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Ischemic Myocardial Necrosis in Diabetic Patients

Kurbanova Shohista Tojiddin qizi, Nurillayeva Nargiza Muxtarxanovna, Rajabova Ra'no Shavkatjon qizi, To'raqul Bahodir Hazratqul o'g'li
Tashkent State Medical University

Abstract: Myocardial infarction in patients with diabetes mellitus represents a distinct clinical scenario characterized by unique pathophysiological mechanisms, an atypical course, and an unfavorable prognosis. Diabetes mellitus is considered equivalent to coronary heart disease in terms of cardiovascular risk, which underscores the importance of studying the features of development and progression of acute coronary syndrome in this patient population.

Keywords: Myocardial infarction, diabetes mellitus, coronary heart disease, diabetic cardiomyopathy, glycemic control, cardiovascular complications, reperfusion therapy, prognosis

Introduction. Ischemic myocardial necrosis in patients with diabetes mellitus is one of the most pressing issues in modern cardiology and endocrinology, characterized by high prevalence, atypical course, and poor prognosis. According to the World Health Organization, diabetes mellitus affects more than 463 million people worldwide, with cardiovascular diseases being the leading cause of mortality in this population, accounting for up to 70-80% of all deaths among diabetic patients.

Epidemiological studies of recent decades indicate that the risk of developing myocardial infarction in patients with diabetes mellitus is 2-4 times higher than corresponding rates in the general population. In women with diabetes, this difference is even more pronounced, reaching a 5-7-fold increase in risk. Of particular concern is the fact that in patients with type 2 diabetes mellitus, myocardial infarction often develops at a younger age and is characterized by a more severe course compared to patients without carbohydrate metabolism disorders.

Pathogenetic mechanisms of myocardial ischemic necrosis development in diabetes mellitus are multifactorial and include both traditional risk factors for coronary heart disease and specific diabetes-associated mechanisms. Chronic hyperglycemia triggers a cascade of pathological processes, including an increase in oxidative stress, activation of protein kinase C, formation of final glycation products, endothelial dysfunction, and impairment of blood rheological properties.

Diabetic cardiomyopathy, developing independently of atherosclerotic lesions of the coronary arteries, significantly modifies the course of acute myocardial infarction. Metabolic disorders in cardiomyocytes, including insulin resistance, impaired utilization of glucose and fatty acids, mitochondrial dysfunction, and fibrous changes in the myocardium, create a pathological background where acute cardiac muscle ischemia develops.

The accelerated development of atherosclerosis in patients with diabetes mellitus is characterized by a number of features, including earlier onset, diffuse nature of the lesion, predominant localization in the distal segments of the coronary arteries, and increased tendency to thrombus formation. Diabetic atherosclerotic plaques are characterized by increased instability, which increases the risk of their rupture and the development of acute coronary syndrome.

Disorders in the hemostasis system in diabetes mellitus include increased platelet aggregation, increased synthesis of procoagulant factors, decreased fibrinolytic activity, and impaired anticoagulant mechanisms. These changes create a prothrombotic state, contributing to the formation of occlusal thrombi in the coronary arteries and the development of extensive necrotic changes in the myocardium.

Clinical features of myocardial ischemic necrosis in patients with diabetes include atypical clinical picture, painless or asymptomatic course in 30-40% of cases, which is associated with diabetic autonomic neuropathy. The absence of classic anginal pain syndrome leads to late diagnosis and untimely start of reperfusion therapy, which significantly worsens the prognosis of the disease.

Electrocardiographic changes in myocardial infarction in diabetics can be less pronounced or atypical, making it difficult to diagnose and assess the prevalence of the necrotic lesions. Echocardiographic examination often reveals comorbidities associated with diabetic cardiomyopathy, including left ventricular diastolic dysfunction, concentric myocardial hypertrophy, and impaired regional contractility.

