

REVIEWS

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Tachycardiomyopathy in Human and Animals – Pathophysiology, Treatment, and Prognosis

Tachykardiomiopatia u ludzi i zwierząt – patofizjologia, leczenie i rokowanie

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Abstract

Tachycardiomyopathy is a form of secondary dilated cardiomyopathy caused by a high heart rate leading to left ventricle dilation and systolic function impairment. It is a result of inadequate systole caused by long-lasting or frequently recurrent supraventricular or ventricular arrhythmias as well as frequent ventricular extrasystole. The signs of tachycardiomyopathy, if treated causally, are fully reversible, in contrast to other types of cardiomyopathy. However, if it is diagnosed too late and is not treated properly, the progressive nature of the process leads to symptoms of severe congestive heart failure or to sudden death caused by ventricular arrhythmias. This disease is difficult to diagnose because dilation of the ventricles of heart may be the cause or the result of tachyarrhythmias. The high prevalence of atrial fibrillation and the increased number of elderly persons with this kind of arrhythmia makes atrial fibrillation-induced tachycardiomyopathy one of the leading causes of congestive heart failure in humans. This article presents the pathophysiology, treatment, and prognosis of tachycardiomyopathy in human and animals (*Adv Clin Exp Med* 2010, 19, 2, 245–249).

Key words: tachycardiomyopathy, heart, arrhythmias.

Streszczenie

Tachykardiomiopatia jest jedną z postaci kardiomiopatii rozstrzeniowej, której przyczyną rozwoju jest wysoka częstotliwość rytmu serca prowadząca do rozstrzeni lewej komory i pogorszenia jej czynności skurczowej. Przyczyną rozwoju tachykardiomiopatii są długo trwające lub często nawracające epizody tachyarytmii zarówno nadkomorowej, jak i komorowej oraz liczna ekstrasystolia komorowa. W odróżnieniu od innych rodzajów kardiomiopatii rozstrzeniowych następstwa tachykardiomiopatii mogą się całkowicie wycofać, jeśli jej przyczyna zostanie odpowiednio wcześniej zdiagnozowana i usunięta. W przeciwnym razie wiedzie do rozwoju objawowej zastoinowej niewydolności serca lub nagłego zgonu sercowego w mechanizmie komorowych zaburzeń rytmu. Coraz częstsze występowanie migotania przedsionków, zwłaszcza w populacji chorych w podeszłym wieku, czyni tę arytmie jedną z wiodących przyczyn rozwoju niewydolności krążenia. Niniejsza praca przedstawia patofizjologię, leczenie oraz rokowanie w tachykardiomiopatii u ludzi i zwierząt (*Adv Clin Exp Med* 2010, 19, 2, 245–249).

Słowa kluczowe: tachykardiomiopatia, serce, arytmie.

Tachycardiomyopathy is a form of secondary dilated cardiomyopathy caused by a high heart rate leading to left ventricle dilation and systolic function impairment. Other forms of cardiomyopathy are primary dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM). DCM is an inherited, genetically caused disorder observed more frequently in large and giant dog breeds such

as the boxer, Doberman pinscher, Great Dane, and Irish wolfhound [1]. DCM is also diagnosed in humans, with symptoms occurring at a relatively young age. Primary dilated cardiomyopathy is a disease with a poor prognosis. The progressive nature of the process leads to symptoms of severe congestive heart failure or to sudden death caused by ventricular arrhythmias. In animals, HCM is

observed mainly in cats, particularly in Maine coon cats. In humans, HCM is diagnosed more rarely than DCM. All the above-mentioned cardiomyopathies are included in the group of non-ischemic disorders. In humans, the most common form of cardiomyopathy is secondary ischemic cardiomyopathy caused by ischemic coronary disease (myocardial hibernation) and/or subsequent myocardial infarction (myocardial necrosis).

