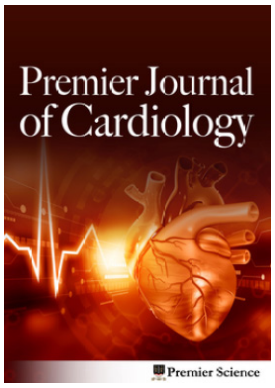

Impact of Moderate and Vigorous Physical Activity on Cardiovascular Health: A Review

Vedran Radonić

ABSTRACT

This article is a narrative review based on literature search primarily on PubMed about connections of physical activity and cardiovascular health. Moderate physical activity increases life expectancy and provides numerous cardiovascular benefits. It reduces the risk of atherosclerosis, atrial fibrillation (AF) incidence, arterial hypertension, hyperlipidemia, and diabetes. Accordingly, the World Health Organization guidelines recommend a minimum of 150 min of moderate physical activity or 75 min of vigorous physical activity per week, or a combination of the intensities of appropriate duration, for adults aged 18–64 years. For additional beneficial health effects, 300 or more minutes of moderate physical activity or 150 or more minutes of vigorous physical activity, with the option of combining training intensities, are recommended. On the other hand, evidence on vigorous physical activity is less clear, and evidence is more conflicting. There is a hypothesis that intense exercise may harm the cardiovascular system, causing enlargement of all heart chambers, myocardial fibrosis (primarily of the right ventricle), and increasing the risk, of coronary artery calcification, AF, and sudden cardiac death. Despite recent advancements, there is no firm evidence on the clinical significance of these conditions. Hence, current recommendations do not advise specific exercise intensity limits. The most important sports medicine task is identifying the athletes with an unacceptably high risk of triggering sudden cardiac death during sports activity and advising them with appropriate recommendations.

Keywords: Cardiovascular health, Moderate physical activity, Vigorous physical activity, Mitochondrial function, Sudden cardiac death

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Introduction

Physical activity is an important segment of human everyday life that improves overall health. The benefits of physical activity have been illustrated by Robert Butler, an American physician and former president of the US National Institute on Aging. He stated that if physical activity could be stored in a pill, it would be the most prescribed medicine in the country.[1] It is estimated that if physically inactive people regularly engaged in at least low-level physical activity, one in six deaths could be postponed, a scenario comparable to the success of programs to reduce tobacco consumption in the general population.[2] However, while moderate physical activity benefits are clear, the effects of vigorous physical activity are still debatable.[3–5] This paper is a narrative review of the relationship between physical activity and cardiovascular health. It covers physiological mechanisms, epidemiologic studies, and prospective trials (historic and latest). A literature search was conducted using PubMed as a primary source of biomedical research using "physical activity," "cardiovascular outcomes," "sudden cardiac death," "atrial fibrillation," "athlete heart syndrome," "coronary artery disease," "mitochondria," and "inflammation." The search date was May 18, 2025.

Basic Terms

Physical activity is defined as the body's movement at a rate greater than at rest. Exercise is planned, structured, repetitive physical activity to improve or maintain physical fitness.[6] It has various modalities based on activity type and intensity. Strength training primarily increases muscle mass and muscle strength. Anaerobic physical activity uses anaerobic mechanisms for energy production, and regular anaerobic physical activity increases acidosis tolerance. Aerobic physical activity predominantly uses aerobic mechanisms for energy production and improves cardiorespiratory fitness. Aerobic capacity is the ability of the cardiorespiratory system to deliver oxygen to the muscles during continuous physical activity.

Physical Activity by Intensity

The unit of physical activity intensity measurement is milliliters of oxygen per kilogram of body weight per minute (ml/kg/min).[7] Absolute aerobic work intensity is the amount of energy expended during aerobic exercise. It is usually expressed in metabolic equivalents (MET). One MET is the amount of oxygen consumed at rest and is approximately 3.5 ml/kg/min. Relative intensity is a percentage of maximum heart rate or maximal aerobic capacity (VO2 max). Moderate-intensity physical activities are those with a relative intensity of 40–60% or an absolute intensity of 4–6 MET, while high-intensity physical activities are those above these values. Mild physical activity implies an energy expenditure of 1.5–3 MET. Sedentary behavior is considered to be that of 1.5 MET or less. For example, slow walking (up to 4 km/h) is considered low-intensity physical activity, fast walking (about 6 km/h) is considered moderate-intensity physical activity, and fast walking uphill or with a load is considered high-intensity physical activity.[8] Top-level sports often require exposure to physical activity significantly above 15 MET.[7]

