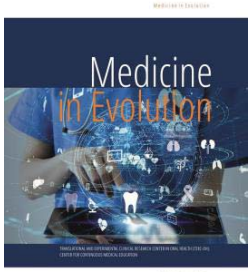
The role and importance of physical exercise in the prevention of cardiovascular disease



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Abstract

Cardiovascular disease (CVD) is the leading health problem of the modern world. They are the leading cause of death in both developed and transition countries. Physical activity (PA) has a beneficial impact on the cardiovascular system, both directly by improving endothelial function and indirectly by normalising atherosclerosis risk factors such as dyslipidaemia, hypertension, obesity and through positive effects on the clotting mechanism. The impact of physical activities on the cardiovascular system is manifested by immediate changes in hemodynamics, blood pressure and heart rate during physical training. After sustained physical training basal heart rate, blood pressure and heart rate response to physical activity stress decrease, indicating good conditioning through increased physical capacity. Prospective epidemiological studies have shown that a sedentary lifestyle has a two-fold increased risk of sudden death and cardiovascular mortality. Physical activity needs to be ongoing to have positive effects on the cardiovascular system; that means 4 to 5 times a week depending on the duration and intensity of exercise. Physical activity in patients with coronary heart disease should be individualised, quantified and monitored. In subjects with impaired heart muscle function, physical activity is limited with characteristic symptoms - dyspnoea and stenocardia. These patients are classified into mild, moderate and high risk groups and based on this the allowable intensity of their physical activity is assessed, as well as the degree of its control. Exercise should be range free and should not exceed this symptom limit. The aim of physical activity and training is to increase the symptom tolerance threshold.

Keywords: Cardiovascular diseases, physical exercises, life style

INTRODUCTION

In 1970 cardiac rehabilitation became synonymous with physical training indicated to selected groups of patients, namely young men with uncomplicated myocardial infarction, showing in these patients increased functional capacity, decreased resting heart rate, decreased systolic blood pressure, increased maximal oxygen volume (VO2max) but also increased ischemic threshold [1]. Subsequently, the notion of cardiac rehabilitation has acquired new meanings, with education, physical training, psychotherapy, counselling and practical guidance as its main components. The programs are varied in terms of content, main focus and major priorities, starting from those based on physical training, which have as a premise that improving physical performance has the effect of quickly solving all other problems, then moving on to those centred on psychotherapy, which have as a central point that improving depression and anxiety has the primary effect of regaining confidence in returning to normal life [2]. Therefore, today, cardiac rehabilitation is seen as an active, integrative, multi-faceted process, medical, family and social, in which the role of the complex team of doctors, nutritionists, psychologists, physiotherapists, kinesiotherapists is essential, these aspects being necessarily complemented by medical education measures, which will involve both the family and the community [3].

Literature data demonstrate that regular physical activity and increased exercise capacity improve survival in subjects without cardiac adaptation. In patients with coronary artery disease, increased exercise capacity is accompanied by increased life expectancy [2, 3]. Physical training is a central component of a multifactorial cardiac rehabilitation program [4]. Rehabilitation programs have demonstrated efficacy in coronary artery disease patients; however, there is less clinical evidence in valve surgery patients [5].

Most of the benefits of physical training are maintained as long as physical exertion is performed regularly, only to disappear almost completely after 2 weeks of physical inactivity [6]. The decrease in circulating catecholamines during daily exercise leads to an increase in the threshold for ventricular fibrillation and a decrease in the risk of sudden death. Decreased body weight is an important benefit of exercise, in addition, regular physical activity has an antidepressant effect [7].

The comprehensive recovery program includes physical training, psycho-social support, relaxation techniques and individual psycho-social counselling for each patient and their partner. Specific psychosocial areas are: depression, anxiety, personality and character elements, social isolation and everyday stress. Quality of life and depression can be improved by specific techniques, regardless of the extent of pre-existing disturbances [8].

