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# **So-called gray zone between athlete's heart and hypertrophic cardiomyopathy- the significance of new imaging techniques in differential diagnosis**

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## **Abstract**

### **Background**

Athlete's heart is characterized by many adaptive changes in the heart in response to physical exertion. The discovery of the "heart of the athlete" phenomenon was made by Henschen

already at the end of the 19th century during physical examination through percussion the chest of cross-country skiers.

### **The aim of the study**

The aim of the paper is to present new imaging techniques aimed at more accurate diagnosis of the differential heart of patients with physiological adaptation to intense physical exercise of left ventricular hypertrophy and patients with hypertrophic cardiomyopathy.

### **Material and method**

Standard criteria were used to review the literature data. The search of articles in English in the PubMed and Google Scholar database was carried out using the following keywords: athlete's heart, hypertrophic cardiomyopathy, tissue doppler method, magnetic resonance (MR) T1, extracellular volume (ECV) mapping, three-dimensional echocardiography (3D).

### **Description of the state of knowledge**

Athlete's heart may occasionally imitate pathological conditions related to sudden death, such as hypertrophic cardiomyopathy — the leading cause of sudden cardiac death in young athletes. Problems in differential diagnosis between the athlete's heart and hypertrophic cardiomyopathy are still existed. In the aspect of the differentiation of adaptive and pathological left ventricular hypertrophy in athletes, the diagnostic problem concerns the thickness of the myocardium (especially the interventricular septum) within 13-16 mm and constituting the so-called gray zone. This is a range of values that can be an expression of physiological LVH in competitive athletes and the symptom of a mild phenotype HCM.

### **Summary**

This kind of lesions require an extended cardiac diagnosis, these include: echocardiography, tissue doppler imaging, cardiovascular magnetic resonance T1, extracellular volume and 3D echocardiography.

**Key words:** Athlete's heart, hypertrophic cardiomyopathy, echocardiography, tissue doppler imaging, cardiovascular magnetic resonance T1, extracellular volume, 3D echocardiography

### **Background**

Morphological and functional changes in the heart muscle, which are the result of intense and long-lasting physical training (EICR, exercise-induced cardiac remodeling) are called the athletic heart syndrome. There are the adaptive changes in the cardiovascular system and their

goal is to protect the growing metabolic needs, which increase during skeletal muscles' activity. Left ventricular hypertrophy (LVH) together with the decreased heart rate is the characteristic components of the clinical picture of the athlete's determined heart.

### **The aim of the study**

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### **Material and method**

Standard criteria were used to review the literature data. The search of articles in English in the PubMed and Google Scholar database was carried out using the following keywords: athlete's heart, hypertrophic cardiomyopathy, tissue doppler method, magnetic resonance (MR) T1, extracellular volume (ECV) mapping, three-dimensional echocardiography (3D).

### **Description of the state of knowledge**

#### **Adaptive changes in the athlete's cardiac muscle**

Dynamic, i.e. isotonic efforts such as running, swimming and cross-country skiing increase venous return and volume overload of the heart, what results in increased left ventricular end-diastolic dimension index, stroke volume and minute capacity of the heart during exercise. The left ventricular becomes thickened, which leads to normalization of its tension. Isotonic effort causes eccentric, i.e. centrifugal cardiac hypertrophy and the ratio of mass to volume remains unchanged [1,2]. However, static exercise i.e. isometric, for example, weight lifting leads to an increase in blood pressure during training, which results in increased after load of the heart. The cardiac muscle grows concentrically and the ratio of mass to volume increases [1,2].

Other factors, such as ethnicity, age, gender, genetic factors and body weight, also affect heart remodeling. In addition, sports training in most disciplines, especially cycling and rowing [4,5] is characterized by a variable combination of endurance and strength exercises. Therefore, the myocardium overgrows eccentrically, i.e. the regular growth of the thickness and the transverse dimension of the ventricle, thus increasing the thickness of the wall, causing it to grow into the center, i.e. increasing the ratio of mass to volume of the heart. There is an increase in the weight and dimensions of the heart, an increase in the resting tension of the parasympathetic system, which leads to a significant release of the heart. Excessive tension of the cranial nerve and reduced sympathomimetic heart activity is the cause of sinus bradycardia in sportsmen and the

heart rate is even 35 / min and less. More often than in the general population, athletes have ECG changes that may suggest the presence of cardiac pathologies: disturbance of supraventricular rhythm, atrioventricular conduction disturbances, atrio-ventricular rhythm, features of left ventricular hypertrophy and repolarization periods. Atrioventricular conduction abnormalities and repolarization disorders in the ECG of athletes disappear under the influence of physical exercise as a result of increased sympathetic activity during this time [2,3].