Historical Studies on Physical Activity

Epidemiological studies on physical activity began in the 1950s, when Morris and colleagues published a historical 'London busmen study' in Lancet, which showed that physically active men at work (bus conductors) had reduced the cardiovascular mortality rate of those in sedentary jobs (bus drivers).[9] In the following decade, Paffenbarger and colleagues showed that men who died of cardiovascular disease were 40–50% less likely to have been physically active during their

lifetime.[10] The prospective Framingham study had a major impact on the knowledge of the beneficial effects of physical activity on the cardiovascular system, showing a significantly reduced cardiovascular mortality rate in physically active men.[11] Subsequently, numerous epidemiological studies have shown the benefits of physical activity for cardiovascular and general health for men and women and all age groups, with cardiovascular and general mortality reductions by 30–40%.[12–17] On the other hand, low maximal aerobic capacity is an important predictor of poorer quality of life and high cardiovascular and general mortality.[18–20]

Physiology of Physical Activity

The striated and heart muscles are made up of muscle fibers. Skeletal muscles are mainly voluntarily controlled by alpha motoneurons, while cardiac muscle is under the control of the autonomic nervous system.[21] Cardiac muscle has a striated structure like skeletal muscle, but with a different fiber organization adapted to the synchronous contraction of the heart. The energy needed for the process is directly provided by adenosine triphosphate (ATP), which is acquired in mitochondria (visualized in Figure 1) primarily by glucose, though molecules like lipids and amino acids can be used as alternatives. Mitochondria are organelles capable of aerobic energy generation in myocytes and can precisely meet the energy needs of myocytes provided that oxygen delivery is adequate and continuous. Mitochondria of normally functioning muscles form a highly organized network.[22,23] When mitochondria stop functioning properly, they can fuse with other mitochondria, preserving the functional region and eliminating the defective one. Alternatively, mitochondria can undergo fission and divide into two independent organelles, which are cleared by lysosome mitophagy.

Physical Activity and Mitochondrial Pool

As mitochondria age and become damaged, mitochondrial function in the cell is maintained through a balance of biogenesis and fusion, as well as fission and mitophagy. Aging and physical inactivity shift the balance of the mitochondrial pool toward fission and mitophagy, which result in sarcopenia and reduced tissue response to energy requests. On the other hand, regular exercise increases the number of mitochondria in the myocytes. Though it increases mitophagy of severely degenerated mitochondria, it also stimulates mitochondrial fusion and biogenesis, improving myocyte function.[22,24–29] Furthermore, healthier mitochondria are less predisposed to myocyte apoptosis initiation.[22] Thus, at the cellular level, exercise helps myocytes maintain their capacity for ATP biosynthesis and ensures that their mitochondrial pool is functional.

Free Oxygen Radical Reduction

Active maintenance of mitochondrial health and function is essential for mitigating age-related sarcopenia and muscle function decline. The same is true for cardiovascular health and functional capacity. Impaired mitochondrial turnover, consequential decreased ATP production, and increased free oxygen radicals are associated with atherosclerosis and cardiomyopathies.[26,30] In one study, patients with coronary artery disease participated in an 8-month exercise regimen, and their total antioxidant capacity increased by up to 137%.[30,31]

Increasing Cardiovascular Capacity

Adequate energy source delivery, primarily oxygen, to myocytes is required to meet metabolic demands. It has been shown that increased metabolic demands in physical activity increase the amount of vascular growth factors, and consequently, arteriogenesis, capillary number, and capillary density.[32,33] Physical activity also increases muscle protein synthesis.[34,35] In cardiac muscle, the stimulus for muscle protein synthesis during physical activity can be increased pressure load for concentric hypertrophy and volume load for eccentric myocardial hypertrophy. The key result is a maximal stroke volume increase and improved functional aerobic capacity.