Emotional support, the benefits of positive thinking and training appear to have a real effect in improving prognosis. Of all the entities presented, the most important on post-disease recovery as prognostic impact is depression, whose diagnosis and treatment immediately after onset leads to immediate positive outcomes [9].

The effect of cardiac recovery on vocational aspects is difficult to assess due to the increased variability of professional entities, regional, economic, political and social differences. For example, obtaining considerable social benefits, even if retirement occurred early in terms of age and length of service, makes the rate of re-employment low due to the satisfaction of individual needs without the need for additional work. However, studies have shown an increase in the return to work of patients included in rehabilitation programs. In a longitudinal study, participation in cardiac rehabilitation programs was an independent factor favoring return to work [10].

Although increased effort capacity is correlated not only with improved prognosis but also with return to work, it is still unclear whether this return to work is due to increased

quality of life and effort capacity, or is the result of specific economic and social conditions and vocational counselling [11].

Cardiovascular recovery thus represents a multifactorial system of intervention that increases exercise capacity, improves emotional state and quality of life, increases return to work and decreases mortality. Cardiac rehabilitation has been shown to be cost-effective in improving patients' lifestyle and emphasizes the importance of applying optimal medical treatment in combination with rehabilitation techniques to achieve maximum benefit [12].

PHYSICAL ACTIVITY

Physical activity (PA) can be defined as any bodily movement of skeletal muscle contraction that results in a substantial increase in caloric requirement over resting energy consumption [3]. During PA, muscles rely on their active contraction in three major pathways, which are the phosphagen system (anaerobic alactacid), the lactic acid system (anaerobic lactacid) and the aerobic system. These three pathways aim to ensure the availability of ATP throughout the contraction and that they are activated in relation to the duration and intensity of the exercise [4]. More specifically, the phosphagen system and the lactic acid system can be referred to as the "anaerobic system". The mechanisms for the first response of muscle are (i) the collection of stored and already disposable ATP in the cell, (ii) the activation of the phosphagen system which consists of the cleavage of high-energy phosphagen and creatine phosphate (PCr) [5]. If these mechanisms are unable to provide adequate metabolic support to the contracting muscle, or another metabolic pathway takes over: non-aerobic carbohydrate breakdown, derived from hepatic and muscle glycogen stores, degraded to pyruvic acid and then lactic acid by glycolysis. [6]. The third, aerobic or oxidative metabolism, involves the burning of carbohydrates and fats, and only in a few cases proteins, in the presence of oxygen [7].

The pattern of activation of these three different pathways depends on the type of exercise chosen: in high-intensity, short-duration exercise, muscle contraction will rely on anaerobic pathways (the phosphagen system and the lactic acid system), whereas in low-intensity to moderate-intensity resistance exercise their contraction will rely only initially on anaerobic metabolism and then switch to aerobic metabolic pathways. Since the pattern of activation of these integrated processes is variable, as well as the main source of energy used, it is reasonable not to think that athletes might benefit from a different type of diet, depending on their main PA program.

Endurance training (ET) is a type of exercise usually performed at constant intensity, with the main aim of progressively increasing the "anaerobic threshold", i.e. the limit above which the body begins to use anaerobic metabolism to restore depleted ATP to the cost of lactate production accumulation [8]. Particularly for submaximal or maximal intensity exercise, the extremely rapid increase in muscle oxygen requirement cannot be immediately met by the aerobic system, thus creating a temporary "oxygen deficit" in which, as previously mentioned, the phosphagen system and lactic acid systems are the main suppliers of ATP synthesis [9]. Once the deficit is filled, a series of coordinated metabolic processes take place to maintain the supply of exogenous substrates. The liver has the primary role of sustaining blood glucose levels through both glycogenolysis and gluconeogenesis and can produce ketone bodies from increased serum fatty acid concentrations that come from adipose tissue lipolysis (activated by beta-adrenergic stimulation during exercise) [10]. In this scenario, where adipose tissue fat is considered a constant source of energy and ketone bodies are considered either an alternative or supplemental source of fuel to sustain endurance exercise [11].

