## Review

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# Treatment of Patients with Myocardial Infarction in Modern Conditions of a Regional Vascular Center

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ABSTRACT The article highlights the problem of providing care for patients with acute coronary syndrome, given the high myocardial infarction (MI) morbidity and mortality among the youth population. The main method of managing acute myocardial infarction is reperfusion therapy, performing revascularization with percutaneous coronary intervention (PCI) in the shortest possible time from the disease onset. Only rational and timely treatment can reduce mortality after MI, the frequency of its complications, as well the period of inpatient treatment and disability of the population.

Keywords: acute coronary syndrome, myocardial infarction, reperfusion therapy, percutaneous coronary intervention, cardiogenic shock, antiplatelet therapy, mechanical support

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IABP – Intra-aortic balloon counterpulsation

MI - Myocardial infarction

NSTEMI - Non-ST-elevation myocardial infarction

STEMI - ST-segment elevation myocardial infarction

LV - Left ventricle

MCSDs - Mechanical circulatory support devices

AMI - Acute myocardial infarction

ACS - Acute coronary syndrome

NSTE-ACS – Non-ST elevation acute coronary syndrome

STEACS - ST-segment elevation acute coronary syndrome

AHF – Acute heart failure

HF - Heart failure

PCI - Percutaneous coronary intervention

ECG - Electrocardiography

ECMO – Extracorporeal membrane oxygenation

CAG - Coronary angiography

CS - Cardiogenic shock

CABG - coronary artery bypass graft

## DEFINITION AND EPIDEMIOLOGY OF MYOCARDIAL INFARCTION, MAIN METHODS OF TREATMENT

Myocardial infarction (MI) is an acute myocardial injury which is characterized by a deviation in the level of acute phase biomarkers in the presence of clinical, electrocardiographic or imaging signs of acute ischemia [1]. Currently, acute myocardial infarction is a widespread disease with persistent high mortality and the risk of complications. The prevalence of MI in adults is about 2-4%. At a younger age (up to 39-40 years old), it is quite low (up to 0.4%), while among people over 80 years old, the proportion of patients with MI can reach 17% [2]. According to foreign literature, the annual incidence of MI ranges from 2 to 16 cases per 1000 population, depending on the age of the studied patients [2]. According to data on the Russian Federation in 2017, it was 138.2 cases per 100,000 people. Moreover, about 25% of the reported MI cases are repeated MI [3].

Along with other forms of ischemic heart disease, acute myocardial infarction remains one of the leading causes of death worldwide [4]. According to various sources, mortality rates from MI are from 3.4 to 14% (I.V. Samorodskaya, 2017; S.S. Virani et al., 2020), and hospital mortality ranges from 4-15% [3,5,6].

Despite the development of prevention and treatment methods in the last decade, the data on the dynamics of MI incidence are rather contradictory: in some studies, a decrease in MI incidence was found, while in others no statistically significant differences were shown [7]. According to the data on the Russian Federation for 2002-2012, a decrease in the incidence of primary MI was found, while the incidence of recurrent MI, on the contrary, increased [8]. On the other hand, the development of methods for the treatment of MI, primarily the introduction of reperfusion into clinical practice in the early stages of the disease, has led to a decrease in mortality from MI, which is confirmed by large-scale epidemiological studies [9]. This trend is also typical for the Russian Federation: for example, when comparing mortality rates for 2006 and 2015, they show a decrease of 14%. In Moscow, for the period 2018-2019, the mortality rate for myocardial infarction was 8.7%. And the number of endovascular interventions (percutaneous coronary interventions - PCI) performed in patients with a heart attack increased in comparison with 2005-2006 and 2019-2020 from 75% to 95%, respectively. Currently, patient comorbidity, age, etc. are not a contraindication to PCI.

Improvement of outcomes in patients with MI is possible with timely, i.e. the earliest possible, myocardial reperfusion. At the same time, ST-segment elevation recorded by an electrocardiogram in a patient with acute coronary syndrome (ACS) is always an indication for reperfusion (PCI) [10], while in the case of ACS without ST-segment elevation (NSTE-ACS), the tactics depend on the severity of the patient's condition and risk assessment results based on laboratory and instrumental examination [11]. The main method of reperfusion is PCI. Pharmacological reperfusion therapy (thrombolysis) is recommended only for ST-elevation MI (STEMI) in case that a transport time to a vascular center where PCI is possible exceeds 120 minutes. If thrombolysis is effective, delayed PCI within 24 hours is feasible in the absence of clinical deterioration of the patient, while the absence of electrographic improvement or an increase in symptoms are indications for salvage PCI immediately after transport to the vascular center. On the other hand, according to a number of studies, the earliest PCI after thrombolysis is more practical [12]. In other cases, the combination of thrombolysis and PCI, i.e. the pharmacoinvasive strategy, is currently subject to discussion. In addition to reperfusion, the use of drugs (dual antiplatelet and anticoagulant therapy, beta-blockers, angiotensin-converting enzyme inhibitors or aldosterone receptor blockers, lipid-lowering therapy, etc.) is important for the treatment of MI. Pharmacological therapy is aimed at preventing a complicated course of MI.

