Physiol. Res. 72 (Suppl. 5): S429-S444, 2023 *https://doi.org/10.33549/physiolres.935238*

REVIEW

Sports Activities and Cardiovascular System Change

Petra ŠTURSOVÁ[1], Xenie BUDINSKÁ[1], Zuzana NOVÁKOVÁ[1], Petr DOBŠÁK[2], Petr BABULA[1]

[1]Department of Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic, [2]Department of Sports Medicine and Rehabilitation, Faculty of Medicine and St. Anne´s Faculty Hospital, Masaryk University, Brno, Czech Republic

Received March 31, 2023
Accepted September 24, 2023

Summary

Sports activity is generally considered to be beneficial to health. The World Health Organization (WHO) recommends physical activity as part of a healthy lifestyle. Sports activities significantly affect the cardiovascular system. A number of studies show that they significantly reduce the risk of cardiovascular disease as well as decrease cardiovascular mortality. This review discusses changes in various cardiovascular parameters in athletes – vagotonia/bradycardia, hypertrophy of heart, ECG changes, blood pressure, and variability of cardiovascular parameters. Because of its relationship to the cardiovascular system, VO_{2max}, which is widely used as an indicator of cardiorespiratory fitness, is also discussed. The review concludes with a discussion of reactive oxygen species (ROS) and oxidative stress, particularly in relation to changes in the cardiovascular system in athletes. The review appropriately summarizes the above issues and points out some new implications.

Key words

Sports activity • Hypertrophy • ECG • Variability • Oxidative stress

Corresponding author

P. Babula, Department of Physiology, Faculty of Medicine, Masaryk University, Brno, Kamenice 5, Brno, CZ-625 00, Czech Republic. E-mail: babula@med.muni.cz

Introduction

Sports activity is generally considered beneficial to health. The World Health Organization (WHO) recommends physical activity as a part of the healthy lifestyle. The result of long-term repeated exercise is adaptation, which can be defined as a purposeful change in the organism that leads to an improved level of homeostasis. From a medical point of view the benefits that accompany sports activities include increased resistance to exercise, weight loss, reduction of blood pressure, reduction of low density lipoprotein (LDL), and increase of high density lipoprotein (HDL) cholesterol and increase of insulin sensitivity [1]. The major changes during long-term exercise are in the cardiovascular system, or in the heart itself.

Resting heart rate (HR) values in the normal middle-aged population are around 70 beats per minute. This number decreases with age with minimal gender differences [2]. As exercise intensity increases, HR also increases. This is due to the fact that every exercise is perceived by our organism as a stress and in the basic regulatory patterns we have in this case an increase in sympathetic activity, which by its action accelerates the formation of excitations in the Sinoatrial node. Maximum exercise intensity is performed at maximal HR, which is the same in athletes and non-athletes [3]. This can be estimated from the formula HR_{max} = 220 - age. This would mean that HR_{max} reaches 200 beats/minute in a 20-year-old male. More recent studies have shown that this formula is not accurate and measurements usually yield higher values [4,5]. After exercise, HR returns to baseline values in a few minutes. This time depends on the individual's training and the size/type of the load. With repetitive endurance exercise, adaptive changes

occur, which have been described as the "sports heart" syndrome. These changes are reversible. They are primarily manifested by a decrease in resting HR (bradycardia) and enlarging of the heart by the mechanism of hypertrophy [6].

There are many different kinds of sports. It can be generally separated into three groups: endurance, strength and combined exercise. Endurance sports, also called aerobic sports, are performed at low loads for long period of time. This includes running, swimming or cycling. Strength or resistance sports are characterized by short, intensive muscle contractions that are repetitive, e.g. weightlifting. It is an anaerobic type of activity. We have to take into account that most sports are not strength- or endurance-oriented. Combined sports include both types of actives – aerobic and anaerobic, e.g. cycling, rowing [7].

Vagotonia/Bradycardia

Cardiac vagotonia has previously been reported to be due to the predominance of the parasympathetic nerve (whose fibers are part of the vagus nerve) over the sympathetic nerve and is manifested by a reduction in resting HR. Hence the term "vagotonia". Currently, it is rather considered that the main changes leading to a reduction in resting HR take place in the sinoatrial node [8]. The increase of vagal tone on the heart comes as part of the adaptation processes to exertion, the decrease in HR at rest is considered a physiological adaptation of the body to episodes of strong sympathetic stimulation by intense muscle work during sports. A comparative study showed lower resting HR in athletes (around 58 beats/minute) compared to healthy non-athletes, with values reaching around 76 beats/minute [9]. Values of around 35 beats/minute have been measured in the best endurance runners [10]. On the other hand, reduced resting HR was not found in strength sports [11]. Combined sports may result in a greater reduction in resting heart rate, for example cricketers showed lower resting heart rate (57 beats per minute) than other athletes and non-athletes in one study [12].

Hypertrophy

Cardiac growth is another manifestation of the "athletic heart" syndrome. Hypertrophy can be divided into concentric and eccentric depending on the type of stimulus. Eccentric hypertrophy occurs in endurance sports in which isotonic exercise occurs. This type of sports is characterized by volumetric loading that primarily leads to an increase in the end-diastolic dimension of the left ventricle [13]. At the cellular level, cardiomyocyte elongation occurs; sarcomeres are arranged in series [14,15]. In some athletes, an increase in left ventricular wall thickness above 13 to 15 mm has been observed, which is considered normal [7].

Concentric hypertrophy is observed in strength sports during isometric exercise. Increased pressure load is observed when the heart has to pump blood against greater resistance. Primarily, there is hypertrophy of the cardiac free wall and interventricular septum, accompanied by growth of the cardiac mass. The increase in wall thickness is disproportionate to the size of the ventricle, but the wall thickness is still within normal limits [7]. At the cellular level, sarcomeres are arranged in parallel, leading to thickening of cardiomyocytes [14,15]. In combined sports, both forms of these adaptations occur.

The role of the right ventricle during exercise is often overlooked. It may be essential for proper left ventricular function [16]. The right ventricle responds to endurance training with a balanced increase of volume and mass [17]. The increase in heart rate volume is achieved by different mechanisms in the two ventricles. In the right ventricle, there is an increased contractility and a decrease in end-systolic volume to 10-20 ml with a concomitant increase in ejection fraction. The heart has to accept a larger volume of blood at diastole, hence the left ventricle responds with an increased end-diastolic volume to 150-180 ml. This is responsible for an increase in venous return leading to increased contractility by the so-called Starling effect, increasing the amount of blood ejected. Due to its enlargement, the "athletic heart" can pump the same blood volumes into the bloodstream at lower HR as the heart of an untrained individual. As a result, the energy cost of left ventricular contraction is optimized and the overall cost is reduced [16]. In contrast, strength training leads to an extreme increase in blood pressure.

As a result of ventricular enlargement, systolic volume increases. Resting values of about 86 ml have been measured in swimmers compared to controls with resting values of about 59 ml [18]. Stress values in non-athletes reach about 100 ml, while in trained athletes of about 180 ml [19].

During exercise, cardiac output must increase, despite the shorter filling time due to increased HR. It is

logical that the increase in reservoirs will play an important role in the accelerated filling of the left ventricle. The physiological response during exercise is a reduction of minimal volume in the atria accompanied by increased emptying function [20]. Athletes have larger atrial volumes than non-athletes. Resting values of minute cardiac output are about 5 l/min in men. In women, it is slightly less. At maximal load, the output increases up to 25 l/min. If we take into account the increased heart volume, increased HR and the adaptive changes caused by cardiac hypertrophy, the resulting minute cardiac output may be greater than 35 l/min [21].

Previously, hypertrophy was divided into physiological and pathological hypertrophy, but the term "hypertrophy" means abnormal growth, so hypertrophy cannot be physiological [22]. Pathological hypertrophy is associated with cardiomyocyte loss, cardiac dysfunction, and increased risk of heart failure and sudden death [23,24]. The growth of the heart after birth, in women during pregnancy, and growth caused by regular physical activity was considered physiological. Today, all types of hypertrophy are considered pathological. The structure of the heart is preserved, and functionality is normal or increased. These changes are due to enlargement of cardiomyocytes, not their proliferation. During early postnatal development, cardiomyocytes lose the ability to proliferate and become terminally differentiated. However, there are studies that support the theory of the ability of adult cardiomyocytes to proliferate as a result of regular sports activity [25-27].

Hypertrophy, resulting from sports activity, is accompanied by the formation of new blood vessels in the process of angiogenesis due to hypoxia [28,29]. Sufficient nutrition of the hypertrophied left ventricular musculature is ensured, unlike pathological hypertrophy, in which new blood vessels do not form [30]. In general, these adaptations are considered to be physiological due to the demands of the sport. Unlike hypertension, these changes are not associated with diastolic dysfunction, arrhythmias, or adverse prognosis. After a long-term termination of sports activity, the indicators return to their original values [31].