Physical training, as a subcategory of PA, is defined as a structural intervention with the goal of increasing or maintaining RFC or health, achieving athletic performance, or both. Maximal oxygen consumption or RFC can be measured directly during the cardiopulmonary exercise test or estimated from the workload achieved on the treadmill or with the cycle ergometer, adjusted for duration. Although considerable epidemiological evidence suggests that moderate to vigorous habitual BP may help reduce chronic stress and protect against the development of atherosclerotic CVD, acute exercise-related cardiac events have been reported in the medical literature [34] as well as in the lay press [12], suggesting that vigorous PA (≥6 metabolic equivalents [METs]; 1 MET = 3.5 mL/kg/min) may trigger cardiac arrest or acute myocardial infarction (AMI) in individuals with known CVD [13]. Several trigger mechanisms have been suggested for plaque rupture and acute coronary thrombosis [14] and life-threatening ventricular arrhythmias (Figure 1) [15].

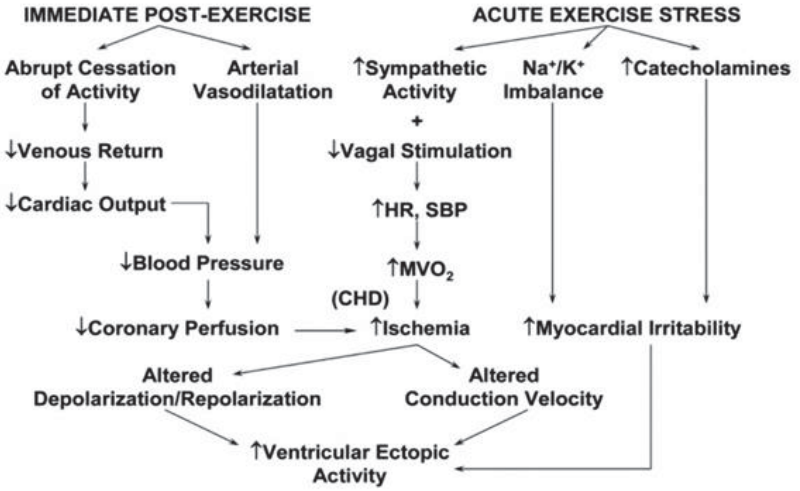

Figure 1. Physiological changes that accompany physical exercises, recovery and their possible sequelae. CHD, coronary artery disease; HR, heart rate; SBP, systolic blood pressure; MVO2, myocardial oxygen consumption [2]

Structural cardiovascular abnormalities, particularly hypertrophic cardiomyopathy (HCM), are major causes of sudden cardiac death (SCD) due to exercise in younger athletes [16]. In contrast, atherosclerotic CVD is the most common autopsy finding in middle-aged and older adults [17]. In a landmark study conducted by the Cleveland Clinic, investigators estimated that ~85% of US individuals aged ≥50 years have subclinical evidence of coronary artery disease [18]. Thus, the combination of vigorous PA and atherosclerotic or structural heart disease, rather than exercise per se, appears to present the trigger for cardiac events associated with strenuous exercise.

The relative risk (RR) for acute cardiac events during or immediately after mild to moderate intensity exercise is similar to that most expected by chance alone. In individuals with known CVD, high-volume, high-intensity or competitive training regimens may be associated with an increased incidence of acute cardiovascular events [19]. The absolute risks of exercise-related cardiovascular events in apparently healthy adults are 1 in 1,124,200 and 1 in 887,526 person-hours for nonfatal and fatal events, respectively [20]. Thus, intense bouts of PA, especially when not habitual, may increase the risk of cardiovascular complications; however, the absolute risk associated with each exercise session remains extremely low.

