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CORONARY HEART DISEASE IN YOUNG AGE: THE ROLE OF CATECHOLAMINES IN PATHOGENESIS

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Abstract. Coronary heart disease (CHD) is a leading cause of death and disability worldwide, affecting millions of people annually. While it is traditionally considered to be more common in older adults, an alarming increase in the incidence among younger patients has been observed in recent decades. In young adults, CHD can present atypically, complicating timely diagnosis and treatment [1]. This circumstance highlights the need for a more in-depth study of CHD diagnostic methods in young patients. The sympathetic-adrenal system mediates its adaptive effects through specific chemical messengers, catecholamines, the ratio and level of which in the myocardium is an important physiological constant and is of wide scientific interest.

Key words: coronary heart disease, catecholamines, young age, CT, MRI, clinical studies.

Catechol amines (epinephrine and norepinephrine) ensure rapid cardiac responses to the body's increasing needs for oxygen and energy substrates, exerting positive inotropic, chronotropic, bathmotropic, and dromotropic effects. Myocardial norepinephrine levels reflect the strength of the sympathetic innervation of the heart and its functional reserves, while a decrease in its level weakens contractile capacity [2]. Norepinephrine (L-1-(3,4-dihydroxyphenyl)-2-aminoethanol) is a hormone (the "rage hormone") of the adrenal medulla and a mediator (the "wakefulness mediator") of the sympathetic branch of the autonomic nervous system. Adrenaline (L-1-(3,4-dihydroxyphenyl)-2-methylaminoethanol) is the main hormone of adrenal chromaffin cells (the "fear hormone") and a neurotransmitter synthesized in sympathetic postganglionic adrenergic neurons in small quantities (up to 20%). The effects of physical activity on the body, like the stress response, are phasic and include sequential acute and long-term adaptations. Even with mild to moderate physical activity, some changes in catecholamine excretion into the blood and urine have been identified, and significant increases occur with severe exercise. During the rapid activation phase at the onset of a stressor, norepinephrine is released into the hypothalamus and other CNS centers, activating adrenergic neurons and the adrenal medulla, increasing adrenaline release and its delivery to the heart. During the acute phase of stress, sympathoadrenal system activity is at its peak, then decreases and increases with additional stimuli. Hypertrophy of the adrenal medulla is observed, the sympathetic nervous system is activated, stimulating an increase in the content of catecholamines in the blood plasma (about 80% adrenaline, 20% norepinephrine) and adaptive responses from the cardiac activity and respiratory system, noted in an increase in blood pressure, heart rate, glucose concentration in the blood, increased redistribution of blood to skeletal muscles, acceleration of metabolism, etc. [2]. Catecholamines enhance the breakdown of glycogen, increase and strengthen the heart rate, improve the conduction of excitation through the myocardium, etc., accelerate the duration of the action potential of cardiomyocytes due to the effect on the slow calcium current. Catecholamines act on cardiomyocytes through β-receptors, activating guanyl nucleotide-binding protein (Gs), which stimulates adenylate cyclase. cAMP-dependent protein kinase (cAMP from ATP) phosphorylates proteins that create channels for the passage of Ca^{2+} and Na^{+} ions, which accelerates cardiomyocyte depolarization, prolongs the plateau phase of the action potential, increases the myocardial contractility, increases the cardiomyocyte demand for O_2, and accelerates slow diastolic depolarization. Studies on isolated right atrial preparations demonstrate that physical exertion increases the role of the inotropic effects of adrenaline and α1-receptors, which serve as a reserve mechanism for acute adaptation. α1-receptors cause a positive inotropic effect associated with an increase in the concentration of cAMP, Ca^{2+} current, a slowdown in K^+ current, and an increase in the duration of the action potential [1, p. 16]. The adrenaline:noradrenaline ratio in the myocardium is an important physiological constant. The motor regime is a factor influencing the change in the adrenaline:noradrenaline ratio. In the work of A.S. Chinkin [3, 10–18] it is indicated that in animals and humans who are not trained to physical exertion, during physical exertion, prolonged hypokinesia, and in an extreme state, the activity of the sympathoadrenal system (hormonal link) increases noticeably, adrenaline secretion increases, its level in the myocardium increases, the chronotropic effect increases, the content of noradrenaline and the inotropic effect decreases slightly, and the heart rate increases without an increase in the stroke volume of blood. The myocardium actively absorbs adrenaline from the circulating blood of the coronary vessels at the onset of physical exertion. During severe physical fatigue, the levels of catecholamines, their precursors, and the enzymes that support their resynthesis decrease in the heart and adrenal glands. Catecholamine reserves are depleted, and blood concentrations drop. A decrease in the adrenal component in the regulation of myocardial contractions and a predominance of the sympathetic nervous system are beneficial for the heart. Developing sympathetic dominance requires repeated acute adaptation with adrenaline excretion, which forms the basis for long-term adaptation.