Heart growth as a result of increased exercise is dependent on many factors including activation of signaling pathways, changes in gene expression, and increases in protein synthesis, including the organization of contractile proteins in sarcomeres [32]. It is also accompanied by an increased capacity of energy production, primarily in the mitochondria.

In animal models, phenotypes associated with hypertrophy have been shown to arise from different stimuli under the activation of different signaling pathways [33]. Genetically engineered mouse models (transgenic, knockout) together with models with different types of hypertrophy (pathological, concentric, eccentric) are powerful tools in such studies [34,35]. Cardiac hypertrophy results from activation of signaling pathways that are triggered through membrane-bound receptors [36-38]. The most used animal models are small rodents like mice and rats, but other models have also been established, for example swine, rabbit and dog models [39]. Larger animals have more similar hearts to humans, but they are more demanding in terms of space and diet, it is very difficult to manipulate them and exercise protocols more complex to implement. The advantages of rodent models are their rapid reaching of adult age (about 2 months), short gestation periods and many offsprings, which leads to cheaper mass production. Although some contractile aspects are different from the human myocardium, structure and grow patterns are well known and are similar to human hearts [40]. To induce cardiac hypertrophy in rodent models, various training schedules are used. Endurance training includes for example treadmill running, voluntary wheel running and swim training. Treadmill running allows for well-controlled and uniform training units [41]. In addition, selected cardiovascular parameters can be reliably monitored. On the other hand, treadmill running requires technical skills and specialized equipment. Experimental animals may experience psychological and physical stress during long-term exercise. It is necessary to mention, that even voluntary exercise induces stress, which seems to be necessary during exercise [42]. The advantages of voluntary wheel training are the minimal technical requirements and activity in a "home environment". On the other hand, the disadvantage is the different length and intensity of the exercise, which can lead to different exercise results [43]. Swim training does not require a lot of space and it can be done with several experimental subjects at once. The question of voluntary training is irrelevant here – if the animal does not swim, it will drown. This is related to the increased stress level due to hypoxia caused by diving and fear of drowning [39].

Resistance training is mainly intended to induce skeletal muscle growth. Various methods have been used for this purpose, for example a model of chronic muscle stretching, compensatory overload and electric stimulation in unconscious rats [44]. More suitable are

models of conscious exercise, where the animal is motivated by a food reward or the movement is stimulated by an electric shock to the tail or leg, but not directly in the muscle tissue [45,46]. A model that mimics squad-training was also created [46]. Today it is the most common used model by many laboratories also in cardiovascular research [47,48].

Usually, two different groups of animals are used in experiments – trained and sedentary. However, these are two extremes, the majority of people are between them and do some sport activity. Other factors that affect the results of experiments are age, sex and strain. It is well known, that younger rats have a higher capacity for cardiomyocyte proliferation [49]. Sex plays an essential role in cardiac growth. Significant differences were observed between males and females mice, with significantly greater gain of heart mass in females [50]. Similarly, differences have been described between strains [51-54]. The final evaluation of the training also has its limitations. Heart growth is assessed in relation to the weight of the individual, but male rats show greater weight loss than females after intensive training [55]. Ultrasound echocardiography has a lower sensitivity and therefore *post mortem* evaluation is preferable.

ECG changes

Electrocardiogram (ECG) is used as a basic diagnostic method in cardiology recording the electrical activity of the heart and excitement conduction, typically used is a modified 12-lead ECG [56].

As mentioned before, athletes have a lower resting HR. This will show up in resting conditions as an extension of the time intervals of each section described on the ECG-RR intervals, QRS complex, QT interval or PQ segment [57]. Even so, in sports medicine there is a diagnosis of sudden cardiac death. Sudden cardiac arrest is the most common cause of death in sports activities [58]. Death can occur as a result of hypertrophic cardiomyopathy (HCM), forms of arrhythmogenic (right ventricular) cardiomyopathy (AVC), ion channel diseases (e.g. Brugada syndrome, long or short QT syndrome), and accessory pathways (e.g. Wolf-Parkinson-White [WPW] syndrome [59-61]. The abnormalities can be hereditary, structural and electrical. This results in an ECG waveform that can be non-standard in up to 50 % of athletes [62]. In general, the greatest abnormalities occur in athletes with the greatest increase in left ventricular cavity size, wall thickness and left atrial dimension [13]. Other indicators are younger age and endurance sport. Changes are also more common in men than in women [10,62]. This may be due to the lower rate of left ventricular remodeling, and also to the lesser involvement of women in sports in which abnormalities are more common.

Sports activity is recommended for the prevention of cardiovascular disease, but atherosclerosis is more common in elite athletes. High-volume and high-intensity training may increase the probability of disease [63-65]. Atherosclerosis is characterized by the formation of plaques: calcified, noncalcified, or mixed (containing both calcified and noncalcified material) with different prognosis. Calcified plaques are associated with best prognosis, mixed plaques are associated with worst prognosis. For endurance sports some studies suggest an increased prevalence of cardiovascular arterial calcification for athletes with the highest weekly workload (more than 2000 min per week vs. less than 1000 min per week) [64]. Another study identifies older age as a risk factor (40 years) [63]. A major risk of strength training is the usage of anabolic steroids, which increase the risk of atherosclerosis [66]. The problem of these studies is the different parameter settings and selection of athletes. Most of them focus on white male athletes. We lack data for female athletes and the race of the athletes needs to be taken into account. In general, sports activity reduces the risk of atherosclerosis. Athletes with a higher workload have a lower biological age of blood vessels of about 30 years [67]. Coronary atherosclerotic plaques are more stable, athletes have a lower incidence of mixed plaques compared to the general population and thus a lower risk of cardiovascular events [64,68].

We must remember that athletes are monitored much more frequently and this may be one reason for the more frequent detection of changes on ECG. We also need to consider which changes are related to the athlete's heart syndrome and are completely physiological, and which changes are classified as pathological. Most diseases remain undetected until a fatal event occurs [69]. For this reason, preventive ECG examinations are recommended. Correct interpretation of the results under the supervision of an experienced specialist is important. The currently valid “International Recommendations for ECG Interpretation in Athletes” date from 2017 [70]. It includes a traffic light that classifies ECG changes into physiological (green), borderline (yellow) and pathological (red).

Blood pressure

When we talk about blood pressure, we are referring to the pressure of blood on the wall of the arteries. Normal systolic/diastolic blood pressure (S/DBP) is 120/80 mm Hg at rest, with the higher number indicating the systolic SBP, i.e. the highest pressure during the ejection phase of the systole of the cardiac cycle. The lowest, diastolic pressure is in the filling phase of the diastole. We speak of hypertension, i.e. high pressure, at values above 140/90 mm Hg, while hypotension (low pressure) is considered to be below 100/65 mm Hg [71,72].

SBP logically depends on the heart rate, which is influenced by the sympathetic system [73-75]. DBP depends on peripheral resistance and does not have a clear answer – the type of load and the person's training play an important role here. Autonomic nervous system (ANS) evaluates the situation and tunes the ratio between sympathetic and parasympathetic activity on the vascular system. If sympathetic tone is increased, peripheral resistance and DBP increase, if sympathetic activity is decreased, peripheral resistance and DBP are lower, or the ratio does not change and DBP remains the same.

Adrenergic receptors (ARs) play a role in blood pressure control. They belong to superfamily of G protein-coupled receptors (GPCR) [76,77]. Nine subtypes of these receptors have been found in humans – three α_1ARs (α_{1A}, α_{1B}, α_{1D}), three α_2ARs (α_{2A}, α_{2B}, α_{2C}) and three βARs (β_1, β_2 and β_3). ARs are expressed in the central nervous system (CNS), in peripheral sympathetic nerves and also in sympathetically innervated tissues throughout the body [78]. Receptors respond to substances from the catecholamine group, specifically norepinephrine (or noradrenaline) and epinephrine (or adrenaline) [79]. Activation of α_1ARs and β_2ARs has the greatest influence on blood pressure control [80]. α_1ARs are located in the smooth muscle cells of blood vessels and their activation leads to smooth muscle contraction and vasoconstriction of peripheral veins and arteries, thereby increasing blood pressure. On the other hand, activation of β_2ARs leads to dilation of blood vessels and blood pressure decreases.

The acute response to exercise is a change in blood pressure depending on the type and intensity of exercise. Systolic pressure which depends on cardiac output increases during dynamic movements [81]. At submaximal intensity, systolic pressure values of over 200 mm Hg can be measured [82]. However, there may be a decrease in diastolic pressure depending on total peripheral resistance. During static exercise, both pressures rise. In terms of short-term effects, decreases in both systolic and diastolic blood pressure have been reported for 8-12 h, independently of exercise intensity [83]. In terms of adaptive changes, endurance athletes show lower systolic blood pressure at rest (110) compared to non-athletes (120) [84]. Exercise 3-5 times per week with exercise intensity between 40-50 % of VO_{2max} was most effective in reducing blood pressure [81]. During extreme strength training (concentric contraction, double-leg press), pressures of 480/350 have been measured in one athlete, and 320/250 mm Hg on average [85].