The signs of tachycardiomyopathy, if treated causally, are fully reversible, in contrast to the other types of cardiomyopathy. The first observations of the causal relationship between atrial fibrillation with high heart rate and reversible left ventricle systolic dysfunction were published in 1949 by Phillips and Levine [2]. The high prevalence of atrial fibrillation assessed in 2 million people in the USA in 1995 and the increased number of elderly persons in whom atrial fibrillation incidence reaches up to 9% in the ninth decade of life make atrial fibrillation-induced tachycardiomyopathy one of the leading causes of congestive heart failure in humans [2, 3].

In dogs and horses, atrial fibrillation is the most common form of arrhythmia [4, 5]. Making the proper diagnosis of tachycardia-induced cardiomyopathy is not easy because of the possibility of a reverse relationship. The primary myocardial disorder can lead to left ventricle dilatation, mitral annulus enlargement, and mitral regurgitation [6]. This causes pressure and volume overload inducing atrial enlargement, mechanical and electrical remodeling, and atrial fibrillation with a relatively high heart rate [7]. The described course of the pathophysiological process is widely described in mitral insufficiency caused by its non-inflammatory degeneration in dogs of small and toy breeds. Atrial fibrillation occurs particularly frequently in dogs with DCM in whom it exacerbates the signs of heart failure because of cardiac output fall, left ventricle ejection fraction decrease, and rapid left ventricle dilatation [8–15].

The main indicator of a tachyarrhythmic origin of left ventricular cardiomyopathy is the improvement in both systolic and diastolic function after effective arrhythmia treatment, in particular effective ventricular rate control. Tachycardiomyopathy is commonly seen in patients with incessant or frequently recurrent supraventricular tachycardia, i.e. atrial tachycardia, atrial fibrillation, or flutter, but can be observed even in atrioventricular nodal reentrant tachycardia or atrioventricular reentrant tachycardia in humans and dogs with pre-excitation syndrome [7, 11, 14, 15]. The cause of ventricular dilatation can also be ventricular tachyarrhythmias. In humans the most common arrhythmia is atrial fibrillation. It can be therefore

assumed that most cases of tachycardiomyopathy originate from this arrhythmia. This could really be the case because atrial fibrillation is particularly common, up to 35%, in patients with congestive heart failure [16]. In dogs, AF is often observed in DCM [1].

Tachycardiomyopathy is a result of inadequate systole caused by long-lasting or frequently recurrent supraventricular or ventricular arrhythmias as well as frequent ventricular extrasystole [14, 15]. This last cause is commonly observed in boxer dogs [11, 12]. Not only heart rate, but also irregularity of the heart rhythm and the presence of possible previous myocardial damage have causative roles in left ventricular function deterioration [17]. The precise mechanism of left ventricle dilatation has not been fully explained. One possible explanation is dysfunction of the systolic apparatus of cardiomyocytes and collagen fiber deposits in the extracellular compartment [18]. The systolic dysfunction could also be caused by coronary circulation abnormalities, in particular in the subendocardial layer, even in the absence of any coronary artery lesions [19]. These changes are probable in the setting of a very high heart rate, i.e. a very short diastolic interval. In tachycardiomyopathy, as well as in other forms of dilated cardiomyopathies, there are increases in end-systolic and end-diastolic left ventricle diameter and left ventricle volume and filling pressure, a decrease in ejection fraction, and increases in pulmonary artery and right ventricular pressure. Left ventricle dilatation is usually accompanied by relative mitral regurgitation, which speeds up the development of chamber dilatation by the mechanism of volume overload [6]. As mentioned above, tachyarrhythmic left ventricle dilatation predisposes to other supraventricular and ventricular arrhythmias. Mitral regurgitation leads to left atrial volume overload, its dilatation, and myocardial fibrosis, which could be the substrate for arrhythmias other than the primary one. An important role in atrial arrhythmia development is played by left ventricle diastolic dysfunction, also inducing left atrial enlargement. In a four-year follow-up study, the development of atrial fibrillation in patients with preexisting diastolic function impairment was as high as 10% [20]. In veterinary medicine there are few data regarding diastolic dysfunction, probably because of the underuse of echocardiography and the technical problems with this technique in various species. One important study dealt with systolic and diastolic dysfunction in dogs with dilated cardiomyopathy. For this reason its results could not be regarded as similar to the situation with previously normal diastolic function deteriorated in the course of tachycardiomyopathy development [21].