Due to the wide prevalence and high mortality rate, MI remains an urgent medical and social problem. It is especially important to study the effectiveness of the treatment methods used in relation to MI and its complications, not only in clinical trials, but also in real practice, for which registries of patients with MI can be used. The analysis of their data allows both assessing adherence to current recommendations for patient management and improving the therapeutic tactics used, as well as formulating hypotheses on the basis of which new fundamental and clinical studies can be conducted [13]. The largest Russian registries of patients with MI and ACS include RECORD (2007-2008, number of patients (n)=796), RECORD-2 (2009-2011, n=1656) and RECORD-3 (March-April 2015, n= 2370); registries of acute MI (AMI): Yakutsk (2004-2006, n=799) Khabarovsk (n=321), Lyubertsy (The LIS study – Lyubertsy study on mortality rate in patients after acute myocardial infarction, 2005-2007, n=1133) , the register of ACS in Krasnodar (2008, n=776), as well as the Federal register of ACS [14,15,16,17,18].

According to epidemiological studies, in recent years in the Russian Federation there has been an increase in the frequency of using PCI as a method of reperfusion. The proportion of patients undergoing coronary angiography (CAG) and primary PCI is especially high in large federal and regional vascular centers (80-90% and 50-70%, respectively). These figures are somewhat lower in the RECORD-3 study (70% and 39% for patients with STEACS, and 48% and 21% for patients with NSTE-ACS, respectively) [14]. Similar results are shown in the Khabarovsk MI registry: CAG was performed in 65% of patients with MI, and primary PCI was performed in 65.5% of patients with STEMI and 42% with NSTEMI. Moreover, when comparing the data of the RECORD-3 registry with the previous RECORD and RECORD-2 registries, the proportion of patients undergoing CAG and PCI increased significantly, along with a decrease in mortality [14,18].

MAJOR MI COMPLICATIONS. THE EFFECT OF REPERFUSION ON THE INCIDENCE OF THEIR DEVELOPMENT

In addition to the treatment of MI, an important aspect is the correction of its complications, which significantly increase mortality in this group of patients. According to the pathophysiological principle, the following groups can be distinguished among the MI complications: mechanical myocardial injury (rupture of left ventricular free wall, interventricular septum or papillary muscles leading to acute mitral regurgitation and true ventricular aneurysm), cardiogenic shock (CS), electrical instability (rhythm and conduction disturbances), inflammatory (peri-infarction pericarditis and post-infarction Dressler syndrome), ischemic (post-infarction angina pectoris, enlargement of the infarct zone or reinfarction), and embolic (parietal thrombus formation and systemic embolism) processes [19]. From a clinical point of view, it is also advisable to single out systolic myocardial dysfunction and acute heart failure (AHF) as separate complications. This paper mainly considers MI complications that develop in the acute and subacute period, which are often urgent conditions with a high probability of death.

Among the MI complications, systolic dysfunction of the left ventricle (LV) is most common, the prevalence of which, according to various data, can range from 23 to 60% in the acute period of MI. AHF is observed in 20-35% of patients with MI at admission and its proportion during hospitalization increases to 40-54% [20]. At the same time, we are mainly talking about LV AHF due to the relatively rare development of right ventricular MI [19]. According to Russian registries, the prevalence of AHF in patients with MI is 21-35%. Rhythm and conduction disturbances are also highly prevalent, ranging from 6% for ventricular arrhythmias to 28% for atrial fibrillation [21]. CS is a less frequent complication and observed in 5-14% of patients with MI and in the vast majority of cases developing on the first day from the onset of the disease in patients with STEMI. CS is characterized by extremely high mortality (up to 45-60%) [19]. The prevalence of such mechanical complications as myocardial ruptures and acute mitral regurgitation, which develop mainly in the acute period of MI (the first week), is quite low and is about 1-7%, but even with timely surgical correction, mortality in case of their development ranges from 25 up to 75% [19]. LV aneurysms develop somewhat more frequently than myocardial ruptures and are recorded in 2-6% of patients with MI [22]. Pericardial complications are currently quite rare (acute pericarditis is detected in 1-5% of patients with MI, Dressler syndrome in about 0.1%) [23].