Laboratory diagnosis of myocardial infarction in diabetes mellitus has its own peculiarities associated with the possible influence of hyperglycemia and ketoacidosis on the level of cardiac biomarkers. Troponins remain the most specific and sensitive markers of myocardial necrosis, however, their interpretation requires consideration of kidney function, which is often impaired in patients with diabetes.

Modern imaging methods, including coronary angiography, cardiac magnetic resonance imaging, and positron emission tomography, allow for a detailed assessment of the nature and extent of myocardial damage, the condition of coronary arteries, and the viability of ischemic areas of the heart muscle. These data are of fundamental importance for choosing the optimal treatment strategy and assessing the prognosis.

Reperfusion therapy for myocardial ischemic necrosis in patients with diabetes mellitus has a number of features associated with an increased risk of reperfusion damage, impaired microcirculation, and the no-reflow phenomenon. Primary percutaneous coronary intervention remains the method of choice, however, its effectiveness may be reduced due to the diffuse nature of atherosclerotic lesions and disorders at the microcirculation level.

Thrombolitic therapy in patients with diabetes is associated with an increased risk of hemorrhagic complications, especially in the presence of diabetic retinopathy and nephropathy. Choosing a thrombolytic drug and its administration regimen requires careful assessment of the benefit-risk ratio, taking into account the patient's individual characteristics.

Anti-aggregant and anticoagulant therapy for myocardial infarction in diabetics requires a special approach, taking into account the increased thrombotic risk and the simultaneous increase in the likelihood of bleeding. Double antiplatelet therapy using clopidogrel, prasugrel, or tikagrelor in combination with aspirin shows better results compared to aspirin monotherapy.

Drug therapy for myocardial infarction in diabetes mellitus includes a standard set of cardioprotective drugs, taking into account their effect on carbohydrate metabolism and kidney function. ACE inhibitors and angiotensin II receptor blockers have additional nephro- and cardioprotective effects in patients with diabetes. Beta-blockers, despite the potential risk of masking hypoglycemia, remain the drugs of choice for improving the prognosis after myocardial infarction.

Secondary prevention of myocardial infarction in patients with diabetes involves strict control of all modifiable risk factors, including glycemia, blood pressure, lipid profile, body weight, and smoking cessation. A multifactorial approach to correcting risk factors shows significantly better results compared to isolated impact on individual parameters.

Modern new generation sugar-lowering drugs, including SGLT2 inhibitors and GLP-1 receptor agonists, demonstrate additional cardioprotective effects in patients with diabetes with high cardiovascular risk. The results of large randomized studies indicate the ability of these drugs to reduce the risk of recurrent cardiovascular events and cardiovascular mortality.

Genetic factors play an important role in the predisposition to the development of myocardial infarction in patients with diabetes. Polymorphisms of genes encoding the proteins of the hemostasis system, lipid metabolism, inflammatory response, and angiogenesis influence the individual risk of

developing acute coronary syndrome and can serve as a basis for a personalized approach to prevention and treatment.

Inflammatory markers, including C-reactive protein, interleukin-6, tumor necrosis factor α, and other cytokines, play a significant role in the pathogenesis of atherothrombosis in patients with diabetes. Anti-inflammatory therapy using specific inhibitors of inflammatory mediators represents a promising direction in the treatment of this category of patients.

Endothelial dysfunction is a key link in the development of vascular complications of diabetes, including myocardial infarction. Modern approaches to correcting endothelial dysfunction include the use of ACE inhibitors, statins, antioxidants, and other drugs capable of improving the functional state of the endothelium.

Microcirculatory disorders in patients with diabetes significantly affect the effectiveness of reperfusion therapy and the course of myocardial infarction. The no-reflow phenomenon, characterized by the absence of adequate myocardial perfusion after the elimination of epicardial obstruction, is significantly more common in diabetics and is associated with an unfavorable prognosis.