However, diagnosing coronary artery disease in young adults remains challenging due to the lack of specific symptoms and the fact that coronary artery disease symptoms often mimic other conditions. In this context, the relevance of our study lies in the comparative analysis of various methods for diagnosing coronary artery disease in young patients. We aim to evaluate the effectiveness, availability, and safety of these methods to determine the most appropriate approaches for this age group. Particular attention will be paid to modern imaging techniques, such as cardiac MRI and CT coronary angiography. Thus, this study aims to improve understanding of the current state of coronary artery disease diagnostic methods in young patients and to identify potential avenues for optimizing diagnostic strategies in this area. The results are expected to contribute to increased diagnostic efficiency and, consequently, improved treatment outcomes for coronary artery disease in young patients.

The aim of this study is to conduct an in-depth comparative analysis of methods for diagnosing coronary heart disease in young patients.

The primary objective is to identify the most effective, safe, and accessible diagnostic approaches, taking into account the specific clinical features of coronary heart disease (CHD) in young patients. To this end, the study has the following key objectives: 1. Analyze the effectiveness of diagnostic methods: Assess the accuracy, sensitivity, and specificity of various CHD diagnostic methods, including ECG, stress testing, coronary angiography, CT, and cardiac MRI. 2. Assess the availability and safety of methods: Analyze the availability of various diagnostic methods for young patients, taking into account the cost of evaluation and the need for specialized equipment. Assessing the safety of the methods is also an important aspect. 3. Study the influence of age-related factors on diagnostic effectiveness: Given that CHD in young patients may have specific clinical features, it is important to evaluate how these factors influence the effectiveness of traditional and new diagnostic methods. Achieving these objectives will not only improve our understanding of the current state of CHD diagnostic methods in young patients but also contribute to the development of more effective diagnostic strategies. This, in turn, may lead to more successful treatment and an improved prognosis in this patient population.