Variability

Sports activity changes not only cardiovascular parameters (HR, BP) but also their variability. Generally, there are 3 parameters described: heart rate variability (HRV), blood pressure variability (BPV), and baroreflex sensitivity (BRS). HRV, BPV and BRS parameters can be estimated with ECG (heart rate) and blood pressure measurements. Variability of these parameters could be studied in time and frequency domains (power spectrum). These parameters can help us for studying reflex mechanisms of cardiovascular regulation during and after exercise, during training and overtraining, sex differences and effects of aging [86].

In the frequency domain we can find three frequency bands: high frequency band (HF, >0.15 Hz), low frequency band (LF, 0.040.15 Hz), and very low frequency band (VLF, <0.04 Hz). Variability in each frequency band has different origin. HF band is influenced by parasympathetic nervous system [87,89]. Variability of cardiovascular parameters in this band could be given by the respiratory sinus arrhythmia [90]. LF variability is given mainly by sympathetic nervous system (sympatho-sympathetic reflexes) [91]. However, at the same time there could be modulations from another factors or systems: activity of the parasympathetic nervous system (inhibition effect), vasomotor effect, and sensitivity of the effectors. LF aim is to maintain stability of the blood pressure *via* baroreflex regulation [92]. VLF origin is given by changes of the peripheral vasomotor tonus; it could be given by middle/long term changes influencing vascular tonus, i.e. changes in hormonal systems (renin-angiotensin system, cortisol fluctuations), thermoregulatory mechanisms [56,57].

Heart rate variability is measured by the variation in the beat-to-beat interval. Parameters of HRV can be used to determine cardiac sympatho-vagal balance, the relation of sympathetic and parasympathetic nerve activity [95]. Increased sympatho-vagal balance leads to a decrease in HRV, which is associated with higher risks of cardiovascular morbidity and mortality [96,97].

Various studies that evaluated the effect of intense resistance exertion on autonomic modulation shows decrease in HF and increase in LF components of HRV [98-100]. Moreover, HF variability returns to initial/baseline values in 48-72 h [11]. The regular resistant workload does not show the significant changes in HRV [101-103], but despite of that, the post-exercise HR recovery is improved [11]. More complicated HRV changes are given by aerobic exercise. HRV is increased in LF and HF bands in young respondents. It could be explained by higher parasympathetic (vagal) or baroreflex modulation [87]. Nevertheless, for HRV in older respondents (60 years old and older) there are still controversial results: regular aerobic activity causes the increase of the parasympathetic tone [104,105], but at the same time others reported only limited or non-significant improvement of vagal activity [105,106]. Which is why we can suggest that adaptation of the parasympathetic nervous system, and HRV are age-dependent, and they decrease with age.

Blood pressure variability is a phenomenon that characterizes continuous and dynamic fluctuations in blood pressure levels. These fluctuations could be short-term (seconds, minutes), mid-term (24 h or day-to-day), and long-term (months). Some studies have reported associations between BPV and end-organ damage, cardiovascular events or mortality, and it is a strong predictor of stroke, independent of mean BP [107,108]. The most frequently analyzed BPV is mid-term or long-term variability. The studies usually compare two types of the exercises – resistance and aerobic, both in acute and chronical application. Separately chronic resistance workload does not change significantly the BPV, but there is a trend to decrease the SBP [108]. Long-term regular aerobic training leads to decrease the BPV [108,109]. Mixed acute workload causes decrease of BPV with non-changed BP [110], whereas chronic mixed workload leads to opposite results: decreased BP, and non-changed BPV [110,111]. SBP and BP variability are two independent cardiovascular risk factors, where we can see a positive correlation between these parameters and cardiovascular incidences and mortality.

Baroreflex sensitivity is defined as the change in inter-beat interval in milliseconds per unit change in BP. Assessment of baroreflex sensitivity is an established tool to assess autonomic control of the cardiovascular system. Changes in the BRS contribute to the changes in the ratio between parasympathetic and sympathetic activity on behalf of sympathetic activity that leads to the development and progression of cardiovascular disease. Therefore, the estimation/analysis of BRS is a source of valuable information in the clinical management of cardiac disease patients, particularly in risk stratification [112]. In all types of the exercises (acute and chronic, aerobic and resistant) the improvement of BRS were registered [113-116].

VO_{2max}

Transport of oxygen to tissues is one of the main tasks of the cardiovascular system, its consumption increases with exertion. It is important for athletes to use as much of the inspired oxygen as possible. This is referred as VO_{2max}, the maximum volume of oxygen the body is able to use. In simple terms, it tells us how fit the athlete is. The resulting number is given in absolute values – i.e. ml/min or converted to kg of body weight – i.e. ml/kg/min. Many fitness watches present a VO_{2max} measurement function, but the most accurate readings are obtained in laboratory conditions using a spiroergometric test. Resting oxygen consumption values are around 3.5 ml/kg/min. Maximum values for average women are about 35 ml/kg/min and for men about 45 ml/kg/min. In athletes we find another of the adaptive changes, where the average athlete can consume 60 ml/kg/min [9]. This is obviously related to the size and filling of the left ventricle.

Oxidative stress

In the following section, we will focus on general characteristics and mainly on endurance sports. The heart needs a constant supply of energy to contract and distribute oxygen and nutrients throughout the body. In a healthy heart, fatty acid oxidation is responsible for 60-70 % of ATP production [117]. Glucose and lactate metabolism is responsible for the remaining 30 % of ATP synthesis. The heart is able to switch between substrates depending on the type of activity performed and the concentration of source molecules in the

bloodstream. This mechanism ensures a constant energy supply under different physiological conditions. During exercise, fatty acid oxidation increases, the ratio of glucose oxidation versus glycolysis increases, and ATP production increases. In the diseased heart, the opposite is the case; in addition, proton production increases and overall efficiency decreases [118].

Mitochondria have an irreplaceable role in cells. They cover energy requirements, provide energy metabolism of the cell along with cellular respiration, calcium homeostasis, contractility of cardiac cells, produce and scavenge reactive oxygen species (ROS), participate in nuclear gene expression and regulate cell death [32]. Unlike normal cells, mitochondria in cardiomyocytes are uniform in size and are nested between contractile elements [119]. The number and size of mitochondria is determined by their fusion and fission. If the balance between fusion and fission is disrupted, cardiovascular and other diseases can arise [120]. Regular aerobic training in rats after myocardial infarction alters the ratios of proteins associated with fusion – mitofusin 2 (mfn2) and optic athrophy 1 (OPA1) or fission – dynamin-related protein 1 (DRP1), preventing a decrease in mfn2+OPA1 and an increase in DRP1 [121]. Mitochondrial fragmentation is not only associated with pathological conditions, it is essential in the physiological regulation of mitochondrial function during stressful conditions such as exercise at submaximal intensity [122]. Physiological mitochondrial fission improves mitochondrial functionality, deactivates mitophagy (mitochondrial autophagy) and is essential for maximal performance. However, autophagy of mitochondria is also essential to maintain their quality [123]. ROS are generated as a product of mitochondrial activity, specifically oxidative phosphorylation. They can also be produced by interaction with external sources such as xenobiotic compounds. These include the superoxide anion ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2) and the hydroxyl radical ($HO^{\bullet}$). When the production of ROS overwhelms the antioxidant capacity of the cell, oxidative stress occurs, which can lead to many diseases such as atherosclerosis, diabetes, cancer, neurodegenerative diseases, and to aging [124-127]. When ROS are overproduced, their potentially harmful effects are removed by sophisticated mechanisms such as their neutralization by antioxidant substances (e.g. reduced thiols, vitamins A and E, catecholamines) or enzymes (e.g. superoxide dismutase, peroxidase, catalase, glutathione reductase) that are synthesized in the body [128]. Paradoxically, ROS serve as essential signaling molecules in cell proliferation and survival. They are involved in the regulation of essential signaling pathways [129].

During exercise, muscles experience increased metabolic demands, which are compensated by an increase in oxygen uptake, increasing blood flow to the muscles. Oxidative stress markers are elevated after aerobic exercise [130,131]. With faster metabolism, more ROS are produced in skeletal muscle and other tissues and organs [132]. ROS production after exercise has been found to be lower in the heart than in the liver and skeletal muscle [133]. Indeed, the concentration of ROS in ventricular cardiomyocytes is tightly regulated. The increase is compensated by an increase in ROS degradation. This may have beneficial effects on the heart [134]. Indeed, in the recovery phase, upregulation of antioxidant defense mechanisms and other adaptive changes occur. It has been found that 10-day treadmill training in rats reduces ROS production, specifically H_2O_2, the potential on mitochondrial membranes is better maintained and redox homeostasis is preserved [135]. These changes protect the heart of trained individuals from arrhythmias. For strength training, the results of studies are inconsistent. Some studies show measurable increased oxidative stress, others have seen no effect after exercise [136,137,130,131]. Oxidative stress in this case is probably dependent on training intensity [138]. After long-term exercise, oxidative capacity is unchanged after strength training [139].