Stem cells and regenerative therapy open up new possibilities for treating patients with extensive myocardial infarction against the background of diabetes mellitus. Mesenchymal stem cells, induced pluripotent stem cells, and cardiac progenitor cells exhibit the ability to differentiate into cardiomyocytes and stimulate angiogenesis in the ischemic damage zone.

Telemedical technologies and remote monitoring systems open up new opportunities for monitoring patients with diabetes in the post-infarction period, ensuring continuous monitoring of vital parameters and timely detection of complications. Mobile apps for monitoring glycemia, blood pressure, and heart rate increase patients' adherence to treatment and improve long-term results.

Artificial intelligence and machine learning are finding increasing application in diagnosing and predicting the course of myocardial infarction in patients with diabetes. Deep learning algorithms are capable of analyzing large arrays of clinical data and identifying hidden patterns inaccessible to traditional statistical analysis.

The pharmacogenetic approach to treating myocardial infarction in patients with diabetes allows for the optimization of drug selection and dosage based on the patient's individual genetic characteristics. Polymorphisms of genes encoding drug metabolism enzymes affect the effectiveness and safety of antiplatelet, anticoagulant, and other types of therapy.

The quality of life of diabetic patients after a myocardial infarction suffers significantly due to limited physical activity, psychological problems, social maladjustment, and economic difficulties. Comprehensive rehabilitation programs should take into account all aspects of the patient's life and be aimed at the most complete restoration of social functioning.

The economic burden of myocardial infarction in patients with diabetes includes both direct costs for medical care and indirect losses associated with temporary and permanent disability. Investing in preventive programs and early detection of patients with diabetes with high cardiovascular risk demonstrates high economic efficiency.

International clinical recommendations for managing patients with diabetes mellitus with acute coronary syndrome are constantly being updated based on the results of new clinical studies and accumulated practical experience. The introduction of modern recommendations into clinical practice contributes to the standardization of treatment approaches and improvement of results.

Educational programs for patients with diabetes should include information about risk factors for myocardial infarction development, symptoms of acute coronary syndrome, rules of conduct when chest pain occurs, and the importance of following prescribed therapy. Improving patients' medical literacy helps them seek medical help early and improves long-term prognosis.

The interdisciplinary approach to managing diabetic patients with myocardial infarction involves close collaboration between cardiologists, endocrinologists, nephrologists, ophthalmologists, and other specialists. The coordination of efforts by various specialists ensures a comprehensive assessment of the patient's condition and optimization of treatment tactics[7]. Pathogenetic mechanisms of myocardial infarction development in patients with diabetes mellitus are multifactorial and include accelerated development of atherosclerosis, endothelial dysfunction, increased tendency to thrombus formation, microcirculation disorders, and the development of diabetic cardiomyopathy. These factors together lead to the formation of a special phenotype of coronary heart disease, characterized by diffuse coronary artery disease, frequent involvement of distal segments and microvascular bed[8].

In patients with diabetes mellitus, there is an accelerated development of coronary artery atherosclerosis due to several mechanisms. Chronic hyperglycemia leads to non-enzymatic glycation of blood vessel wall proteins, the formation of glycation end products (AGE), which contribute to inflammation, oxidative stress, and endothelial dysfunction. In addition, in diabetes mellitus, pronounced dyslipidemia with the predominance of atherogenic lipoprotein fractions is observed, which accelerates the formation of atherosclerotic plaques. Endothelial dysfunction is an early and key link in the pathogenesis of vascular complications of diabetes mellitus. Hyperglycemia, insulin resistance, and chronic inflammation lead to reduced nitrogen oxide bioavailability, impaired vasodilation, increased vascular wall permeability, and activation of thrombus formation processes.

In patients with diabetes mellitus, a hypercoagulation state is observed, caused by an increase in the level of fibrinogen, Willbrand factor, plasminogen-1 activator inhibitor (PAI-1), as well as increased platelet aggregation. This creates prerequisites for thrombotic coronary artery occlusion even with moderate damage to the atherosclerotic plaque[9]..