Although AMI and SCD can be triggered by vigorous PA, the risk decreases with increasing frequency (days/week) of vigorous PA. RR appears to be highest for inactive individuals with known CVD who perform unusual vigorous PA. For example, in the

Determinants of Myocardial Infarction Onset Study [21], the risk of AMI was 5.9-fold higher during 1-hour periods of vigorous BP up to high intensity compared with periods of lower levels of activity or rest. The RR of AMI was highest among those who exercised <1 time per week (RR, 107) compared with those who exercised ≥5 times per week (RR, 2.4) [22]. Accordingly, 1-2 sessions of vigorous exercise alone per week reduced the risk of exercise-related AMI by nearly 80%.

COMMON ACTIVITIES ASSOCIATED WITH ACUTE CARDIAC EVENTS

Physical activities involving sudden bursts or high levels of anaerobic metabolism may transiently increase the risk of acute exercise-related cardiac events. These include alpine skiing [23], racquet sports [24], high-intensity interval training [25] and competitive sports activities (e.g. basketball) [26] compared to other more moderate activities. Neural and psychological stimuli secondary to competition can simultaneously increase sympathetic activity and catecholamine levels and lower the threat threshold for ventricular arrhythmias [27]. Other recreational and domestic activities associated with increased cardiac demands and a higher incidence of cardiovascular events include activities such as hunting [28] and snow removal [29], as well as marathon running [30] and triathlon participation [31].

Marathon running analyzed in the RACER (Race Associated Cardiac Event Registry) study evaluated the incidence and outcomes of cardiac arrest associated with marathon and half-marathon races in the US over a 10.5-year period. The study population included 10.9 million registered runners (mean age ± SD, 42 ± 13 years) [32]. Of the 59 cases of cardiac arrest, 42 (71%) were fatal. The incidence rate was 3.75 times higher during full marathons than half marathons and 5.6 times higher among men than women. Almost half of all SCDs occurred during the last mile. The overall risk of a cardiac event during marathons and half marathons was relatively low compared to other competitive endurance activities. Autopsy findings showed that HCM and atherosclerotic CVB were the most common underlying abnormalities.

Triathlon participation. The frequency of cardiac arrest and SCD has also been reported in >9 million triathlon participants from 1985 to 2016 [31]. There were 135 SCDs, or 1.74 per 100,000 participants, which exceeded the previously reported incidence rate for marathon running (1.01 per 100,000 participants) [30]. The incidence of cardiovascular events was also 3.5 times lower in women than in men. Most SCD occurred during the swimming segment (67%), while the remaining deaths occurred during the cycling, running and post-race recovery segments, respectively. Race experience was available for 68 participants, of whom 26 (38%) were competing in their first triathlon. Autopsies were performed on 61 victims, of whom 27 (44%) had either atherosclerotic coronary artery disease or cardiomyopathy.

Altogether, these data suggest that cardiac arrest and SCD during marathon running and triathlon participation occur occasionally and that physicians evaluating race participants should be aware of the increased risks of HCM and atherosclerotic coronary artery disease in this patient population [32], both of which can often be detected by appropriate medical screening. An increased risk among "novice" triathlon participants suggests inadequate preparation or poor training as potential contributors to some of the exercise-related deaths [31]. Finally, participants should also be advised to heed warning symptoms and avoid sprinting during the last minutes of the race, when cardiovascular events are most common [33]. Symptomatic athletes should be strongly advised to cease training and competition until a medical evaluation and clearance is obtained.

Among individuals participating in high-volume, high-intensity resistance training regimens, the use of cardioprotective medications is lower than among their less physically

active counterparts [34]. These data, along with reports documenting the impressive risk factor profiles and superb cardiac performance of marathon runners, as well as the anti-aging effects that regular endurance exercise provides [35], have led a growing number of health enthusiasts to adopt the idea that "more exercise is invariably better" [36].

Conventional long-term resistance training or isotonic exercise alters cardiac structure and function, and such adaptations are considered to be benign. These include: enlargement of all cardiac chambers; improved ventricular compliance and distensibility; and electrical remodelling, such as sinus bradycardia, sinus arrhythmia and first-degree atrioventricular block. However, emerging evidence suggests that, over time, high-volume, high-intensity training regimens may induce cardiac maladaptations, such as an increased incidence of atrial fibrillation (AF) and accelerated coronary artery calcification (ACC) [37]. Consequently, there is debate as to whether intense exercise may be harmful to the heart, particularly in some individuals.