Overview of Diagnostic Methods for Coronary Heart Disease (CHD) CHD is a complex disease that requires a comprehensive approach to diagnosis. Existing diagnostic methods for CHD can be divided into several categories: noninvasive, minimally invasive, and invasive. Noninvasive methods include ECG, echocardiography, stress tests, and various types of imaging, such as cardiac MRI and CT. Minimally invasive methods include stress echocardiography and nuclear medicine. Invasive methods, such as coronary angiography, remain the "gold standard" in the diagnosis of CHD, but their use is limited due to the high risk of complications [3]. A detailed analysis and comparison of studies for each method: ECG in the diagnosis of CHD ECG occupies a central place in the diagnostic algorithm for CHD. This method, widely available and cost-effective, allows for the assessment of the electrical activity of the heart and the identification of potential abnormalities associated with CHD. However, despite its widespread use, the ECG has limitations, particularly when used for diagnosis in certain patient groups. A meta-analysis [4] including the results of 40 studies involving over 5,000 patients showed that the sensitivity and specificity of the ECG in diagnosing coronary artery disease can vary significantly. This is particularly true for young patients with atypical disease manifestations. In this context, the ECG may fail to detect ischemic changes, especially in the early stages of the disease or in the presence of non-specific ECG changes. Additionally, a study [5] conducted on a group of 2,000 young patients showed that a standard ECG can miss up to 30% of coronary artery disease cases due to the absence of typical ischemic changes, such as the ST segment or T wave. This highlights the importance of combining the ECG with other diagnostic methods, such as stress testing or imaging techniques, which improve diagnostic accuracy. Furthermore, it is important to note that the interpretation of ECG results requires a high level of qualification and experience of the specialist, since some ischemic changes may be subtle or misinterpreted. For example, a study [6] conducted among cardiologists showed that the accuracy of ECG interpretation may fluctuate, especially in complex clinical cases. Although the ECG is an important tool in the diagnosis of coronary artery disease, its limitations necessitate the use of additional methods and approaches, especially when working with young patients and in cases of atypical disease manifestations. This emphasizes the importance of a comprehensive approach to the diagnosis of coronary artery disease, incorporating both traditional and new diagnostic technologies. Stress tests in the diagnosis of coronary artery disease Stress tests, such as the treadmill test or bicycle ergometry, play an important role in assessing the functional state of the heart under stress and are widely used in the diagnosis of coronary artery disease. These tests are especially valuable for identifying hidden forms of coronary artery disease that may not manifest at rest. A meta-analysis [7] including the results of 50 studies involving over 10,000 patients showed that stress tests are effective in identifying functional impairments associated with coronary artery disease. This is especially true in cases where standard methods, such as ECG, do not reveal obvious signs of the disease. Stress tests can reveal ischemic changes, such as reduced blood flow and oxygen supply to the myocardium, which are not detected during a routine examination. However, the accuracy of stress tests can vary depending on a number of factors. A study [8] conducted among 2,000 patients showed that the patient's physical fitness significantly affects the test results. Patients with a high level of physical activity may have better exercise tolerance, which may mask some symptoms of coronary artery disease. On the other hand, in patients with a low level of physical activity, even a small load can cause symptoms unrelated to coronary artery disease, which can lead to false-positive results. In addition, the choice of the type of stress test is an important aspect. A study comparing treadmill testing and bicycle ergometry in 3,000 patients found that each method has its own advantages and limitations depending on individual patient characteristics, including age, gender, physical condition, and comorbidities.

A comparative analysis of the results of our review with data from other studies reveals key trends and differences in methods for diagnosing coronary artery disease in young patients. This comparison is particularly important for understanding the effectiveness and applicability of various diagnostic approaches in different clinical contexts. Studies have shown that ECG combined with stress testing can be an effective tool for the initial diagnosis of coronary artery disease in young patients. However, other studies have shown that this combination may have limited sensitivity, particularly in patients without typical coronary artery symptoms. This underscores the need for additional diagnostic methods to improve accuracy. Several studies have highlighted the high diagnostic value of CT coronary angiography, particularly in young patients with low and intermediate risk of coronary artery disease. This method allows for accurate visualization of the anatomy of the coronary arteries and the detection of early stages of atherosclerosis. A comparison with traditional coronary angiography suggests that CT coronary angiography may be preferable due to its noninvasive nature and lower risk of complications. Stress echocardiography and cardiac magnetic resonance imaging (MRI) are frequently used to assess myocardial function and identify areas of ischemia. Comparative studies indicate the high efficacy of these methods in diagnosing coronary artery disease (CAD), particularly when ECG and stress test results are inconclusive. MRI, in particular, demonstrates high accuracy in determining the degree and extent of myocardial ischemia and fibrosis. Comparison of the results of our review with other studies confirms that diagnosing CAD in young patients requires a comprehensive approach that takes into account both the characteristics of specific methods and individual patient characteristics. Despite significant advances in diagnostic technologies, there is a continuing need for further research to optimize approaches to diagnosing and treating CAD, particularly in young patients. This underscores the importance of continually updating clinical guidelines and protocols based on the latest scientific evidence, as well as the need to integrate new technologies into clinical practice to improve treatment outcomes.

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