In combined sports, there is an increase in oxidative stress after exercise and after long-term exercise, oxidative capacity is increased [140,141].

Conclusions

A sedentary lifestyle brings many disadvantages, the most common of which are the risk of high blood pressure, skeletal muscle wasting, obesity, atherosclerosis or myocardial infarction, which can lead to premature death. Through regular sports activity, we can reduce many of these risks. However, it also depends on the type of sport and the amount of time the sport is performed. Although the classic division into endurance training and strength training is generally accepted, it is far more common to combine both types of sporting activity in different proportions. Long-term and regular sports activity leads to changes in the cardiovascular system primarily manifested by bradycardia (mainly in the case

of endurance training) and hypertrophy. Reduced resting HR may be related to improved VO_{2max} in athletes. A direct relationship between these two variables has been found [142,143]. In addition to the aforementioned, bradycardia may be considered in relation to the type of cardiac hypertrophy [144]. Other factors may also be involved in cardiac remodeling. Among genetic factors, attention has been drawn to polymorphisms in angiotensinogen and angiotensin-converting enzyme (ACE) [145]. In addition, polymorphisms in the IGF-1 (insulin-like growth factor), IGF-1 receptor and myostatin genes have been implicated [146]. Exercise is a known strategy to cope with oxidative stress, however the relationships between them are very complicated depending on the mode, intensity and duration of exercise [147]. Aerobic training is the most widely used type of exercise across studies [148]. It appears to be a suitable activity for improving redox balance, increasing the efficiency of antioxidant defensive mechanisms, leading to an increased capacity for ROS scavenging in the mitochondria [149]. In terms of strength training, there are no consistent results, however, across studies, moderate improvements in redox balance or no changes have been observed [148]. This happens as a result of differently chosen training methods, be it the number of repetitions of a given exercise, the number of sets or rest intervals. In the future, it would be necessary to standardize the training protocols to obtain relevant data.

Conflict of Interest

There is no conflict of interest.

Acknowledgements

This work was supported by grant of Ministry of Education, Youth and Sports – Specific university research MUNI/A/1343/2022: "Loads on the cardiovascular system from A to Z".

References

1. Myers J. Exercise and Cardiovascular Health. Circulation 2003;107:e2-5. https://doi.org/10.1161/01.CIR.0000048890.59383.8D
2. Garavaglia L, Gulich D, Defeo MM, Thomas Mailland J, Irurzun IM. The effect of age on the heart rate variability of healthy subjects. PLoS One 2021;16:e0255894. https://doi.org/10.1371/journal.pone.0255894
3. Stickland MK, Welsh RC, Petersen SR, Tyberg JV, Anderson VD, Jones RL, Taylor DA, ET AL. Does fitness level modulate the cardiovascular hemodynamic response to exercise? J Appl Physiol 2006;100:1895-1901. https://doi.org/10.1152/japplphysiol.01485.2005
4. Støylen A, Nes B, Karlsen T. Maksimal forventet hjertefrekvens. Tidsskr Den Nor Legeforening 2012;132:1729-1729. https://doi.org/10.4045/tidsskr.12.0503
5. Nes BM, Janszky I, Wisløff U, Støylen A, Karlsen T. Age-predicted maximal heart rate in healthy subjects: The HUNT Fitness Study: Maximal heart rate in a population. Scand J Med Sci Sports 2013;23:697-704. https://doi.org/10.1111/j.1600-0838.2012.01445.x
6. Maron BJ. Structural features of the athlete heart as defined by echocardiography. J Am Coll Cardiol 1986;7:190-203. https://doi.org/10.1016/S0735-1097(86)80282-0
7. Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The Upper Limit of Physiologic Cardiac Hypertrophy in Highly Trained Elite Athletes. N Engl J Med 1991;324:295-301. https://doi.org/10.1056/NEJM199101313240504
8. D'Souza A, Sharma S, Boyett MR. CrossTalk opposing view: Bradycardia in the trained athlete is attributable to a downregulation of a pacemaker channel in the sinus node. J Physiol 2015;593:1749-1751. https://doi.org/10.1113/jphysiol.2014.284356
9. Shin K, Minamitani H, Onishi S, Yamazaki H, Lee M. Assessment of Training-Induced Autonomic Adaptations in Athletes with Spectral Analysis of Cardiovascular Variability Signals. Jpn J Physiol 1995;45:1053-1069. https://doi.org/10.2170/jjphysiol.45.1053
10. Gademan MG, Uberoi A, Le VV, Mandic S, Van Oort ER, Myers J, Froelicher VF. The effect of sport on computerized electrocardiogram measurements in college athletes. Eur J Prev Cardiol 2012;19:126-138. https://doi.org/10.1177/1741826710392669
11. Kingsley JD, Figueroa A. Acute and training effects of resistance exercise on heart rate variability. Clin Physiol Funct Imaging 2016;36:179-187. https://doi.org/10.1111/cpf.12223

12. Biswas S. A Study on Resting Heart Rate and Heart Rate Variability of Athletes, Non-athletes and Cricketers. Am J Sports Sci 2020;8:95. https://doi.org/10.11648/j.ajss.20200804.13
13. Pelliccia A, Maron BJ, Culasso F, Di Paolo M, Spataro A, Biffi A, Caselli G, Piovano P. Clinical Significance of Abnormal Electrocardiographic Patterns in Trained Athletes. Circulation 2000;102:278-284. https://doi.org/10.1161/01.CIR.102.3.278
14. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975;56:56-64. https://doi.org/10.1172/JCI108079
15. Bernardo BC, McMullen JR. Molecular Aspects of Exercise-induced Cardiac Remodeling. Cardiol Clin 2016;34:515-530. https://doi.org/10.1016/j.ccl.2016.06.002
16. Ruijsink B, Velasco Forte MN, Duong P, Asner L, Pushparajah K, Frigiola A, Nordsletten D, Razavi R. Synergy in the heart: RV systolic function plays a key role in optimizing LV performance during exercise. Am J Physiol Heart Circ Physiol 2020;319:H642-H650. https://doi.org/10.1152/ajpheart.00256.2020
17. Arbab-Zadeh A, Perhonen M, Howden E, Peshock RM, Zhang R, Adams-Huet B, Haykowsky MJ, Levine BD. Cardiac Remodeling in Response to 1 Year of Intensive Endurance Training. Circulation 2014;130:2152-2161. https://doi.org/10.1161/CIRCULATIONAHA.114.010775
18. Wasfy MM, Weiner RB, Wang F, Berkstresser B, Deluca J, Hutter AM Jr, Picard MH, Baggish AL. Myocardial Adaptations to Competitive Swim Training. Med Sci Sports Exerc 2019;51:1987-1994. https://doi.org/10.1249/MSS.0000000000002022
19. Vella CA. A review of the stroke volume response to upright exercise in healthy subjects. Br J Sports Med 2005;39:190-195. https://doi.org/10.1136/bjsm.2004.013037
20. Schnell F, Claessen G, La Gerche A, Claus P, Bogaert J, Delcroix M, Carré F, Heidbuchel H. Atrial volume and function during exercise in health and disease. J Cardiovasc Magn Reson 2017;19:104. https://doi.org/10.1186/s12968-017-0416-9
21. Schlader ZJ, Mündel T, Barnes MJ, Hodges LD. Peak cardiac power output in healthy, trained men: CPO peak in healthy, trained men. Clin Physiol Funct Imaging 2010;30:480-484. https://doi.org/10.1111/j.1475-097X.2010.00959.x
22. Rakusan K, Ostadal B. "Physiological hypertrophy of the heart" is a misnomer. Curr Res Cardiol 2016;3:32. https://doi.org/10.4172/2368-0512.1000060
23. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic Implications of Echocardiographically Determined Left Ventricular Mass in the Framingham Heart Study. N Engl J Med 1990;322:1561-1566. https://doi.org/10.1056/NEJM199005313222203
24. Cohn JN, Bristow MR, Chien KR, Colucci WS, Frazier OH, Leinwand LA, Lorell BH, ET AL. Report of the National Heart, Lung, and Blood Institute Special Emphasis Panel on Heart Failure Research. Circulation 1997;95:766-770. https://doi.org/10.1161/01.CIR.95.4.766
25. Bergmann O, Bhardwaj RD, Bernard S, Zdunek S, Barnabé-Heider F, Walsh S, Zupicich J, ET AL. Evidence for Cardiomyocyte Renewal in Humans. Science 2009;324:98-102. https://doi.org/10.1126/science.1164680
26. Senyo SE, Steinhauser ML, Pizzimenti CL, Yang VK, Cai L, Wang M, Wu T-D, ET AL. Mammalian heart renewal by pre-existing cardiomyocytes. Nature 2013;493:433-436. https://doi.org/10.1038/nature11682
27. Bergmann O, Zdunek S, Felker A, Salehpour M, Alkass K, Bernard S, Sjostrom SL, ET AL. Dynamics of Cell Generation and Turnover in the Human Heart. Cell 2015;161:1566-1575. https://doi.org/10.1016/j.cell.2015.05.026
28. Shweiki D, Itin A, Soffer D, Keshet E. Vascular endothelial growth factor induced by hypoxia may mediate hypoxia-initiated angiogenesis. Nature 1992;359:843-845. https://doi.org/10.1038/359843a0
29. Bloor CM. Angiogenesis during exercise and training. Angiogenesis 2005;8:263-271. https://doi.org/10.1007/s10456-005-9013-x
30. Oláh A, Németh BT, Mátyás C, Hidi L, Lux Á, Ruppert M, Kellermayer D, ET AL. Physiological and pathological left ventricular hypertrophy of comparable degree is associated with characteristic differences of in vivo hemodynamics. Am J Physiol Heart Circ Physiol 2016;310:H587-H597. https://doi.org/10.1152/ajpheart.00588.2015
31. Lattanzi F, Di Bello V, Picano E, Caputo MT, Talarico L, Di Muro C, Landini L, ET AL. Normal ultrasonic myocardial reflectivity in athletes with increased left ventricular mass. A tissue characterization study. Circulation 1992;85:1828-1834. https://doi.org/10.1161/01.CIR.85.5.1828