The development of MI therapy methods, primarily reperfusion, has led to a decrease in the incidence of most MI complications. In particular, after the introduction of PCI into routine practice, the incidence of AHF decreased to 12-20% [24]. Also, a statistically significant decrease in incidence was noted for LV systolic dysfunction. A similar trend is observed for CS: for example, one of the recent studies showed a decrease in the incidence of early CS in patients with MI from 2.2% to 1.2%, while the incidence of prehospital CS remained the same, which indirectly confirms the connection between the decrease in the incidence and the development of methods for MI treatment. The same study showed a decrease in mortality in early and late CS from 35.9% and 64.7% to 15.8% and 39.1%, respectively [25]. In another study, mortality in patients with MI-related CS who underwent PCI was even lower and amounted to 13.2%. Also, the widespread use of PCI may explain the observed decrease in the incidence of rhythm and conduction disorders, since the restoration of blood flow in the infarct-associated artery is the main method of treating rhythm and conduction disorders in the acute period by correcting ischemia of the pacemaker cells or the conduction system [26]. Similar prevalence dynamics is noted for mechanical and pericardial MI complications.

The effect of particular myocardial reperfusion strategies on the incidence of MI complications has been little studied. A direct comparison of the effect of PCI with thrombolysis on the risk of MI complications has not been conducted, and most large-scale studies comparing PCI with the pharmacoinvasive strategy did not include the risk of developing HF or CS as a separate endpoint. On the other hand, it has been shown that HF is registered less frequently when thrombolysis is combined with subsequent PCI compared to primary PCI,

however, in the case of the pharmacoinvasive strategy, the risk of developing hemorrhagic stroke increases [27]. The risk of developing CS is also lower when thrombolysis is combined with PCI, if the latter cannot be performed early (compared to primary PCI). However, these results do not allow unambiguous conclusions about the advantage of the pharmacoinvasive strategy in relation to the development of CS or AHF in patients with MI.

THERAPY OF AHF AND CARDIOGENIC SHOCK IN MI

Since AHF and CS are quite common complications of MI leading to worse outcomes and associated with a higher risk of death in this group of patients, the study of methods for their diagnosis and treatment is of particular importance [28]. AHF is diagnosed based on the typical clinical presentation and chest x-ray findings. ECG and echocardiography are used to determine the cause of AHF which may include loss of viable myocardium and consequent LV systolic dysfunction, mechanical complications, or arrhythmias. Criteria for CS are a tendency to persistent hypotension (systolic blood pressure less than 90 mm Hg and/or need for inotropic support) with satisfactory filling of the vascular bed and the signs of hypoperfusion or pulmonary congestion. In 2019, a new classification of CS was proposed, according to which 5 stages are distinguished: stage A is "at risk" for cardiogenic shock (patients with acute MI, AHF or decompensated chronic HF without clinical signs of CS); stage B is "beginning" shock (relative hypotension without signs of hypoperfusion); stage C is "classic" cardiogenic shock (hypoperfusion requiring additional interventions besides the correction of volemia); stage D is "deteriorating" (no response to intensive care within 30 minutes); and E is "extremis", terminal stage (circulatory collapse).

Revascularization remains the main treatment option that can improve outcomes in patients with infarct-related HF and CS. In this case, the main method used is PCI, which, according to various studies, is comparable in efficiency to surgical revascularization with CABG and is more effective than pharmacological reperfusion. It should be noted that the development of CS in hemodynamically stable patients during CAG and PCI, on the contrary, is quite rare (about 0.2%) and is associated with more severe coronary artery disease (multivascular stenosis or damage to the left coronary artery trunk) and STEMI. The effectiveness of primary PCI in patients with MI complicated by CS has been confirmed in large-scale studies, while it is noted that that delay in revascularization is associated with increased mortality rate in this group of patients. On the other hand, in real clinical practice, revascularization is often performed in these high-risk patients less frequently and at a later stage than in patients without CS, which can lead to high mortality (A. Kochar et al., 2018) [29, 30]. In this regard, an important aspect is the development of optimal algorithms to reduce the time before PCI.

Since multivessel coronary artery disease is common in patients with MI and CS, an important issue in PCI is the amount of revascularization performed. According to large-scale trials and meta-analyses, PCI with only infarct-related artery revascularization has the advantage of less short-term mortality and a lower risk of acute kidney injury compared to multivessel revascularization. On the other hand, a recent study found no statistically significant difference in survival or development of acute kidney injury between groups undergoing infarct-related artery revascularization or multivascular PCI, and therefore the choice of PCI tactics in these patients requires further study. A decision on multivascular PCI still needs to be made individually, taking into account the hemodynamic and clinical parameters of each patient.