Anti-Inflammatory Effect

Besides increasing cardiac functional capacity, physical activity exerts significant anti-inflammatory effects at cellular and molecular levels. During exercise, contracting skeletal muscles release interleukin-6 (IL-6), which acts as a myokine with anti-inflammatory properties by stimulating the production of anti-inflammatory cytokines such as IL-10 and IL-1 receptor antagonist, and by inhibiting the production of pro-inflammatory cytokines like tumor necrosis factor-alpha. Exercise reduces the expression of toll-like receptors on monocytes, leading to decreased activation of inflammatory pathways and lower production of inflammatory mediators. Additionally, regular physical activity promotes the mobilization and activity of regulatory T cells, further contributing to the suppression of chronic inflammation and enhancing immune regulation at the tissue level. These mechanisms collectively explain how exercise helps maintain an anti-inflammatory environment, reducing the risk of chronic diseases associated with low-grade systemic inflammation, preventing the risk of atherosclerosis, and certain malignancies.[36–39]

Current Recommendations on Physical Activity

Regular physical activity extends lifespan, providing cardiovascular and other health benefits.[40–44] Accordingly, the World Health Organization guidelines recommend a minimum of 150 min of moderate physical activity or 75 min of vigorous physical activity per week, or a combination of the intensities of appropriate duration, for adults aged 18–64 years. For additional beneficial health effects, 300 or more minutes of moderate physical activity or 150 or more minutes of vigorous physical activity, with the option of combining training intensities, are recommended. Aerobic training should last at least 10 min, and muscle strength training is advised at least twice a week. For adults over 65 years, the same recommendations apply, with the caveat that people who cannot comply with the recommendations due to their health condition should

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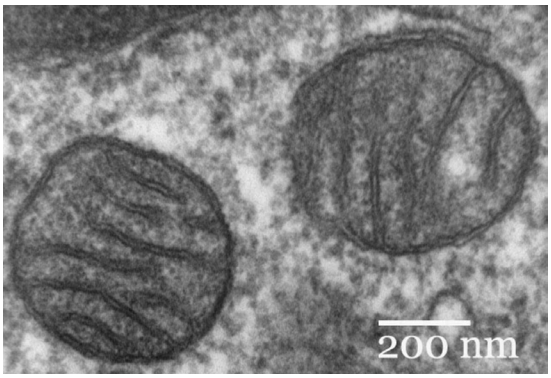

Fig 1 | Physical activity increases mitochondrial pool capacity for ATP biosynthesis

do as much physical activity as their condition allows. In addition, it is emphasized for all age groups that any amount of physical activity, including that below the recommended level, is better for health than complete inactivity.[45] This has also been recommended by the European Society of Cardiology and the American Heart Association.[46,47]

Physical Activity and Cardiometabolic Conditions

Obesity and Hyperlipidemia

Physical activity increases energy expenditure and stimulates lipolysis. Consequently, fat mass is reduced if energy expenditure is not compensated by increased calorie intake.[48] Previous studies have shown that higher physical activity levels reduce gains in body mass or waist circumference over the lifespan.[49,50] There is also evidence that reducing sedentary lifestyles (avoiding prolonged television viewing, taking more opportunities to walk) is beneficial for body mass control independently of the amount of exercise.[51,52] Regarding hyperlipidemia, numerous studies have shown that both aerobic activity and strength training have a beneficial effect on blood lipid levels. This includes decreased serum concentrations of low-density lipoprotein, total cholesterol, and triglycerides, and increased high-density lipoprotein levels. The level of effectiveness of physical activity in optimizing serum lipids directly correlates with the amount of energy expended during exercise.[48,53,54] Physical activity increases the ability of muscles to burn more fat instead of glycogen. This is achieved by activating specific enzymes in skeletal muscles necessary for this metabolic change.[55] There is also evidence that physical activity is directly associated with an increased capacity for cholesterol elimination from the periphery through the liver.[56]