32. Bernardo BC, Ooi JYY, Weeks KL, Patterson NL, McMullen JR. Understanding Key Mechanisms of Exercise-Induced Cardiac Protection to Mitigate Disease: Current Knowledge and Emerging Concepts. Physiol Rev 2018;98:419-475. https://doi.org/10.1152/physrev.00043.2016
33. Gupta S, Sen S. Animal Models for Heart Failure. In: *Cardiovascular Disease, Volume 2: Molecular Medicine*. WANG QK (ed.), Vol 129, Humana Press, 2006, pp 97-114. https://doi.org/10.1385/1-59745-213-0:97
34. McMullen JR, Shioi T, Zhang L, Tarnavski O, Sherwood MC, Kang PM, Izumo S. Phosphoinositide 3-kinase(p110α) plays a critical role for the induction of physiological, but not pathological, cardiac hypertrophy. Proc Natl Acad Sci U S A 2003;100:12355-12360. https://doi.org/10.1073/pnas.1934654100
35. McMullen JR, Shioi T, Zhang L, Tarnavski O, Sherwood MC, Dorfman AL, Longnus S, ET AL. Deletion of ribosomal S6 kinases does not attenuate pathological, physiological, or insulin-like growth factor 1 receptor-phosphoinositide 3-kinase-induced cardiac hypertrophy. Mol Cell Biol 2004;24:6231-6240. https://doi.org/10.1128/MCB.24.14.6231-6240.2004
36. Kim J, Wende AR, Sena S, Theobald HA, Soto J, Sloan C, Wayment BE, ET AL. Insulin-like growth factor I receptor signaling is required for exercise-induced cardiac hypertrophy. Mol Endocrinol 2008;22:2531-2543. https://doi.org/10.1210/me.2008-0265
37. Ikeda H, Shiojima I, Ozasa Y, Yoshida M, Holzenberger M, Kahn CR, Walsh K, ET AL. Interaction of myocardial insulin receptor and IGF receptor signaling in exercise-induced cardiac hypertrophy. J Mol Cell Cardiol 2009;47:664-675. https://doi.org/10.1016/j.yjmcc.2009.08.028
38. Riehle C, Wende AR, Zhu Y, Oliveira KJ, Pereira RO, Jaishy BP, Bevins J, ET AL. Insulin Receptor Substrates Are Essential for the Bioenergetic and Hypertrophic Response of the Heart to Exercise Training. Mol Cell Biol 2014;34:3450-3460. https://doi.org/10.1128/MCB.00426-14
39. Wang Y, Wisloff U, Kemi O. Animal models in the study of exercise-induced cardiac hypertrophy. Physiol Res 2010;59:633-644. https://doi.org/10.33549/physiolres.931928
40. Hasenfuss G. Animal models of human cardiovascular disease, heart failure and hypertrophy. Cardiovasc Res 1998;39:60-76. https://doi.org/10.1016/S0008-6363(98)00110-2
41. Høydal MA, Wisløff U, Kemi OJ, Ellingsen Ø. Running speed and maximal oxygen uptake in rats and mice: practical implications for exercise training. Eur J Cardiovasc Prev Rehabil 2007;14:753-760. https://doi.org/10.1097/HJR.0b013e3281eacef1
42. Droste SK, Chandramohan Y, Hill LE, Linthorst ACE, Reul JMHM. Voluntary Exercise Impacts on the Rat Hypothalamic-Pituitary-Adrenocortical Axis Mainly at the Adrenal Level. Neuroendocrinology 2007;86:26-37. https://doi.org/10.1159/000104770
43. Lambert MI, Van Zyl C, Jaunky R, Lambert EV, Noakes TD. Tests of running performance do not predict subsequent spontaneous running in rats. Physiol Behav 1996;60:171-176. https://doi.org/10.1016/0031-9384(96)00012-1
44. Melo SFS, Júnior NDS, Baraúna VG, Oliveira EM. Cardiovascular Adaptations Induced by Resistance Training in Animal Models. Int J Med Sci 2018;15:403-410. https://doi.org/10.7150/ijms.23150
45. Nicastro H, Zanchi NE, Da Luz CR, Chaves DFS, Lancha AH. An Experimental Model for Resistance Exercise in Rodents. J Biomed Biotechnol 2012;2012:1-7. https://doi.org/10.1155/2012/457065
46. Tamaki T, Uchiyama S, Nakano S. A weight-lifting exercise model for inducing hypertrophy in the hindlimb muscles of rats. Med Sci Sports Exerc 1992;24:881-886. https://doi.org/10.1249/00005768-199208000-00009
47. Barauna VG, Junior MLB, Costa Rosa LFB, Casarini DE, Krieger JE, Oliveira EM. CARDIOVASCULAR ADAPTATIONS IN RATS SUBMITTED TO A RESISTANCE-TRAINING MODEL. Clin Exp Pharmacol Physiol 2005;32:249-254. https://doi.org/10.1111/j.1440-1681.2005.04180.x
48. de Araujo AJS, dos Santos ACV, dos Santos Souza K, Aires MB, Santana-Filho VJ, Fioretto ET, Mota MM, Santos MRV. Resistance training controls arterial blood pressure in rats with L-NAME-induced hypertension. (Article in English, Portuguese) Arq Bras Cardiol 2013;100:339-346. https://doi.org/10.5935/abc.20130051
49. Rosa EF, Silva AC, Ihara SSM, Mora OA, Aboulafia J, Nouailhetas VLA. Habitual exercise program protects murine intestinal, skeletal, and cardiac muscles against aging. J Appl Physiol 2005;99:1569-1575. https://doi.org/10.1152/japplphysiol.00417.2005