In patients with congestive heart failure, neurohumoral changes predispose to arrhythmias. The increased level of catecholamines and angiotensin II leads to structural changes in the myocardium such as cardiomyocyte hypertrophy, collagen accumulation, and fibrosis [13]. Long-lasting atrial fibrillation and their fibrosis induce a decrease in atrial natriuretic peptide (ANP) secretion leading to hemodynamic changes partially responsible for congestive heart failure development [17]. Experimental animal model studies on rapid heart pacing indicate a decrease in beta-adrenergic receptor density on the cardiomyocyte membrane surface [3]. It is important to emphasize the role of the electrical remodeling of the left ventricle. In patients with congestive heart failure caused by chamber dilatation there are changes in the number and regional density of ion channels. Potassium (I_{to} , I_{kr} , I_{ks}) and calcium channel abnormalities lead to increased action potential duration and predispose to ventricular arrhythmias [20, 22].

The probable pathophysiological mechanism of the development of dilated cardiomyopathies such as tachycardiomyopathy is the combination of left ventricle systolic dysfunction inducing a complex neurohumoral response and the cardiomyocyte calcium ion disturbances caused by rapid electrical ventricular activation [23–26]. Inappropriate, rapid, and often hemodynamically ineffective ventricular contractions induce sympathetic nervous system and renin-angiotensin-aldosterone system responses, with all their harmful influences [27]. In particular, frequent ventricular arrhythmia disturbs the proper ventricular systolic function. Prolonged sympathetic activation leads to adrenergic receptor density and function disturbances, ion channel dysfunction, and degenerative changes in cardiomyocytes. These processes end in a loss of structural integrity and in left ventricle enlargement [28].

A high electrical activation rate causes myocyte calcium ion disturbances commonly seen during repeated short-lasting or chronic ischemia [29]. A short diastolic phase increases the calcium ion level within the sarcoplasm, which could not be moved to the sarcoplasmic reticulum. This causes diastolic dysfunction as it decreases the lusitropic properties of the left ventricle. The long-lasting increase in calcium level is responsible for systolic function impairment regarding the Frank-Starling mechanism (only partial diastole) and, combined with prolonged sympathetic stimulation, induces involutive changes in the systolic apparatus resembling the changes described as frozen myocardium [30].

As the described changes are fully functional ones, it is obvious that after the achievement of a normal activation rate, i.e. eliminating the

cause of tachycardiomyopathy, its signs subside. However, in the presence of long-lasting tachyarrhythmia and pronounced chamber enlargement, the sequels, i.e. mitral regurgitation and electrical remodeling could be prolonged and not fully reversible, leading to a shortening of life expectancy.

The sole evidence of an arrhythmic origin of left ventricle dysfunction is its disappearance after sinus rhythm restoration or heart rate control achievement by pharmacotherapy. It has been demonstrated that after successful electrical or pharmacological cardioversion of atrial fibrillation in humans as well as in dogs with tachyarrhythmic left ventricle systolic function impairment, improvement in left ventricle performance can be observed within the first week, with its maximum one month after the procedure [16]. Successful radio-frequency ablation of the arrhythmogenic substrate in dogs with tachyarrhythmias also led to improvement in left ventricle function [14, 15]. It should be emphasized that even tachyarrhythmic cardiomyopathy could not be fully reversible if there was any previous heart damage or the cause was very long lasting. In some patients with chronic atrial fibrillation, congestive heart failure could develop despite pharmacological heart rate control. In these patients, satisfactory rate control may probably be achieved only at rest. Even slight physical exercise, such as everyday activities, cause an inappropriate high heart rate, commonly above 120 bpm, resulting from sympathetic activation [17].