Intensive pharmacological therapy and circulatory support techniques are also extremely important components of the treatment of patients with HF and CS due to MI. The two main lines of HF therapy are the correction of congestion and hypoperfusion. In case of LV AHF, diuretics and nitrates are used to reduce congestion, and oxygen therapy and morphine can be used to correct respiratory failure [31]. To correct hypotension after exclusion of mechanical complications, infusion therapy with crystalloids is used. In addition, as in case of uncomplicated MI, patients need early treatment with ACE inhibitors or angiotensin II receptor blockers (unless contraindicated) and beta-blockers. In the case of right ventricular AHF, in contrast, nitrates, diuretics, and beta-blockers which reduce preload, should be avoided.

With the development of CS in patients with MI, an important component of therapy is the maintenance of adequate perfusion, for which pharmacological agents or mechanical methods of circulatory support can be used. However, there is not enough data on the effectiveness of particular drugs for CS treatment. According to current recommendations, the predominance of hypotension requires the prescription of vasopressors (norepinephrine), while the prescription of inotropic drugs (dobutamine) is recommended for low cardiac output.

If pharmacological methods for correcting hypoperfusion in patients with MI complicated by AHF and CS are not effective, methods of mechanical hemodynamic support are used. The main circulatory support techniques are intra-aortic balloon counterpulsation (IABP) and implantable mechanical circulatory support devices (MCSDs). For patients with refractory CS, extracorporeal membrane oxygenation (ECMO) may be used [32]. The principle of IABP operation is to decrease the afterload in order to reduce myocardial oxygen consumption, and increase diastolic pressure, which improves coronary circulation in the area of damage. Implantable MCSDs act by actively pumping blood from the heart cavity into the great vessels, which allows maintaining an adequate level of perfusion regardless of ventricular myocardial contractility and cardiac output. In modern practice, MCSDs are used to pump blood both from the left heart into the aorta or its branches, and from the right heart (or large veins of the major circle) into the pulmonary artery.

Currently, a degree of efficiency of routine use of mechanical circulatory support in patients with MI complicated by AHF or CS is widely discussed. Thus, in the largest IABP-SHOCK II trial and meta-analyses, statistically significant differences between the group of patients who used IABP and the comparison group were not unambiguously confirmed, and therefore this method is not recommended for routine use in patients with advanced CS [33]. No large clinical trials have been conducted on the effectiveness of routine use of MCSDs, although small studies have confirmed better survival rates in the group of patients with early implantation of MCSDs (before the introduction of inotropic and vasopressor drugs and PCI), in this connection, the possible effectiveness of the early use of this method in selected patients with MI and CS is noted. Besides, there is insufficient data on the comparative efficacy of IABP and MCSDs, although a small study did not confirm a statistically significant difference in 30-day mortality between groups in which IABP was used or an Impella MCSD was implanted [34]. The results of a meta-analysis of studies on the use of IABP and MCSDs in patients undergoing high-risk PCI showed no statistically significant differences in mortality [35].

In addition to maintaining hemodynamics, increasing attention is being paid to the use of circulatory support techniques for unloading the myocardium, which may represent an alternative method of pathogenetic therapy for MI. It is assumed that a decrease in the hemodynamic load on the myocardium when using implantable assistive devices can help reduce the size of the infarct zone and weaken myocardial remodeling. To date, the effectiveness of "unloading" for MI has been shown in in vitro and ex vivo studies. On the other hand, clinical trials have not confirmed that the combination of unloading with delayed PCI is superior to primary PCI in terms of outcomes or the size of the infarction area. For final conclusions about the effectiveness of MCSDs for patients with MI, especially in the case of its complication in the form of AHF or CS, it is necessary to obtain the results of currently ongoing studies.

A number of authors recommend to apply – timely and according to indications – mechanical hemodynamic support techniques.

### CONCLUSION

Given the widespread occurrence of MI and its high mortality, the search for effective methods of treating MI, as well as the evaluation of their use in real clinical practice, remains an urgent problem in modern medicine. To date, the main method of treatment for MI is reperfusion in the early stages of the disease, with preference given to primary PCI, which, according to the registries of patients with MI, is currently performed in about 50-70% of patients. On the other hand, the increasing number of vascular centers makes primary PCI more accessible, and therefore this procedure has become more frequent in recent years.

The spread of PCI has reduced the lethality of MI and the incidence of most of its complications, including AHF, CS, CARDIAC ARRHYTHMIAS, MECHANICAL AND PERICARDIAL COMPLICATIONS. DESPITE THIS, AHF AND CS REMAIN fairly common complications of MI. The main method to improve outcomes in this group of patients is revascularization with PCI, although data on comparative efficacy with the pharmacoinvasive reperfusion strategy are scarce. In addition, an important aspect of the management of these patients is the symptomatic therapy of AHF and CS, including pharmacological and mechanical inotropic support. It should be noted that the latter can also be used as an alternative strategy for the pathogenetic treatment of MI by unloading the myocardium, however, its effectiveness in patients with MI, especially if MI is complicated by AHF and CS, requires further research.

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