50. Konhilas JP, Maass AH, Luckey SW, Stauffer BL, Olson EN, Leinwand LA. Sex modifies exercise and cardiac adaptation in mice. Am J Physiol Heart Circ Physiol 2004;287:H2768-H2776. https://doi.org/10.1152/ajpheart.00292.2004
51. Barbato JC, Koch LG, Darvish A, Cicila GT, Metting PJ, Britton SL. Spectrum of aerobic endurance running performance in eleven inbred strains of rats. J Appl Physiol 1998;85:530-536. https://doi.org/10.1152/jappl.1998.85.2.530
52. Koch LG, Britton SL, Barbato JC, Rodenbaugh DW, DiCARLO SE. Phenotypic differences in cardiovascular regulation in inbred rat models of aerobic capacity. Physiol Genomics 1999;1:63-69. https://doi.org/10.1152/physiolgenomics.1999.1.2.63
53. Lerman I, Harrison BC, Freeman K, Hewett TE, Allen DL, Robbins J, Leinwand LE. Genetic variability in forced and voluntary endurance exercise performance in seven inbred mouse strains. J Appl Physiol (1985) 2002;92:2245-2255. https://doi.org/10.1152/japplphysiol.01045.2001
54. Kilikevicius A, Venckunas T, Zelniene R, Carroll AM, Lionikaite S, Ratkevicius A, Lionikas A. Divergent physiological characteristics and responses to endurance training among inbred mouse strains: Training and genetic effects in mice. Scand J Med Sci Sports 2013;23:657-668. https://doi.org/10.1111/j.1600-0838.2012.01451.x
55. Pitts GC. Body composition in the rat: interactions of exercise, age, sex, and diet. Am J Physiol Regul Integr Comp Physiol 1984;246:R495-R501. https://doi.org/10.1152/ajpregu.1984.246.4.R495
56. Mason RE, Likar I. A new system of multiple-lead exercise electrocardiography. Am Heart J 1966;71:196-205. https://doi.org/10.1016/0002-8703(66)90182-7
57. Trachsel LD, Wilhelm M. Das Elektrokardiogramm des Sporttreibenden und der Sport-assoziierte plötzliche Herztod: The athletes' ECG and the exercise related sudden cardiac death. Ther Umsch 2015;72:303-309. https://doi.org/10.1024/0040-5930/a000680
58. Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of Sudden Cardiac Death in National Collegiate Athletic Association Athletes. Circulation 2011;123:1594-1600. https://doi.org/10.1161/CIRCULATIONAHA.110.004622
59. Drezner JA, Sharma S, Wilson MG. Sports cardiology: preventing sudden cardiac death. Br J Sports Med 2014;48:1133-1133. https://doi.org/10.1136/bjsports-2014-093922
60. Marijon E, Uy-Evanado A, Reinier K, Teodorescu C, Narayanan K, Jouven X, Gunson K, ET AL. Sudden Cardiac Arrest During Sports Activity in Middle Age. Circulation 2015;131:1384-1391. https://doi.org/10.1161/CIRCULATIONAHA.114.011988
61. Finocchiaro G, Papadakis M, Robertus JL, Dhutia H, Steriotis AK, Tome M, Mellor G, ET AL. Etiology of Sudden Death in Sports. J Am Coll Cardiol 2016;67:2108-2115. https://doi.org/10.1016/j.jacc.2016.02.062
62. Karagjozova I, Petrovska S, Nikolic S, Maleska-Ivanovska V, Georgievska-Ismail L. Frequency of Electrocardiographic Changes in Trained Athletes in the Republic of Macedonia. Open Access Maced J Med Sci 2017;5:708-713. https://doi.org/10.3889/oamjms.2017.174
63. Mohlenkamp S, Lehmann N, Breuckmann F, Bröcker-Preuss M, Nassenstein K, Halle M, Budde T, ET AL. Running: the risk of coronary events : Prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. Eur Heart J 2008;29:1903-1910. https://doi.org/10.1093/eurheartj/ehn163
64. Aengevaeren VL, Mosterd A, Braber TL, Prakken NHJ, Doevendans PA, Grobbee DE, Thompson PD, ET AL. Relationship Between Lifelong Exercise Volume and Coronary Atherosclerosis in Athletes. Circulation 2017;136:138-148. https://doi.org/10.1161/CIRCULATIONAHA.117.027834
65. Merghani A, Maestrini V, Rosmini S, Cox AT, Dhutia H, Bastiaenan R, David S, ET AL. Prevalence of Subclinical Coronary Artery Disease in Masters Endurance Athletes With a Low Atherosclerotic Risk Profile. Circulation 2017;136:126-137. https://doi.org/10.1161/CIRCULATIONAHA.116.026964
66. Santora LJ, Marin J, Vangrow J, Minegar C, Robinson M, Mora J, Friede G. Coronary Calcification in Body Builders Using Anabolic Steroids. Prev Cardiol 2006;9:198-201. https://doi.org/10.1111/j.1559-4564.2006.05210.x
67. Shibata S, Levine BD. Biological aortic age derived from the arterial pressure waveform. J Appl Physiol 2011;110:981-987. https://doi.org/10.1152/japplphysiol.01261.2010

68. Nerlekar N, Ha FJ, Cheshire C, Rashid H, Cameron JD, Wong DT, Seneviratne S, Brown AJ. Computed Tomographic Coronary Angiography-Derived Plaque Characteristics Predict Major Adverse Cardiovascular Events: A Systematic Review and Meta-Analysis. Circ Cardiovasc Imaging 2018;11:e006973. https://doi.org/10.1161/CIRCIMAGING.117.006973
69. Maron BJ. Sudden Death in Young Competitive Athletes: Clinical, Demographic, and Pathological Profiles. JAMA 1996;276:199. https://doi.org/10.1001/jama.1996.03540030033028
70. Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, ET AL. International Recommendations for Electrocardiographic Interpretation in Athletes. J Am Coll Cardiol 2017;69:1057-1075. https://doi.org/10.1016/j.jacc.2017.01.015
71. Walker HK, Hall WD, Hurst JW. *Clinical Methods: The History, Physical, and Laboratory Examinations. Third Edition*. Butterworths, 1990. Accessed January 26, 2023. http://www.ncbi.nlm.nih.gov/books/NBK201/
72. Al-Makki A, DiPette D, Whelton PK, Murad MH, Mustafa RA, Acharya S, Beheiry HM, ET AL. Hypertension Pharmacological Treatment in Adults: A World Health Organization Guideline Executive Summary. Hypertension 2022;79:293-301. https://doi.org/10.1161/HYPERTENSIONAHA.121.18192
73. Charkoudian N, Rabbitts JA. Sympathetic neural mechanisms in human cardiovascular health and disease. Mayo Clin Proc 2009;84:822-830. https://doi.org/10.4065/84.9.822
74. Joyner MJ, Charkoudian N, Wallin BG. Sympathetic nervous system and blood pressure in humans: individualized patterns of regulation and their implications. Hypertens Dallas Tex 1979 2010;56:10-16. https://doi.org/10.1161/HYPERTENSIONAHA.109.140186
75. Berg T, Jensen J. Simultaneous parasympathetic and sympathetic activation reveals altered autonomic control of heart rate, vascular tension, and epinephrine release in anesthetized hypertensive rats. Front Neurol 2011;2:71. https://doi.org/10.3389/fneur.2011.00071
76. Bylund DB, Eikenberg DC, Hieble JP, Langer SZ, Lefkowitz RJ, Minneman KP, Molinoff PB, ET AL. International Union of Pharmacology nomenclature of adrenoceptors. Pharmacol Rev 1994;46:121-136.
77. Hieble JP, Bylund DB, Clarke DE, Eikenburg DC, Langer SZ, Lefkowitz RJ, Minneman KP, Ruffolo RR Jr. International Union of Pharmacology. X. Recommendation for nomenclature of alpha 1-adrenoceptors: consensus update. Pharmacol Rev 1995;47:267-270.
78. Perez DM. *The Adrenergic Receptors: In the 21st Century.* Humana Press, 2006, 404 p. https://doi.org/10.1385/1592599311
79. Ciccarelli M, Santulli G, Pascale V, Trimarco B, Iaccarino G. Adrenergic receptors and metabolism: role in development of cardiovascular disease. Front Physiol 2013;4:265. https://doi.org/10.3389/fphys.2013.00265
80. Motiejunaite J, Amar L, Vidal-Petiot E. Adrenergic receptors and cardiovascular effects of catecholamines. Ann Endocrinol 2021;82:193-197. https://doi.org/10.1016/j.ando.2020.03.012
81. Fagard RH. Exercise characteristics and the blood pressure response to dynamic physical training: Med Sci Sports Exerc 2001;33(Supplement):S484-S492. https://doi.org/10.1097/00005768-200106001-00018
82. Wielemborek-Musial K, Szmigielska K, Leszczynska J, Jegier A. Blood Pressure Response to Submaximal Exercise Test in Adults. BioMed Res Int 2016;2016:1-8. https://doi.org/10.1155/2016/5607507
83. Pescatello LS, Fargo AE, Leach CN, Scherzer HH. Short-term effect of dynamic exercise on arterial blood pressure. Circulation 1991;83:1557-1561. https://doi.org/10.1161/01.CIR.83.5.1557
84. Mittal S, Jaiswal MK. Pathophysiology of Cardiac Output in Athletes and Non-Athletes. J Adv Med Dent Sci Res 2018;6:56-58.
85. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. J Appl Physiol (1985) 1985;58:785-790. https://doi.org/10.1152/jappl.1985.58.3.785
86. Aubert AE, Seps B, Beckers F. Heart rate variability in athletes. Sports Med Auckl NZ 2003;33:889-919. https://doi.org/10.2165/00007256-200333120-00003
87. Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science 1981;213:220-222. https://doi.org/10.1126/science.6166045

