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Editorial

Physical activity and coronary artery disease: Looking beyond risk factors

Alves A[1,2]

[1] Higher Institute of Educational Sciences, Felgueiras, Portugal
[2] Research Centre in Physical Activity, Health, and Leisure, Faculty of Sport, University of Porto, Porto, Portugal

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Physical activity has been described as a "miracle drug" due to its extensive health benefits (2). Indeed, participation in physical activity is associated with a decrease in cardiovascular events (26). The cardiovascular risk reduction attributed to increased physical activity is as significant as that promoted by current pharmacological therapies such as statins (14). The reasons behind the effectiveness of physical activity are most likely related to its multiple positive effects on cardiovascular risk factors and atherosclerosis biology.

Coronary atherosclerosis is a chronic inflammation disease, which develops over decades in response to the biological effects of traditional risk factors such as hypertension, diabetes, hypercholesterolemia and obesity.

It is well established that increased physical activity can prevent cardiovascular risk factors such as hypertension, metabolic syndrome and type 2 diabetes from developing in the first place (10, 11). In addition, aerobic and resistance training can decrease blood pressure in people with hypertension (3); improve body composition, inflammation and lipid profile in overweight and obese people (8); and improve blood glucose levels, body composition and insulin sensitivity in patients with type 2 diabetes mellitus (13). Exercise training also attenuates chronic inflammation in coronary artery and heart failure patients (5). This shows that structured physical activity may act against coronary artery disease by tackling its most prevalent predisposing factors. However, the attenuation of cardiovascular risk factors – in particular inflammation, hemostatic biomarkers, hypertension lipids and diabetes (15) – does not fully explain the reduction in incidences of cardiovascular events, suggesting that structured physical activity directly improves the health of coronary arteries.

Coronary atherosclerosis begins with a focal endothelial cell dysfunction, which follows a series of biochemical and inflammatory events that cause endothelial and smooth muscle cells to proliferate, produce extracellular matrix molecules and form a fibrous cap over the developing atheromatous plaque (16). This plaque formation can lead to flow-limiting stenosis, producing clinical symptoms such as stable angina.

Regular physical activity improves endothelial dysfunction and arterial stiffness as well as myocardial perfusion in patients with coronary artery disease (7). Positive modifications occur in endothelial function as a result of vasoactive substances such as nitric oxide, but the reparation of abnormalities in the endothelial cell structure could happen as well. The mechanisms of endothelial repair are not completely understood, but evidence supports that endothelial progenitor cells (EPC) are mobilized from the bone marrow into sites of endothelial damage in response to structured physical activity, supporting a potential role in the regeneration and repair of the damaged endothelium (19). Compelling evidence shows that aerobic exercise training significantly increases the circulating levels of EPC in patients with coronary and peripheral arterial disease, heart failure and acute coronary syndromes, as well as in patients following cardiac surgery (19). These changes have been associated with improvements in flow-mediated dilation in patients with coronary artery disease, supporting the notion that EPC are an important mechanism for endothelial repair and neovascularization. Researchers are still trying to identify the molecular mechanisms that exercise activates for EPC mobilization and integration into endothelial networks. Nonetheless, important steps in this process seem to include the activation of endothelial nitric oxide synthase, the production of nitric oxide, the activation of extracellular matrix proteins and the expression of cytokines, growth factors and cell-surface receptors (22).

Corresponding author:
Alberto Alves, PhD: Research Centre in Physical Activity, Health and Leisure, Faculty of Sports, University of Porto, Rua Dr. Plácido Costa, 91, 4200 - 450 Porto, Portugal • Tel: 00351 225 074 786 • Fax: 00351 225500689 • Email: aljo.alves@gmail.com

These observations are promising, as they suggest that physical exercise is an effective, inexpensive lifestyle strategy for restoring markers of vascular regeneration capacity, which otherwise decreases with age and chronic vascular diseases (9, 23).

However, there are a number of questions yet to be resolved. Prospective studies showing that physical activity can increase circulating levels of EPC and reverse cardiovascular outcomes are rare (24). Moreover, the many differences in exercise programs make any advice concerning intensity and duration of physical activity programs difficult at this point. Furthermore, not all patients seem to respond to exercise with an increase in circulating levels of EPC. Thus, factors that may influence the training response, such as lifestyle changes, training regimes and genetic profile, should be identified.

Regular structured physical activity may also prevent acute coronary events by preventing the physical disruption of the atheromatous plaque. Plaque rupture exposes its contents to coagulation proteins and platelets, triggering thrombi formation , which can lead to acute coronary events. Some studies support that sustained physical activity reduces platelet reactivity and improves blood coagulation and fibrinolytic systems activity, thus inhibiting fibrin formation (12). However, there is only limited evidence demonstrating that sustained physical activity can reduce the risk of plaque rupture or improve its vulnerability. The impact of sustained physical activity on plaque progression is also unclear.

Other potential mechanisms of exercise-mediated cardioprotection could include myocardial ischemic preconditioning and myocardial collaterization (4).

For any treatment to be effective, it needs to be prescribed with the correct dosage. One of the most prominent debates nowadays centers on the amount and intensity of physical activity that elicits the greatest benefit in primary and secondary prevention, as well as in cardiac rehabilitation. A recent meta-analysis concluded that individuals who achieved 300 min per week of moderate-intensity physical activity had a greater coronary artery disease risk reduction than those who met the minimum recommendations (150 min per week) (21). However, those who completed only half of the minimum amount of physical activity achieved a similar risk reduction as those who reached the minimum (21). This finding suggests that there is no such thing as a minimum threshold for achieving health benefits, indicating instead that more physical activity is better than less. It should be noted that men had lower coronary artery disease risk reduction compared with women for the same amounts of moderate-intensity physical activity (21), suggesting that men need greater stimulus to be protected. On the other hand, women did not show greater benefits with further increases in physical activity, indicating that a maximum limit may exist in women. Therefore, future studies should investigate the differentiating mechanisms in men and women.

Vigorous physical activity also appears to result in greater benefits for cardiovascular health when compared to moderate-intensity physical activity. A significant number of epidemiological studies have not controlled for total volume, but those that did reported a lower incidence of coronary events (18).

High-intensity interval exercise training has also proved to be more powerful than moderate exercise for improving cardiac and skeletomuscular function in heart failure patients (25). The question is whether high-intensity physical activity is as safe as moderate-intensity activity with regard to cardiac and skeletomuscular complications (20). Further questions could be made: are the results convincing enough to abandon the old recipe? Is the superior impact of high-intensity interval training maintained during long-term exercise programs? High-intensity interval training also seems to be more enjoyable for participants, although long-time adherence to such programs has never been tested (1).

Despite these numerous benefits, the role of physical activity is still underappreciated. Physical inactivity remains highly prevalent worldwide, (6) and adherence to cardiac rehabilitation programs is still lower than expected (2). Compliance with long-term physical activity programs is also a problem that needs to be solved (17). Nonetheless, these data strongly suggest that structured physical activity is a powerful yet inexpensive therapeutic and preventive strategy against cardiovascular diseases.

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