Reviews

Muscular exertion in selected cardiovascular disorders

Wysiłek mięśniowy w wybranych chorobach układu sercowo-naczyniowego

Katarzyna Podgórska-Gumulak[1,B–D], Szymon Suwiczak[2,B,C,E], Ewa Szahidewicz-Krupska[1,B,C,E], Adrian Doroszko[1,A,C–F]

[1] Department and Clinic of Internal and Occupational Diseases and Hypertension, Faculty of Medicine, Wroclaw Medical University, Wrocław, Poland
[2] Department of Rehabilitation in Internal Medicine, Faculty of Physiotherapy, University School of Physical Education in Wroclaw, Wrocław, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

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Address for correspondence
Adrian Doroszko
E-mail: adrian.doroszko@umed.wroc.pl

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Abstract

According to the recommendation of European Society of Cardiology (ESC), regular physical activity is a key factor in reducing cardiovascular mortality in both primary and secondary prevention of cardiovascular disease (CVD). Mechanisms of beneficial effects of physical activity are multi-directional and differ among each other depending on the type of effort being undertaken and the conditions coexisting in the exercising person. By closely affecting vascular endothelial cells, physical activity affects their inflammatory, pro- and anti-angiogenic and vasodilatory properties, determining the maintenance of normal cardiovascular homeostasis. Based on the available data, it can be unequivocally stated that none of the known therapeutic interventions reduces the risk of so many diseases at the same time as physical activity does. This paper summarizes the contemporary data concerning the role of physical exercise in modifying the course of different types of CVD at different stages of their pathophysiology.

Key words: muscular exertion, vascular endothelium, atherosclerosis, cardiovascular risk

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Streszczenie

Zgodnie z obowiązującymi obecnie rekomendacjami Europejskiego Towarzystwa Kardiologicznego (European Society of Cardiology – ESC) regularny wysiłek fizyczny stanowi kluczowy czynnik zmniejszający śmiertelność z przyczyn sercowo-naczyniowych zarówno w profilaktyce pierwotnej, jak i wtórnej chorób układu krążenia. Mechanizmy korzystnego oddziaływania aktywności fizycznej na układ krążenia są wielokierunkowe i różnią się między sobą zależnie od rodzaju podejmowanego wysiłku oraz schorzeń współistniejących u osoby ćwiczącej. Poprzez ścisłe oddziaływanie na komórki śródbłonka naczyniowego wysiłek fizyczny wpływa na ich właściwości zapalne, pro- i antyangiogenne oraz wazodylatacyjne, determinując tym samym utrzymanie na prawidłowym poziomie homeostazy układu sercowo-naczyniowego. Na podstawie dostępnych danych literaturowych można jednoznacznie stwierdzić, że żadna ze znanych obecnie interwencji terapeutycznych nie ma podobnej wysiłkowi fizycznemu skuteczności w redukcji ryzyka tak wielu chorób jednocześnie. Praca niniejsza w zwarty sposób podsumowuje dostępne współcześnie dane literaturowe dotyczące roli wysiłku fizycznego w modyfikowaniu przebiegu wybranych schorzeń układu sercowo-naczyniowego na różnych etapach ich patofizjologii.

Słowa kluczowe: wysiłek mięśniowy, ryzyko sercowo-naczyniowe, śródbłonek naczyniowy, zmiany miażdżycowe

Introduction

According to the WHO report, noncommunicable diseases are currently the most common causes of death in the world. Cardiovascular disease (CVD) represents approx. 50% of this group and accounts for more than 36 million deaths each year. More than 9 million patients died at the age of 18–60, which is the period of greatest activity of life and, in most cases, these deaths could have been prevented with appropriate prophylaxis.[1] At the basis of most CVD cases lies the endothelial dysfunction as well as impaired platelet function leading to excessive platelet aggregation.

The benefits related to physical exercise depend on the type of activity and its intensity, and are still a subject of discussion and much controversy. Regular activity of medium intensity maintains the correct function of endothelial cells and supports the antioxidant effects, which can prevent the development of CVD. However, it is worth noting that exhaustive effort increases the oxidative metabolism.[2]

Patients with known vascular endothelial function impairment relatively benefit more from physical activity. However, the difficulties in proving the improvement of health status though physical activity among healthy subjects should be taken into account. Improving the function of endothelial cells is expressed in increased bioavailability of nitric oxide (NO); however, the mechanisms underlying it are complex and still not fully understood. Furthermore, further research requires elaborating the details of an optimal training plan and assessing the duration of beneficial changes depending on the type of training exercises and initial conditions.[3]