88. Japundzic N, Grichois ML, Zitoun P, Laude D, Elghozi JL. Spectral analysis of blood pressure and heart rate in conscious rats: effects of autonomic blockers. J Auton Nerv Syst 1990;30:91-100. https://doi.org/10.1016/0165-1838(90)90132-3
89. Izraeli S, Alcalay M, Benjamini Y, Wallach-Kapon R, Tochner Z, Akselrod S. Modulation of the dose-dependent effects of atropine by low-dose pyridostigmine: quantification by spectral analysis of heart rate fluctuations in healthy human beings. Pharmacol Biochem Behav 1991;39:613-617. https://doi.org/10.1016/0091-3057(91)90136-P
90. Perini R, Veicsteinas A. Heart rate variability and autonomic activity at rest and during exercise in various physiological conditions. Eur J Appl Physiol 2003;90:317-325. https://doi.org/10.1007/s00421-003-0953-9
91. Tonhajzerová I, Javorka K. Evaluation of heart rate variability and its usefulness. (Article in Slovak) Cesk Fysiol 2000;49:51-60.
92. Sayers BM. Analysis of heart rate variability. Ergonomics 1973;16:17-32. https://doi.org/10.1080/00140137308924479
93. Javorka K, Javorková J, Petrásková M, Tonhajzerová I, Buchanec J, Chromá O. Heart rate variability and cardiovascular tests in young patients with diabetes mellitus type 1. J Pediatr Endocrinol Metab JPEM 1999;12:423-431. https://doi.org/10.1515/JPEM.1999.12.3.423
94. Kawamoto M, Kaneko K, Hardian, Yuge O. Heart rate variability during artificial ventilation and apnea in brain-damaged rabbits. Am J Physiol 1996;271:H410-H416. https://doi.org/10.1152/ajpheart.1996.271.2.H410
95. Wong A, Figueroa A. Effects of Acute Stretching Exercise and Training on Heart Rate Variability: A Review. J Strength Cond Res 2021;35:1459-1466. https://doi.org/10.1519/JSC.0000000000003084
96. Pal GK, Adithan C, Ananthanarayanan PH, Pal P, Nanda N, Durgadevi T, Lalitha V, ET AL. Sympathovagal imbalance contributes to prehypertension status and cardiovascular risks attributed by insulin resistance, inflammation, dyslipidemia and oxidative stress in first degree relatives of type 2 diabetics. PLoS One 2013;8:e78072. https://doi.org/10.1371/journal.pone.0078072
97. Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. Int J Cardiol 2010;141:122-131. https://doi.org/10.1016/j.ijcard.2009.09.543
98. Chen JL, Yeh DP, Lee JP, Chen C-Y, Huang C-Y, Lee S-D, Chen C-C, ET AL. Parasympathetic nervous activity mirrors recovery status in weightlifting performance after training. J Strength Cond Res 2011;25:1546-1552. https://doi.org/10.1519/JSC.0b013e3181da7858
99. Heffernan KS, Sosnoff JJ, Jae SY, Gates GJ, Fernhall B. Acute resistance exercise reduces heart rate complexity and increases QTc interval. Int J Sports Med 2008;29:289-293. https://doi.org/10.1055/s-2007-965363
100. Kingsley JD, Hochgesang S, Brewer A, Buxton E, Martinson M, Heidner G. Autonomic modulation in resistance-trained individuals after acute resistance exercise. Int J Sports Med 2014;35:851-856. https://doi.org/10.1055/s-0034-1371836
101 Karavirta L, Tulppo MP, Laaksonen DE, Nyman K, Laukkanen RT, Kinnunen H, Häkkinen A, Häkkinen K. Heart rate dynamics after combined endurance and strength training in older men. Med Sci Sports Exerc 2009;41:1436-1443. https://doi.org/10.1249/MSS.0b013e3181994a91
102. Wanderley FAC, Moreira A, Sokhatska O, Palmares C, Moreira P, Sandercock G, Oliveira J, Carvalho J. Differential responses of adiposity, inflammation and autonomic function to aerobic versus resistance training in older adults. Exp Gerontol 2013;48:326-333. https://doi.org/10.1016/j.exger.2013.01.002
103. Kingsley JD, McMillan V, Figueroa A. The effects of 12 weeks of resistance exercise training on disease severity and autonomic modulation at rest and after acute leg resistance exercise in women with fibromyalgia. Arch Phys Med Rehabil 2010;91:1551-1557. https://doi.org/10.1016/j.apmr.2010.07.003
104. Levy WC, Cerqueira MD, Harp GD, Johannessen KA, Abrass IB, Schwartz RS, Stratton JR. Effect of endurance exercise training on heart rate variability at rest in healthy young and older men. Am J Cardiol 1998;82:1236-1241. https://doi.org/10.1016/S0002-9149(98)00611-0
105. Raffin J, Barthélémy JC, Dupré C, Pichot V, Berger M, Féasson L, Busso T. Exercise Frequency Determines Heart Rate Variability Gains in Older People: A Meta-Analysis and Meta-Regression. Sports Med 2019;49:719-729. https://doi.org/10.1007/s40279-019-01097-7

106. Verheyden B, Eijnde BO, Beckers F, Vanhees L, Aubert AE. Low-dose exercise training does not influence cardiac autonomic control in healthy sedentary men aged 55-75 years. J Sports Sci 2006;24:1137-1147. https://doi.org/10.1080/02640410500497634
107. Asayama K, Schutte R, Li Y, Hansen TW, Staessen JA. Blood pressure variability in risk stratification: What does it add? Clin Exp Pharmacol Physiol 2014;41:1-8. https://doi.org/10.1111/1440-1681.12091
108. Seidel M, Pagonas N, Seibert FS, Bauer F, Rohn B, Vlatsas S, Mühlberger D, ET AL. The differential impact of aerobic and isometric handgrip exercise on blood pressure variability and central aortic blood pressure. J Hypertens 2021;39:1269-1273. https://doi.org/10.1097/HJH.0000000000002774
109. Chehuen M da R, Cucato GG, de Carvalho CRF, Zerati AE, Leicht A, Wolosker N, Ritti-Dias RM, de Moraes Forjaz CL. Walking Training Improves Ambulatory Blood Pressure Variability in Claudication. (Article in English, Portuguese) Arq Bras Cardiol 2021;116:898-905. https://doi.org/10.36660/abc.20190822
110. Matias LAS, Mariano IM, Batista JP, de Souza TCF, Amaral AL, Dechichi JGC, de Lima Rodrigues M, ET AL. Acute and chronic effects of combined exercise on ambulatory blood pressure and its variability in hypertensive postmenopausal women. Chin J Physiol 2020;63:227-234. https://doi.org/10.4103/CJP.CJP_61_20
111. Mariano IM, Dechichi JGC, Matias LAS, de Lima Rodrigues M, Batista JP, de Souza TCF, Amaral AL, ET AL. Ambulatory blood pressure variability and combined exercise training: comparison between hypertensive and normotensive postmenopausal women. Blood Press Monit 2020;25:338-345. https://doi.org/10.1097/MBP.0000000000000480
112. La Rovere MT, Pinna GD, Raczak G. Baroreflex sensitivity: measurement and clinical implications. Ann Noninvasive Electrocardiol Off J Int Soc Holter Noninvasive Electrocardiol Inc 2008;13:191-207. https://doi.org/10.1111/j.1542-474X.2008.00219.x
113. Teixeira AL, Ritti-Dias R, Antonino D, Bottaro M, Millar PJ, Vianna LC. Sex Differences in Cardiac Baroreflex Sensitivity after Isometric Handgrip Exercise. Med Sci Sports Exerc 2018;50:770-777. https://doi.org/10.1249/MSS.0000000000001487
114. Rodríguez-Núñez I, Pontes RB, Romero F, Campos RR. Effects of physical exercise on baroreflex sensitivity and renal sympathetic nerve activity in chronic nicotine-treated rats. Can J Physiol Pharmacol 2021;99:786-794. https://doi.org/10.1139/cjpp-2020-0381
115. Tomoto T, Repshas J, Zhang R, Tarumi T. Midlife aerobic exercise and dynamic cerebral autoregulation: associations with baroreflex sensitivity and central arterial stiffness. J Appl Physiol (1985) 2021;131:1599-1612. https://doi.org/10.1152/japplphysiol.00243.2021
116. Kingsley JD, Tai YL, Marshall EM, Glasgow A, Oliveira R, Parks JC, Mayo X. Autonomic modulation and baroreflex sensitivity after acute resistance exercise: responses between sexes. J Sports Med Phys Fitness 2019;59:1036-1044. https://doi.org/10.23736/S0022-4707.18.08864-3
117. van der Vusse GJ, Glatz JF, Stam HC, Reneman RS. Fatty acid homeostasis in the normoxic and ischemic heart. Physiol Rev 1992;72:881-940. https://doi.org/10.1152/physrev.1992.72.4.881
118. Masoud WGT, Ussher JR, Wang W, ET AL. Failing mouse hearts utilize energy inefficiently and benefit from improved coupling of glycolysis and glucose oxidation. Cardiovasc Res 2014;101:30-38. https://doi.org/10.1093/cvr/cvt216
119. Ong SB, Hall AR, Hausenloy DJ. Mitochondrial Dynamics in Cardiovascular Health and Disease. Antioxid Redox Signal 2013;19:400-414. https://doi.org/10.1089/ars.2012.4777
120. Disatnik MH, Hwang S, Ferreira JCB, Mochly-Rosen D. New therapeutics to modulate mitochondrial dynamics and mitophagy in cardiac diseases. J Mol Med 2015;93:279-287. https://doi.org/10.1007/s00109-015-1256-4
121. Jiang HK, Wang YH, Sun L, He X, Zhao M, Feng Z-H, Yu X-J, Zang W-J. Aerobic interval training attenuates mitochondrial dysfunction in rats post-myocardial infarction: Roles of mitochondrial network dynamics. Int J Mol Sci 2014;15:5304-5322. https://doi.org/10.3390/ijms15045304
122. Coronado M, Fajardo G, Nguyen K, Zhao M, Kooiker K, Jung G, Hu D-Q, ET AL. Physiological Mitochondrial Fragmentation Is a Normal Cardiac Adaptation to Increased Energy Demand. Circ Res 2018;122:282-295. https://doi.org/10.1161/CIRCRESAHA.117.310725
123. Twig G, Hyde B, Shirihai OS. Mitochondrial fusion, fission and autophagy as a quality control axis: The bioenergetic view. Biochim Biophys Acta 2008;1777:1092-1097. https://doi.org/10.1016/j.bbabio.2008.05.001