It is very important to understand these changes due to the need to distinguish them from those caused by pathological conditions. Therefore, a need to clarify and refine the study of the exponents of physiological adaptation of the circulatory system to physical effort appeared, which requires differentiation especially with hypertrophic cardiomyopathy (HCM), which is a significant threat of sudden cardiac death.

The evaluation of the athlete's heart should start with a full echocardiographic examination. In recent years, apart from classic echocardiographic examinations, new achievements have been used, such as: tissue Doppler imaging, three-dimensional echocardiography, as well as using magnetic resonance imaging (CMR) T1 and extracellular volume (ECV) mapping.

### **Echocardiography as the basic method used in differential diagnosis**

Echocardiography plays a fundamental role in differential diagnosis of left ventricular hypertrophy and HCM. The adaptive LVH is homogeneous and symmetrical. The ratio between the thickness of the ventricular septum and the posterior left ventricular wall does not exceed 1.5: 1. People with HCM are characterized by generalized left ventricular hypertrophy or asymmetric Ventricular Septal hypertrophy, most often in the basal segment (HCM from LVOTO, Left Ventricular Outflow Tract Obstruction of Hypertrophic Cardiomyopathy) [6].

Pelliccia et al. conducted a study which involved 947 athletes. The results showed that 98.3% of the subjects in the study group had values for left ventricular wall thickness (LVWT) not exceeding 12 mm. In 16 people (1.7%), in whom LVWT was equal to or larger than 13 mm, an enlargement of the ventricular diastolic dimension (55-63 mm) was also observed. This group includes canoeists, rowers and one cyclist. In the aspect of the differentiation of adaptive and pathological left ventricular hypertrophy in athletes, the diagnostic problem concerns the thickness of the myocardium (especially the interventricular septum) within the limits of 13-16 mm and constituting the so-called gray zone. This is a range of values that can be an expression of physiological LVH and a symptom of benign phenotypic HCM in professional sportsmen. Such changes require extended cardiac diagnosis [7,8,9,10].

### **Tissue Doppler (TDI) imaging**

The use of tissue Doppler extends the possibilities of classic echocardiography in the differential diagnosis of physiological LVH and HCM. The adaptation to physical exertion is expressed as an improvement of left ventricular diastolic function and an increase in its susceptibility. The ejection fraction of the echo-cardiographic evaluation at rest does not change or decrease, while the shrinkage reserve used during maximal efforts increases. However, diastolic dysfunction, characterizes the heart of the patient with HCM and it may be the first expression of the disease and may precede the development of left ventricular hypertrophy [6]. The E / A ratio is a marker of the left ventricular function, calculated using Doppler echocardiography. In sportsmen, the E / A ratio is often greater than 2, with a typical low speed of peak flow caused by atrial contraction (wave A). This parameter is useful to distinguish adaptation to physical exercise from pathological hypertrophy of the left ventricle, in which the E / A ratio is less than 1, and peak flow velocity in early diastole (wave E) is extended to 9 [11]. In sportsmen, the early diastolic velocity of the myocardium ( $e'$ ) of the primary septum and the base of the lateral wall are increased. The measurement is possible thanks to the use of TDI imaging. Patients with HCM are characterized by a reduced value of this parameter. It was suggested that the peak velocity threshold  $<11.5$  cm / s can be used to differentiate patients with HCM and sportsmen [12]. In sportsmen there is no regional diastolic dysfunction ( $E / a' < 1$ ). This is evident in 25% of myocardial segments of patients with HCM and patients with hypertension [13]. TDI provides additional information on systolic myocardium at rest. The characteristic for the sportsmen's heart are supra-normal values, hypertrophy of the left ventricle coexisting with normal EF and systolic peak speed ( $s'$ )  $> 9$  cm / s. In patients with HCM is  $< 9$  cm / s and EF is clearly reduced. The E /  $e'$  ratio is low in sportsmen, but in HCM patients it increases, suggesting that the left ventricle, which pumps blood to the circulation, cannot properly fill with blood in the period between contractions, which is referred to as diastolic dysfunction and can ultimately lead to symptoms of heart failure [14].