Type 2 Diabetes

Physical activity decreases blood glycated hemoglobin (HbA1c) levels.[57] Physical activity increases insulin sensitivity in trained muscle and muscle contraction-induced glucose uptake into muscle. Mechanisms include increased insulin postreceptor signaling, increased expression of glucose transporter type 4, and increased glucose transport to muscle due to an expanded muscle capillary network and increased blood flow.[57,58] Aerobic and strength training are effective, and the effectiveness of optimizing insulin sensitivity is directly related to the volume of physical activity. Studies have shown a prophylactic effect of physical activity on type 2 diabetes, as well as a significant improvement in glycemic control in physically active patients.[59,60]

Arterial Hypertension

Physical activity provides benefits in blood pressure control. It is associated with better endothelial function, including endothelium-mediated vasodilation. This is due to the increased bioavailability of nitric oxide, which is a vasodilator, and the reduced vasoconstriction mediated by catecholamines, as well as the activity of the renin-angiotensin system.[17,61,62] According to studies conducted in animal models, these changes are mediated by specific gene expression as a result of physical activity.[17,63] Research has shown that physical activity chronically lowers arterial blood pressure in both normotensive and hypertensive individuals.[64–68] The antihypertensive effect of physical activity is also evident acutely after physical activity.[68] Both endurance and strength training have been shown to have antihypertensive effects, although the evidence for strength training is more conflicting.[69–71]

Atherosclerosis

Obesity, hyperlipidemia, type 2 diabetes, and arterial hypertension are components of the metabolic syndrome, which is the key prerequisite for atherosclerotic changes in the arteries all over the body. Since physical activity reduces the risk of every metabolic syndrome component, it decreases the risk of atherosclerosis as well.[47] Lower oxidative stress and inflammation levels further decrease the atherosclerotic plaque formation. Reducing the risk of atherosclerotic plaque formation implies a lower risk of coronary heart disease and peripheral atherosclerosis, and thus myocardial infarction, stroke, and limb ischemia.[17] Besides prevention, physical activity is beneficial for people suffering from atherosclerotic conditions. The so-called cardiac preconditioning in physically active individuals leads to a reduced level of myocardial injury and a reduced risk of arrhythmias during ischemia.[22,72] It has also been shown that physical activity as part of cardiac rehabilitation has a beneficial effect on cardiovascular and general mortality in patients with coronary artery disease.[48,72,73] Numerous molecular and intracellular processes have been identified for these effects.[74] Among patients who have had a stroke, those who were previously physically active have been shown to have a less extensive stroke and a better long-term prognosis.[75] The beneficial effect of physical activity in patients with intermittent claudication due to limb ischemia due to peripheral atherosclerosis is also known.[76]

Arrhythmia Reduction and Other Benefits

Studies have also shown a beneficial effect of physical activity on baroreflex sensitivity and heart rate

variability, with an increase in parasympathetic tone and a decrease in sympathetic tone.[77,78] Animal models have shown that this mechanism reduces the likelihood of malignant arrhythmia in conditions of myocardial ischemia.[77] Furthermore, it may contribute to the proven atrial fibrillation (AF) risk reduction connected with moderate physical activity.[79] Physical activity is thought to increase blood plasma volume, reduce blood viscosity, increase the extent of erythrocyte deformation, and increase fibrinolytic activity.[64]

Cardiovascular System and Top-Level Sport

Athlete's Heart

While the cardiovascular benefits of moderate physical activity are well known, vigorous physical activity is still the subject of debate. The set of heart changes caused by regular intense physical activity is called the sports heart. Echocardiography shows a mildly dilated left ventricle and, in a smaller number of cases, thickened walls (Figure 2). Sometimes, a reduced ejection fraction at rest is also observed, but this condition is not pathological because, due to the dilation of the left ventricle, the stroke volume remains preserved.[65] The diagnosis of an athlete's heart does not have a bad prognosis. However, the finding needs to be differentiated from pathological conditions such as hypertrophic or dilated cardiomyopathy, coronary artery disease, arrhythmogenic right ventricular cardiomyopathy (ARVC), etc. Sports heart is a reversible condition, and after stopping training for approximately 3 months, the changes disappear in 80% of athletes, while in 20% of them they persist. Electrocardiographic findings include sinus arrhythmia and bradycardia, atrial and ventricular ectopy, wandering conduction, sometimes first- and second-degree atrioventricular block (usually type 1), tall QRS complex with T wave changes due to hypertrophy, and incomplete right bundle branch block.[66,67]