124. Ishikawa K, Takenaga K, Akimoto M, Koshikawa N, Yamaguchi A, Imanishi H, Nakada K, ET AL. ROS-generating mitochondrial DNA mutations can regulate tumor cell metastasis. Science 2008;320:661-664. https://doi.org/10.1126/science.1156906
125. Radak Z, Chung HY, Goto S. Systemic adaptation to oxidative challenge induced by regular exercise. Free Radic Biol Med 2008;44:153-159. https://doi.org/10.1016/j.freeradbiomed.2007.01.029
126. Shukla V, Mishra SK, Pant HC. Oxidative Stress in Neurodegeneration. Adv Pharmacol Sci 2011;2011:1-13. https://doi.org/10.1155/2011/572634
127. Ray PD, Huang BW, Tsuji Y. Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling. Cell Signal 2012;24:981-990. https://doi.org/10.1016/j.cellsig.2012.01.008
128. Birben E, Sahiner UM, Sackesen C, Erzurum S, Kalayci O. Oxidative stress and antioxidant defense. World Allergy Organ J 2012;5:9-19. https://doi.org/10.1097/WOX.0b013e3182439613
129. Powers SK, Talbert EE, Adhihetty PJ. Reactive oxygen and nitrogen species as intracellular signals in skeletal muscle. J Physiol 2011;589:2129-2138. https://doi.org/10.1113/jphysiol.2010.201327
130. Bloomer RJ, Goldfarb AH, Wideman L, McKenzie MJ, Consitt LA. Effects of Acute Aerobic and Anaerobic Exercise on Blood Markers of Oxidative Stress. J Strength Cond Res 2005;19:276. https://doi.org/10.1519/14823.1
131. Fisher-Wellman K, Bloomer RJ. Acute exercise and oxidative stress: a 30 year history. Dyn Med 2009;8:1. https://doi.org/10.1186/1476-5918-8-1
132. Radak Z, Taylor AW, Ohno H, Goto S. Adaptation to exercise-induced oxidative stress: from muscle to brain. Exerc Immunol Rev 2001;7:90-107.
133. Traverse JH, Nesmelov YE, Crampton M, Lindstrom P, Thomas DD, Bache RJ. Measurement of myocardial free radical production during exercise using EPR spectroscopy. Am J Physiol Heart Circ Physiol 2006;290:H2453-H2458. https://doi.org/10.1152/ajpheart.00412.2005
134. Schieber M, Chandel NS. ROS Function in Redox Signaling and Oxidative Stress. Curr Biol 2014;24:R453-R462. https://doi.org/10.1016/j.cub.2014.03.034
135. Alleman RJ, Tsang AM, Ryan TE, Patteson DJ, McClung JM, Spangenburg EE, Shaikh SR, ET AL. Exercise-induced protection against reperfusion arrhythmia involves stabilization of mitochondrial energetics. Am J Physiol Heart Circ Physiol 2016;310:H1360-H1370. https://doi.org/10.1152/ajpheart.00858.2015
136. Lee J, Goldfarb AH, Rescino MH, Hegde S, Patrick S, Apperson K. Eccentric exercise effect on blood oxidative-stress markers and delayed onset of muscle soreness. Med Sci Sports Exerc 2002;34:443-448. https://doi.org/10.1097/00005768-200203000-00010
137. McAnulty SR, McAnulty LS, Nieman DC, Morrow JD, Utter AC, Dumke CL. Effect of resistance exercise and carbohydrate ingestion on oxidative stress. Free Radic Res 2005;39:1219-1224. https://doi.org/10.1080/10725760500317536
138. Quindry JC, Stone WL, King J, Broeder CE. The Effects of Acute Exercise on Neutrophils and Plasma Oxidative Stress: Med Sci Sports Exerc 2003;35:1139-1145. https://doi.org/10.1249/01.MSS.0000074568.82597.0B
139. Radovanovic D, Bratic M, Nurkic M, Cvetkovic T, Ignjatovic A, Aleksandrovic M. Oxidative stress biomarker response to concurrent strength and endurance training. Gen Physiol Biophys 2009;28(Spec Issue):205-211.
140. Brites FD, Evelson PA, Christiansen MG, Nicol MF, Basílico MJ, Wikinski RW, Llesuy SF. Soccer players under regular training show oxidative stress but an improved plasma antioxidant status. Clin Sci (Lond) 1999;96:381-385. https://doi.org/10.1042/cs0960381
141. Hadžović - Džuvo A, Valjevac A, Lepara O, Pjanić S, Hadžimuratović A, Mekić A. Oxidative stress status in elite athletes engaged in different sport disciplines. Bosn J Basic Med Sci 2014;14:56. https://doi.org/10.17305/bjbms.2014.2262
142. D'Souza A, Bucchi A, Johnsen AB, Logantha SJRJ, Monfredi O, Yanni J, Prehar S, ET AL. Exercise training reduces resting heart rate via downregulation of the funny channel HCN4. Nat Commun 2014;5:3775. https://doi.org/10.1038/ncomms4775
143. D'Souza A, Pearman CM, Wang Y, Nakao S, Logantha SJRJ, Cox C, Bennett H, ET AL. Targeting miR-423-5p Reverses Exercise Training-Induced HCN4 Channel Remodeling and Sinus Bradycardia. Circ Res 2017;121:1058-1068. https://doi.org/10.1161/CIRCRESAHA.117.311607

144. Azevedo L, Perlingeiro P, Hachul D, Gomes-Santos IL, Brum PC, Allison TG, Negrão CE, De Matos LDNJ. Sport Modality Affects Bradycardia Level and Its Mechanisms of Control in Professional Athletes. Int J Sports Med 2014;35:e3-e3. https://doi.org/10.1055/s-0034-1384589
145. Alves GB, Oliveira EM, Alves CR, Rached HRS, Mota GFA, Pereira AC, Rondon MU, ET AL. Influence of angiotensinogen and angiotensin-converting enzyme polymorphisms on cardiac hypertrophy and improvement on maximal aerobic capacity caused by exercise training. Eur J Cardiovasc Prev Rehabil 2009;16:487-492. https://doi.org/10.1097/HJR.0b013e32832c5a8a
146. Karlowatz RJ, Scharhag J, Rahnenfuhrer J, Schneider U, Jakob E, Kindermann W, Zang KD. Polymorphisms in the IGF1 signalling pathway including the myostatin gene are associated with left ventricular mass in male athletes. Br J Sports Med 2011;45:36-41. https://doi.org/10.1136/bjsm.2008.050567
147. Ye Y, Lin H, Wan M, Qiu P, Xia R, He J, Tao J, ET AL. The Effects of Aerobic Exercise on Oxidative Stress in Older Adults: A Systematic Review and Meta-Analysis. Front Physiol 2021;12:701151. https://doi.org/10.3389/fphys.2021.701151
148. de Sousa CV, Sales MM, Rosa TS, Lewis JE, de Andrade RV, Simões HG. The Antioxidant Effect of Exercise: A Systematic Review and Meta-Analysis. Sports Med 2017;47:277-293. https://doi.org/10.1007/s40279-016-0566-1
149. Chandwaney R, Leichtweis S, Leeuwenburgh C, Ji LL. Oxidative stress and mitochondrial function in skeletal muscle: Effects of aging and exercise training. AGE 1998;21:109-117. https://doi.org/10.1007/s11357-998-0017-5