### **Magnetic resonance (MR) T1 and extracellular volume (ECV) mapping**

Magnetic resonance imaging enables accurate assessment of the location and severity of hypertrophy. Contrast medicines containing gadolinium also allow identifying foci of fibrosis in the myocardium in patients with HCM [15]. Peter P. Swoboda et al. [16] conducted a study aimed at differentiating left ventricular hypertrophy of sportsmen and patients diagnosed with hypertrophic cardiomyopathy, especially focusing on people with undefined maximum thickness of the wall defined as 12 to 15 mm. For this purpose, magnetic resonance (CMR) T1

and extracellular volume (ECV) mapping were used. It provides a quantitative assessment of the composition of the myocardium [17].

ECV is a marker of remodeling of myocardial tissue. It constitutes an intuitive unit of measure. The correct values in healthy subjects are  $ECV 25.3 \pm 3.5\%$  [1.5 T] [18]. The increased ECV value is most often caused by excessive collagen deposition and thus myocardial fibrosis. Low ECV values are characteristic for thrombus and fat / lipomatousmetaplasia. It is possible to calculate and visualize ECV maps for specific regions of the myocardium [19].

The interesting study is also the examination in which 40 sportsmen, 50 patients with HCM and 35 volunteers have been examined 3.0-T CMR including 5 beats (3 seconds) 3 beats Modified Look-Locker Inversion (MOLLI) T1 maps before and 15 min after administration of 0.15 mmol / kg intravenous gadobutrol [17]. 40 sportsmen (11 runners, 13 triathletes and 16 cyclists) had a training that lasted 6 hours a week. The volunteers practiced less than 3 hours per week. Independently, HCM was identified according to current guidelines. Native T1 and ECV were measured at the thickest segment, and the maximum wall thickness was determined on the basis of diastolic short-axis cine images. The sportsmen and people with HCM were compared using the U Mann-Whitney test. In sportsmen, along with the increase in LV hypertrophy, there was a decrease in ECV, while in patients with HCM, the ECV value increased. The different correlation between ECV and LV in sportsmen and patients with hypertrophic cardiomyopathy suggests that in the healthy heart there is a cellular hypertrophy, whereas the cells disintegrate and the extracellular matrix extends in the heart with hypertrophic cardiomyopathy. Therefore, CMR using T1 mapping has a potential role in exclusion of HCM in sportsmen presenting left ventricular hypertrophy [19].

### **Three-dimensional Echocardiography (3D)**

Three-dimensional echocardiography (3D) allows the assessment of heart anatomy, ventricular function, blood flow velocity and valve disease, as well as LV volume and mass in a manner similar to the magnetic resonance of the heart. However, 3D echocardiography is a more accessible study that generates lower costs and it is therefore widely used for sportsmen.

### **3D echocardiography**

3D echocardiography provides more detailed information than two-dimensional echo technique (2D), determining the values of remodeling and LV function. 3D better describes morphological features, showing differences in the length and shape of the LV chamber, which are not adequately assessed using the 2D technique [20].

A study conducted by Caselli et al. with 3D has shown the increased values of the left ventricular end-diastolic volume and weight in sportsmen compared to the control group. The

gender and type of sport had the greatest impact on left ventricular remodeling. Men performing endurance sports were characterized by the highest value of left ventricular end-diastolic volume and left ventricular mass. An important factor in the LV remodeling was also the body surface area (BSA). However, arterial blood pressure and age had only minimal effects. The left ventricular systolic function was similar for both sportsmen and people who do not do exercises [21].

### **Summary**

Hypertrophic cardiomyopathy is characterized by an echocardiographic image or a magnetic resonance image of the heart resembling the sportsmen's heart. This pathology is known as an important cause of the sudden death of young people and sportsmen, and therefore disqualification from practicing intense sports of patients presenting such a disease entity is justified.

The differential diagnosis can be a clinical dilemma, considering that the sportsmen's heart is a physiological condition and is not essential for disqualification from high-performance sports. It is important to distinguish healthy, physiological modifications of the sportsmen's heart from pathological conditions, such as cardiomyopathy. In the diagnosis of cardiovascular diseases in sportsmen, imaging is necessary, which should certainly be interpreted based on the patient's symptoms, history of his illness, age, sex, ECG and sometimes also genetic analysis.

The most important role in the diagnosis of the sportsmen's heart is played by echocardiography, however, due to the presence of the so-called diagnostic gray area, the latest achievements such as TDI, MR, ECV and 3D allow for more reliable identification of physiological traits and exclusion of pathology. These methods require a wider application in more diverse populations of sportsmen and HCM patients who are involved in competitive sports.

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