Apart from the cited effects on the endothelium, which are released by muscle cells myokines to encourage the growth of muscle mass, angiogenesis and metabolism should also be mentioned. All of these functional and structural changes lead to the reconstruction and the increase in mass of the heart muscle, heart rate acceleration, centralization, and modulation of the immune system, and neurohormonal mechanisms.[4]

Coronary artery disease

Muscular exertion increases the demand for oxygen. During significant activity, a 6-fold increase in oxygen demand of the left ventricle of the heart results in a 5-fold increase in coronary flow in healthy subjects. The dependence of the coronary flow on the cardiac oxygen demand is associated with the effect of the neurohormonal mediators and perivascular vapor pressure of oxygen, as well as on the functional coronary reserve.[5] Muscular exertion influences the increase in coronary flow also through adaptation of microcirculation by increasing the diameter of the capillary vessels or their density along with changes in vasomotor reactivity. The modification in the volume of coronary flow is achieved through the involvement of angiogenesis together with the hypertrophy of the heart muscle, so the capillary density remains within the normal range. However, after exercise, the area of coronary exchange is greater due to changes in vascular resistance and changes in the exchange and distribution of blood flow. This is a result of structural changes and modifications in vasoreactivity of coronary vessels. Regular training increases the adrenergic responsiveness, which is confirmed by no change in α- and β-adrenergic musculature tension at relatively lower levels of circulating catecholamines. In response to a stretch, there is a change in the activity of the voltage-dependent calcium channels, which in turn results in an increase in the tension of coronary vascular smooth muscle cells. Animal models did not provide conclusive evidence on the effect of physical exercise on atherosclerotic changes. It is possible that the beneficial effects of physical activity are not a result of its direct impact on the coronary artery walls.[6]

The increase of blood flow due to exercise may also reduce the level of blood viscosity, resulting in an increase in shear forces. Such increase releases vasodilation substances (including NO and prostacyclin) and then reduces the permeability to lipoproteins and the adhesion of leukocytes. At present, no optimal change in the flow has been established that would correspond to the intensity of pro- or anti-atherosclerotic processes. Moreover, the differential effect of the abovedescribed hemodynamic changes was confirmed, depending on the size of the vessel and the type of tissue.[7]

The stiffness of the vessels shows a strong correlation with CVD, and the common denominator is atherosclerosis. There are studies demonstrating the relationship of pulse wave velocity (PWV) to the endothelium, vasodilation and higher pulse waves. It was found that increased PVW contributes to the elimination of an existing endothelial dysfunction. The relationship of PWV with the risk of developing atherosclerosis has been shown according to Framingham Risk Score, regardless of other factors. Left ventricular ejection fraction has a negative relationship with PWV and the number of elastic fibers in the walls – great vessels become stiffer, affecting the increase of the total vascular resistance and increasing the load on the left ventricle.[8] Pulse pressure as the stiffness index of large arteries has also been used as a prognostic value in coronary artery disease and acute coronary syndromes. Increase in the stiffness of the aorta causes ischemia of the heart and progression of atherosclerosis. Aerobic exercise, by increasing flexibility and improving endothelial function, can contribute to the inhibition of these negative changes.[9] The intensity of the exercise and its repeatability seem to play a key role in the reduction of the inflammatory processes.[10] However, the mechanisms through which the abovedescribed processes progresses require further research. One hypothesis considers the impact of interleukin (IL)-6 released from muscle cells, which not only enhances the production of the anti-inflammatory IL-1 and IL-10, but also inhibits the production of pro-inflammatory agent tumor necrosis factor α (TNF-α). Interleukin 6 lipolysis also intensifies the oxidation of lipids.[11]

Lipid peroxidation, as a source of reactive oxygen species (ROS), negatively affects the function of the endothelium, reduces the bioavailability of NO and impairs its active vasodilation function as well as increases the severity of the nitrogen stress, which, through post-translational modification of numerous proteins, may accelerate the development of atherosclerosis. Increased lipid peroxidation favors also formation of foam cells from macrophages, which limits the clearance of lipid deposits and promotes vascular inflammation, leading to the formation of atherosclerotic plaques.