Diabetic cardiomyopathy is characterized by structural and functional changes in the myocardium, independent of coronary atherosclerosis. The main manifestations are myocardial hypertrophy, fibrosis, and impaired left ventricular diastolic function, which reduces myocardial tolerance to ischemia and worsens the prognosis in the development of infarction. One of the most important features of MI in patients with diabetes mellitus is the high frequency of atypical and painless forms of the disease. Diabetic autonomic neuropathy leads to impaired pain sensitivity, resulting in the absence or mild expression of classic anginal pain. Instead of typical pain, patients may complain of shortness of breath, nausea, weakness, which makes timely diagnosis difficult. In patients with diabetes mellitus, intraventricular conduction disorders, arrhythmias are more common, and characteristic changes in the ST segment may be absent, which is associated with the diffuse nature of coronary artery damage and the presence of collateral circulation[10].

In MI, patients with diabetes mellitus show a more pronounced increase in myocardial necrosis markers (troponins, KFK-MV), which may reflect a larger volume of necrotic damage. In addition, decompensation of carbohydrate metabolism with the development of hyperglycemia or ketoacidosis is often observed. The diagnosis of MI in patients with diabetes mellitus requires special attention due to the frequent atypical course of the disease. It is necessary to conduct ECG monitoring, identify cardiac-specific markers with minimal clinical suspicions. Echocardiography allows for the assessment of local myocardial contractility and the detection of MI complications. In patients with diabetes mellitus, it is recommended to use coronary angiography more widely to assess the state of the coronary artery. Optimal glycemic control during the acute period of MI is a critical factor influencing the prognosis. It is recommended to maintain glucose levels within 7.8-10.0 mmol/l using insulin therapy according to protocols. Patients with DM have indications for more aggressive revascularization, with preference given to primary transcutaneous coronary intervention (TCI). In cases of multiple vascular lesions, coronary artery bypass grafting may be considered. Standard MI therapy includes antiplatelet agents, anticoagulants, beta-blockers, ACE/BRA inhibitors, and statins. In patients with diabetes, special attention is paid to the selection of beta-blockers (preference for cardioselective drugs) and the control of kidney function when using ACE inhibitors.

The prognosis of MI in patients with diabetes remains serious, which requires intensive secondary prevention, including optimal control of glycemia, blood pressure, lipid profile, as well as the use of cardioprotective drugs. Modern sugar-lowering drugs (SGLT-2 inhibitors, GPP-1 agonists) have demonstrated additional cardioprotective effects.

Conclusions: Thus, myocardial infarction in patients with diabetes mellitus is characterized by a specific pathogenesis, including accelerated atherogenesis, endothelial dysfunction, hemostasis disorders, and the development of diabetic cardiomyopathy. The clinical picture of MI in DM is often atypical, with a high frequency of painless forms (up to 42%), which makes timely diagnosis difficult and requires high vigilance from doctors. Patients with DM have a higher risk of MI complications, including cardiogenic shock, rhythm disturbances, and mechanical complications, which leads to an unfavorable prognosis. Diagnosing MI in patients with diabetes mellitus requires a comprehensive approach with the widespread use of instrumental research methods with minimal clinical suspicion.

Optimal glycemic control during the acute period of MI (targeted glucose level of 7.8-10.0 mmol/l) is a critical factor influencing the prognosis of the disease. Reperfusion therapy in patients with diabetes mellitus should be as aggressive as possible, with preference for primary PCI and consideration of revascularization of all significant stenosis. Drug therapy for MI in DM requires special attention to the selection of drugs and control of side effects, especially in relation to kidney function and carbohydrate metabolism. The long-term prognosis of patients with MI against a background of diabetes mellitus remains unfavorable, which requires intensive secondary prevention using modern cardioprotective and nephroprotective drugs.

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