Phidippides Cardiomyopathy

Although an athlete's heart is considered a benign condition, negative consequences on cardiac remodeling due to prolonged intensive physical activity cannot be ruled out. The increased volume load during endurance sports training can strain both ventricles, especially the right ventricle, which is naturally weaker and hence more susceptible to damage in extreme conditions. Markers of cardiac damage (troponin, creatine kinase, B-type natriuretic peptide) have been shown to increase after marathon running, as well as acute dilatation of the right heart chambers with impaired right ventricular systolic function. Although the changes generally return to a physiological state, long-term exposure to prolonged intense physical activity may be associated with chronic enlargement of all heart chambers and the development of myocardial fibrosis, primarily of the right ventricle, where the majority of ventricular extrasystoles originate in athletes.[69] There is also a hypothesis that prolonged intensive exercise increases the coronary artery calcification risk, which increases the risk for significant coronary artery disease.[70] Some scientists call all these changes together Phidippides cardiomyopathy after an ancient Greek soldier who died after running a long distance. Studies of extremely intense physical activity in animal models have shown that exertion significantly affects cardiovascular changes. These include concentric and eccentric hypertrophy of both ventricles, dilation of both atria with increased collagen deposition and fibrosis in the atria and ventricles, and a significantly greater possibility of inducing atrial and ventricular arrhythmias compared to animals that were not exposed to exertion.[71]

The recent Cooper Center Longitudinal Study (CCLS) found increased risk for acute myocardial infarction among people who self-reported prolonged very intense physical activity (≥3000 MET-min/week) compared to those with 500–1499 and 1500–2999 MET-min/week. On the other hand, all-cause mortality was the lowest in the ≥3000 MET-min/week group. Therefore, despite possible undesired impact on the cardiovascular system, it does not appear that prolonged intensive exercise leads to a shorter lifespan in otherwise healthy athletes.[70,80] However, more data are needed on the clinical significance of Phidippides cardiomyopathy.

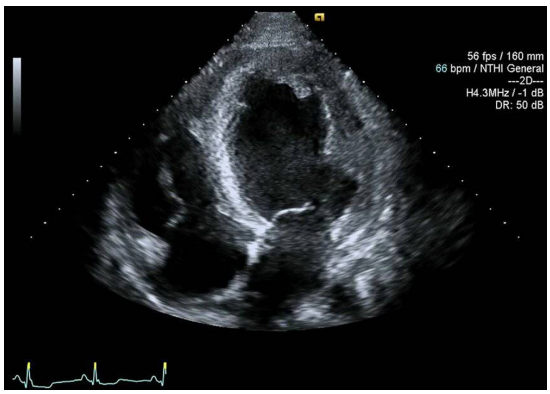

Fig 2 | Echocardiographic representation of a professional soccer player's heart by Kim et al.[68]

AF

AF is a condition whose possible association with vigorous physical activity has been examined in a large sample. The association between physical activity and AF is often described in the literature as a "U"-shaped curve, in which moderate physical activity reduces the incidence of AF, and intense physical activity may increase it.[79,81–83] Enlarged atria increase the AF risk, and prolonged dynamic physical activity is associated with dilation of both atria. The mechanism is not completely clear, but in addition to the pronounced parasympathetic activity that shortens the fraction of the atrial refractory period, prolonged dynamic physical activity is associated with echocardiographic findings of increased lateral wall strain of the left atrium and elevated levels of a marker of atrial stress (pro-atrial natriuretic peptide) after exercise.[81] A meta-analysis compared the risk of AF in 6816 athletes and 63,662 non-athletes and found a significantly higher risk of AF among athletes. The risk is more pronounced for

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endurance sports and those younger than 55 years compared to their peers.[82] It has also been found that prolonged exposure to high levels of physical activity in youth increases the risk of developing AF during active sports, but also in later life.[84] However, AF incidence among active athletes is low (less than 1%) despite possibly increased AF risk compared to their peers, mostly due to their young age.[85] Furthermore, the randomized controlled trial ACTIVE-AF found that people exposed to 150 min/week of moderate physical activity had a higher AF burden than those with a more intensive exercise program.[79]

