturation, cardiac index, mean arterial pressure and ejection fraction, and a decrease in atrial pressure. In 70% of patients in the study, removal of mechanical support for hemodynamics was successful, with long-term survival observed in a large proportion of patients [32]. The available publications on explantation of mechanical support devices are limited, with algorithms and recommendations based on expert consensus. The main principles are - the patient should be stable with a mean arterial pressure > 60-65 mm Hg on low dose vasopressor and/or inotropic support without the presence of pulmonary congestion. There is no generally accepted approach available to suggest when the right time is for explantation of mechanical devices for hemodynamic support [9].

Conclusion

Despite significant advances in cardiology, the prognosis for CS remains bleak. Treatment of CS should begin with intravenous infusion of crystalloid solutions, inotropes/vasopressors, and urgent revascularization in people with myocardial infarction. Mechanical circulatory support has its place in refractory CS. For a long time, IABP was used in all cases of CS until data from various studies favoring the hemodynamic effects of other percutaneous mechanical circulatory support devices came out [23]. Many questions regarding mechanical circulatory support remain unanswered. The key to the process is proper patient selection and timing of device implantation. It has been shown in multiple studies, as well as in the IABP-SHOCK II registry, that only about 50% of CS patients would have survived without device implantation. At the same time, implantation of such a device in the remaining 50% may not only have no positive effect, but may also lead to complications that eventually result in lethality [7, 11]. Proper patient selection depends on a balance between efficacy, team experience, and complications associated with different devices. The choice of the device may also be influenced by the types that are available or reimbursed in the country concerned [7]. Despite the lack of large randomized trials, the use of mechanical
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References