The symptoms of tachycardiomyopathy are related to left ventricle enlargement and systolic and diastolic dysfunction. Left ventricle dysfunction is manifested in the form of heart failure. Its severity depends on the gravity of ventricle dilation and preexisting dysfunction. Exercise intolerance, dyspnea by exertion or at rest, and signs of fluid congestion in the pulmonary and systemic circulation are variously manifested.

Tachycardiomyopathy is characterized by long-lasting and frequent recurrences of arrhythmias before heart failure symptoms become evident. It should be stressed, on the other hand, that particularly atrial arrhythmias can be caused by atrial enlargement and atrial and ventricular electrical remodeling. Thus it becomes obvious that not all arrhythmias in the dilated heart are responsible for its dysfunction. Tachycardiomyopathy can develop without symptoms in humans not recognizing any rhythm disturbances and in animals without any signs of arrhythmia during an event. In this setting, a proper diagnosis becomes difficult if the existing arrhythmia is the cause of the disease or its consequence.

In a clinical evaluation of a patient with tachycardiomyopathy, typical signs of congestive heart

failure can be observed, such as peripheral edema and hepatic or lung congestion. In some patients, additional heart sounds can be heard. Apart from the presence of arrhythmia (atrial fibrillation, atrial flutter, atrial tachycardia, frequent ventricular ectopic beats, ventricular tachycardia), other abnormalities such as left ventricle hypertrophy or enlargement can be observed in the electrocardiogram. In this setting the most useful diagnostic tool in the assessment of arrhythmia is the 24-hour electrocardiography. It enables the recognition of asymptomatic tachyarrhythmias [20]. In chest X-ray, heart enlargement, pulmonary circulation fluid retention, or event pleural congestive effusions can be found. The most important diagnostic information can be achieved from echocardiography. Enlargement of the left and right cardiac chambers and impairment of systolic and diastolic function usually correlate with disease progression. Abnormalities in left ventricle wall motion are usually global and not regional. Functional mitral regurgitation is common due to mitral fibrous annulus dilatation [7]. The presence of tachyarrhythmia or a medical history indicating its frequent recurrence in patients with left ventricle enlargement, in particular if arrhythmia preceded the signs and symptoms of congestive heart failure, deserves a detailed and careful evaluation, often including an invasive electrophysiological assessment. This is important especially in patients with pre-excitation syndrome and atrioventricular reentrant tachycardias. This procedure always precedes radio-frequency ablation.

As mentioned above, reversion of the cause of tachycardiomyopathy always leads to improvement in left ventricular performance and usually to a decrease in chamber diameters. It is obvious that therapy should be primarily focused on removing arrhythmia. Today the leading role, especially in younger patients, is ablation, whereas pharmacotherapy is used if the arrhythmia is not reversible, as in the case of chronic atrial fibrillation [15]. In the latter case, a careful assessment of appropriate heart rate control not only at rest, but also during exercise is essential to eliminate symptoms. A possible therapeutic option in some patients is atrioventricular node ablation and artificial heart pacemaker implantation for ventricular stimulation. Ozcan et al. showed that in humans with atrial fibrillation and heart failure, atrioventricular node ablation led to left ventricular systolic function improvement in 68% of cases and in 29% the ejection fraction exceeded 45% [7]. The deteriorating effect of right ventricle stimulation on heart function makes this solution not fully acceptable. To date, this kind of procedure has not been performed in veterinary medicine.

What must be borne in mind is the proper pharmacological treatment of heart failure itself until ventricle performance improves. The necessary therapeutic approach should consist of beta-adrenergic receptors blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, and aldosterone antagonists. Other drugs, such as nitrates or loop diuretics, should be used according to the patient's fluid volume status.

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