Diabetes

Diseases of affluence, associated with the progress of civilization and with the lack of physical activity, such as obesity, insulin resistance and type 2 diabetes, have in the last decades achieved the stage of a global epidemic. In many clinical studies, it has been proven that well-chosen physical training is the best method to prevent complications associated with these disorders or at least delay the onset of such complications.[12] Both short-term and regular exercise lowers blood glucose levels by increasing insulin sensitivity, reduces the amount of body fat and thereby improves the function of the cardiovascular system. Because of improved glycemic levels, exercise could be a part of the therapy in patients with disturbances in carbohydrate metabolism. However, attention should be paid to possible post-exercise hypoglycemia due to the increased uptake of glucose by the working muscles. In view of the foregoing, diet must be customized and the medications used must be appropriate for the planned exercises.[13]

Diabetes is also linked to the process of chronic inflammation and oxidative stress as a result of several cell types being produced, along with C-reactive protein (CRP), TNF-α or ILs (IL-6, IL-1 or IL-β).[14,15] The effect of physical exercise on oxidative stress and inflammatory processes has been a subject of many studies.[16,17] According to their results, sudden sharp effort contributes to an increase in oxidative stress and to the severity of the inflammatory process (such rapid physical activity can also worsen a course of an infection), while undertaking regular activity results in their reduction.[18–21]

Stiffening of the arteries develops earlier and faster in people with diabetes. Increase in the PWV results in faster development of micro- and macrovascular diseases. This is due to the glycation of proteins in the vascular walls combined with parallel developing changes responsible for atherosclerosis. This process applies to plasma proteins, proteins contained in the morphotic elements of the blood, tissue proteins, and proteins of the walls. The most important cause of microvascular disease is non-enzymatic glycosylation of proteins. People with diabetes present an increased stiffness of blood vessels compared with people without diabetes. The formation of advanced glycation end-products (AGEs) plays an important role in the pathogenesis of accelerated stiffness – AGEs are responsible for changing the structure and function of vessels.[23] The relationship between the stiffness of vascular and inflammatory markers such as CRP, amyloid A, sialic acid, fibrinogen, and leukocytosis, was stated in an analysis of the relationship between disorders of the carbohydrate metabolism and the process of arterial stiffness, which was carried out, among others, in Hoorn Study examinations. The stiffness of blood vessels correlates with the presence of chronic microvascular complications of diabetes (retinopathy, neuropathy, microalbuminuria), as well as with impaired myocardial function and calcification of coronary arteries in patients with diabetes mellitus – and may be partly averted through regular physical training.[24] In the available literature, there is data indicating the relationship of vascular endothelial growth factor (VEGF) levels and physical exertion. Wahl et al. proved the relationship of VEGF concentrations (and thus angiogenesis) with the intensity of the workout. The tests performed after medium-intensity exercise have not shown an upward trend, while high-intensity exercise resulted in an increase in the concentration of VEGF.[25] According to the results of studies carried out by Czarkowska et al., the increase in VEGF concentration was the result of an inflammatory response induced by damage to the muscle fibers due to excessive physical effort.[26] Comparison of VEGF density in response to exercise with a similar intensity in people who do not exercise and athletes allowed Jensen et al. to observe a greater response among non-training people and its decrease along with the repeatability of their workout.[27] Richardson et al. presented in their study a similar effect of adaptation to physical exertion on reducing the concentration of VEGF.[28]

Heart failure

Heart failure results in the deterioration of muscle strength and shifts the homeostatic balance towards catabolic processes.[29] One of the reasons for this may be the observed increased apoptosis of skeletal muscle cells[30,31] and the structural changes of sarcomeres, which in an obvious way transform into modulation of muscle strength, endurance and activity ergoreceptors. Ergoreceptors are free nerve endings in muscles that have been demonstrated to increase the concentrations of lactic acid, potassium and prostaglandins with an accompanying reduction of the pH during physical exercise. They are responsible for ventilation, standalone hemodynamic response, as well as for the maintenance of a balance between the needs of the working muscles and the quantity of blood supply. In heart failure, metabolic disorders and rapid reduction in pH cause excessive activation of ergoreceptors, leading to an increased hemodynamic response and limited ventilation effort.[32,33] For many years, this relationship resulted in the recommendation to limit the exercise in these patients. These changes and further limited physical effort led to reduced strength, the effect of which was increased tiredness. The results of subsequent clinical studies have confirmed the positive effect of well-chosen physical training (including free weights and resistance exercises) in people diagnosed with heart failure.[34–36]

Conclusions

Physical exercise is the only risk-free form of primary and secondary prevention of CVD. Taking into account its pleiotropic and beneficial effects on diseases of affluence and the low cost of its implementation, it is crucial to promote physical activity in the general population and to educate the medical staff on the selection of the optimal training in the therapy of patients with a specific risk profile and coexisting diseases.

ORCID iDs

Katarzyna Podgórska-Gumulak https://orcid.org/0000-0002-5087-1790
Szymon Suwiczak https://orcid.org/0000-0001-9184-6957
Ewa Szahidewicz-Krupska https://orcid.org/0000-0002-4446-6991
Adrian Doroszko https://orcid.org/0000-0001-5472-028X

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