RESEARCH IN THE FIELD OF CARDIOMYOPATHY

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Abstract: *Cardiomyopathies are a group of diseases of the heart muscle characterized by structural and functional changes in the myocardium that are not associated with arterial hypertension, congenital heart defects, or ischemic disease. These pathologies are an important cause of heart failure and sudden cardiac death. Depending on the clinical and morphological features, dilated, hypertrophic, restrictive, and arrhythmogenic cardiomyopathies are distinguished, as well as specific forms that arise against the background of systemic diseases and genetic disorders.*

Keywords: *Sudden cardiac death, MOGE, Takotsubo cardiomyopathy, cardiomyopathy, hypertrophic cardiomyopathy.*

Relevance:

According to the World Health Organization, the prevalence of cardiomyopathies is up to 1 case per 500 people for the hypertrophic form and about 1 per 250 people for dilated cardiomyopathy. Causes include genetic mutations, viral infections, toxic exposures (e.g., alcohol and drugs), autoimmune diseases, and metabolic disorders. The relevance of this topic is due to the increasing number of cases, the difficulties of early diagnosis, and the need to develop new therapeutic approaches.

Main Part:

Clinical trials were identified by PubMed up to March 30, 2021. The search keywords were “cardiomyopathies, sudden cardiac arrest, dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic cardiomyopathy, takotsubo syndrome.” Studies were selected and their references were reviewed for potential inclusion. Studies written in languages other than English were excluded. All selected studies were qualitatively analyzed. Cardiomyopathies are a heterogeneous group of pathologies characterized by structural and functional changes in the heart [1]. The recently proposed MOGE(S) nosology system embodies all these characteristics and describes the morphofunctional phenotype (M), organ(s) involvement (O), genetic inheritance pattern (G), etiological annotation (E), including genetic defect or disease/substrate, and functional status (S) of the disease, using both the American College of Cardiology/American Heart Association stage and the New York Heart Association functional class. The proposed nomenclature is supported by a web application and helps describe symptomatic or asymptomatic patients with cardiomyopathy and their family members in the context of genetic testing. Dilated cardiomyopathy is one of the main causes of heart failure, usually characterized by dilation and impaired function of one or both ventricles. Patients may develop heart failure, and the most common symptoms may be arrhythmias, atrial or ventricular, and sudden cardiac death [3,4]. This disease can be classified as primary or secondary DCM. Primary DCM is considered idiopathic, and the diagnosis can only be made after excluding secondary causes [5]. Dilated cardiomyopathy is one of the main causes of heart failure. Its prevalence among the population with heart failure is 1:250-400 patients, and among the general population - 1:2500 patients. The incidence of dilated cardiomyopathy is 7 cases per 100,000 people per year [6,7]. In addition, in the 1990s, idiopathic dilated cardiomyopathy was

identified as the leading cause of heart transplantation in the United States [8]. In the pediatric population, dilated cardiomyopathy accounts for 60% of cardiomyopathies, and children under 12 months of age have the highest incidence [9,10]. [3,4]. Hypertrophic cardiomyopathy (HCM) is the most common hereditary cardiomyopathy, caused by mutations in numerous genes. Restrictive cardiomyopathy (RCM) is a disease of the heart muscle characterized by stiffness of the ventricular walls, leading to diastolic dysfunction, increased end-diastolic pressure, and atrial enlargement [1]. Arrhythmogenic cardiomyopathy (ACM) is a pathology characterized by replacement of the myocardium with fibrous and fatty tissue, which leads to the development of arrhythmias, decreased systolic function, and sudden cardiac death, especially in young patients [1]. Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy or broken heart syndrome, is defined as the sudden onset of left ventricular dysfunction in response to severe emotional or physiological stress [1].