Sudden Cardiac Death

Incidence

Sudden cardiac death is defined as sudden death due to cessation of circulation of cardiac origin, occurring within 1 h of the onset of symptoms, in the absence of other possible causes. The incidence varies from 1 in a million to 1 in 5000 young athletes yearly.[47] The incidence can be 2–3 times higher than in non-athletes, though the relative risk doubles during physical activity. Research has shown that sudden cardiac death occurs in almost all sports.

Mechanism

An arrhythmogenic substrate is crucial for the occurrence of sudden cardiac death. However, the arrhythmogenic substrate itself does not produce fatal arrhythmias—it requires a trigger, usually extrasystoles or a sudden increase in heart rate, which occurs with pronounced sympathetic activity in sport, which may start and maintain the malignant arrhythmia.[86] Another way to trigger malignant arrhythmia is heart concussion as a result of a blow, and it occurs above all in contact sports.[87]

Causes and Workup

Genetic and congenital disorders associated with sudden cardiac death include ARVC, hypertrophic cardiomyopathy (the two most common causes of death in athletes under 35 years of age), coronary artery anomalies, long QT syndrome, untreated Wolff-Parkinson-White syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia. Acquired conditions include coronary artery disease, which is the leading cause of sudden cardiac death in athletes over 35 years of age, and myocarditis. Electrocardiography serves as a critical noninvasive tool in detecting high-risk features associated with sudden cardiac death in athletes, including ST segment depression, T wave inversion in lateral or inferior leads, pathologic Q waves, ventricular pre-excitation, prolonged or shortened QT interval, complete left bundle branch block, Brugada pattern, and frequent or complex premature ventricular contractions. High-risk ECG findings warrant further evaluation with imaging modalities like echocardiography and cardiac magnetic resonance imaging, functional testing such as exercise ECG or Holter monitoring, and, in select cases, genetic testing or electrophysiological studies, to identify potentially life-threatening cardiac conditions. European literature lists ARVC as the most common cause of sudden cardiac death, while American literature attributes most cases of sudden cardiac death in young athletes to hypertrophic cardiomyopathy. These differences are probably because in Europe, a larger number of athletes with hypertrophic cardiomyopathy are excluded from participation in sports promptly due to detection during mandatory ECG recordings during systematic examinations of athletes. On the other hand, systematic examinations in the USA are exclusively based on physical examination.[47,86] In many cases, the cause of sudden cardiac death is not known.[85]

Conclusion

Despite the potential adverse effects of intense exercise on the cardiovascular system, most of the beneficial effects are not absent in people who regularly engage in intense physical activity, including elite athletes. Vigorous exercise results in even higher cardiovascular capacity. Thus, there is a hypothesis that health benefits are more pronounced.[88] Although epidemiological studies comparing the overall and cardiovascular mortality of elite athletes and the general population occasionally show conflicting results, a large meta-analysis has shown that elite athletes have lower overall and cardiovascular mortality than the general population.[89] Studies that compare outcomes of moderate and intense exercise often yield opposite results.[3–5,70,90,91] Increased myocardial infarction incidence along with reduced absolute mortality among people with the highest exercise volume in the CCLS study tells how complex the interactions of vigorous physical activity and the human body are. Although the cardiovascular harm from vigorous exercise cannot be excluded, multiple other beneficial effects might compensate for it. In conclusion, a time-intensity exercise threshold above which physical activity becomes significantly harmful is almost certain, but it is not yet clear where exactly it lies. Performing randomized controlled trials to answer this question is challenging and that is why rare examples like ACTIVE-AF are extremely valuable. Accordingly, guidelines from leading institutions currently still do not have sufficient data to recommend the specific upper physical activity limit. Further studies are needed to provide more knowledge about this important subject. For now, the most important sports medicine task is identifying the athletes with an unacceptably high risk of triggering sudden cardiac death during sports activity and advising them with appropriate recommendations.

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