Results:

The American Heart Association describes a classification system that categorizes cardiomyopathy as primary or secondary. In primary cases, the disease process is mainly confined to the heart. Secondary cardiomyopathy describes conditions in which heart damage occurs as part of a systemic condition. This classification system is imperfect, and overlap is often observed. Hypertrophic cardiomyopathy (HCM) is the most common primary cardiomyopathy, with a prevalence of 1:500 individuals. Many patients with HCM are asymptomatic and are diagnosed during family screening. Dilated cardiomyopathy (DCM) has a prevalence of 1:2500 and is the main indication for heart transplantation. DCM can occur at any age, but is most common in patients aged 40 to 59 years. Characteristic symptoms of DCM include arrhythmias and thromboembolic events. Pathogenic or likely pathogenic

variants have been identified in eight genes, 20% of which are not included in the standard commercially available dilated cardiomyopathy panel. LV involvement in ARF is characterized by clinical and cardiac magnetic resonance findings that differ from those seen in DCM. The most distinctive feature of the ARF-LV phenotype is the large amount of fibrosis, which directly impairs LV systolic function. Restrictive cardiomyopathy is the least common of the major cardiomyopathies, accounting for 2% to 5% of cases. The restrictive category includes a variety of underlying etiologies and is defined by physiological function rather than anatomy. Genetic RCM can be caused by mutations in genes encoding non-sarcomeric, sarcomeric, and sarcomere-associated proteins. Takotsubo cardiomyopathy is defined as the sudden onset of left ventricular dysfunction in response to severe emotional or physiological stress. Postmenopausal women are most commonly affected. [11].

Treatment of cardiomyopathies

Therapy is aimed at slowing the progression of the disease, eliminating symptoms, and preventing complications.

1. Dilated cardiomyopathy (DCM):

- Drug therapy:
- ACE inhibitors (enalapril, lisinopril) or angiotensin II receptor antagonists (losartan) to reduce the load on the heart.
- Beta-blockers (metoprolol, bisoprolol) to improve heart function and control heart rate.
- Diuretics (furosemide, spironolactone) to reduce edema and fluid retention.
- Anticoagulants (warfarin) if there is a risk of thrombosis.
- Implantation of devices:
- Cardioverter-defibrillators to prevent sudden cardiac death.
- Pacemakers if necessary to correct arrhythmias.

- Heart transplantation: in cases of severe heart failure that does not respond to drug therapy.

2. Hypertrophic cardiomyopathy (HCMP):

- Drug therapy:
- Beta-blockers or calcium channel blockers (verapamil, diltiazem) to reduce heart rate and improve diastolic function.
- Disopyramide to reduce obstruction of the left ventricular outflow tract.
- Invasive methods:
- Septal myectomy to eliminate obstruction.
- Alcohol septal ablation (injection of alcohol into the septal artery to reduce hypertrophy).
- Implantation of a cardioverter-defibrillator: in cases of high risk of sudden cardiac death.

3. Restrictive cardiomyopathy:

- Treatment is aimed at eliminating the symptoms of heart failure and maintaining a normal heart rhythm.
- Diuretics to reduce fluid retention.
- Antiarrhythmic drugs for arrhythmias.
- Treatment of the underlying disease (e.g., amyloidosis or sarcoidosis).

4. Arrhythmogenic right ventricular cardiomyopathy:

- Medication to prevent arrhythmias. Treatment: antiarrhythmic drugs for
- Implantation of a cardioverter-defibrillator: if there is a risk of life-threatening arrhythmias.
- Restriction of physical activity to reduce the risk of arrhythmias.

General approaches:

- Genetic cardiomyopathies. Counseling for hereditary forms
- Prevention of thromboembolic complications in the presence of risk factors.
- Echocardiography. Using ECG and regular monitoring of heart function.

Treatment should be individualized and carried out under the supervision of a cardiologist, taking into account the characteristics of each patient.

Conclusions:

In particular, it has been reported that HCMP is the most important cause of sudden death on sports fields in the United States. Needless to say, it is important to know which changes in the heart due to physical activity are normal and when they are pathological. However, it is very important to achieve the goal of reaching a point where pharmacological and invasive procedures are no longer the only measures for treating cardiomyopathies, preventing sudden death, or performing heart transplants. There is hope that further understanding of the molecular genetics of cardiomyopathies may lead to clinical advances. In particular, future therapeutic approaches will include repurposed molecularly targeted drugs, siRNA-based gene silencing, and genome editing.

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