PREVENTION OF CARDIAC EVENTS

There is now considerable evidence that acute cardiovascular events can be triggered by various physical, chemical and psychological stressors, including intense physical exertion [38]. The underlying mechanisms may involve biomechanical, prothrombotic and arrhythmogenic stimuli, largely mediated by associated increased sympathetic nervous system output.

Fortunately, regular exercise, stress management, smoking cessation, and favorable modification of other coronary risk factors may attenuate the response to and protect against trigger-induced coronary events [39]. The beneficial role of regular moderate to vigorous exercise may be due to multiple mechanisms, including cardiovascular, neurological, and biochemical adaptations, as well as psychological effects (Figure 2). Concurrent favorable autonomic adaptations include increases in heart rate variability, a strong prognostic indicator that is inversely related to mortality [35]. In addition, exercise preconditioning provides immediate cardioprotective benefits against AMI, conferring transient antiarrhythmic and antiischemic effects against ischemic injury [27, 34]. The impact of even brief PA seizures reaching a minimum threshold of ≥50% of functional capacity appears to provide the impetus for improved clinical outcomes following acute cardiac events [33].

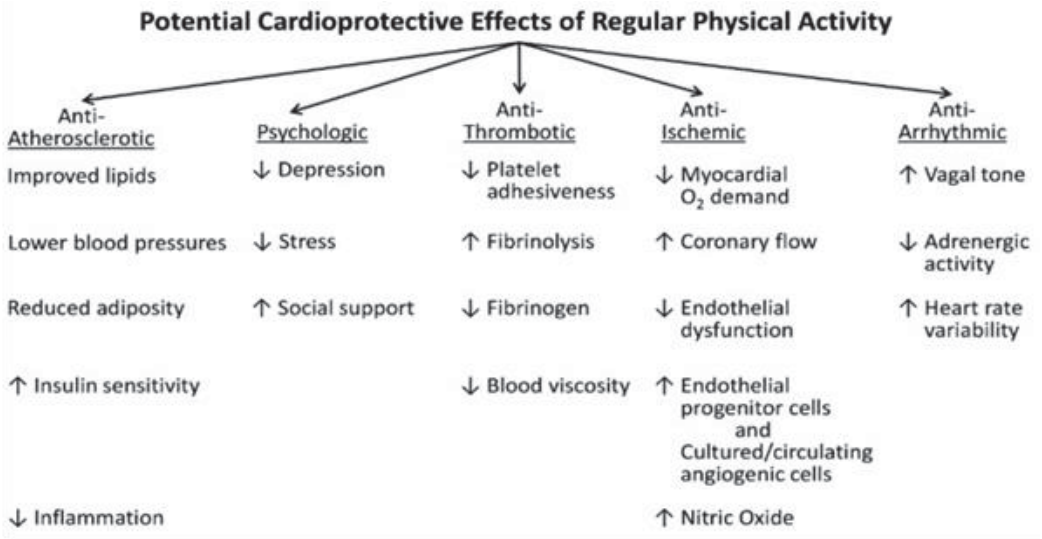

Figure 2. Mechanisms by which moderate to vigorous physical activity may reduce the risk of initial and recurrent cardiovascular events. ↑, increased; ↓, low; O2, oxygen [2]

PROPHYLACTIC USE OF CARDIOPROTECTIVE DRUGS BEFORE INTENSE EXERCISE

Although some have suggested that recreational athletes with known or suspected CVD may benefit from taking aspirin or beta-blockers shortly before competitive exercise, there are no definitive data to indicate that these agents (despite their proven efficacy for secondary prevention) decrease acute exercise-related cardiopathy [32]. Accordingly, related reports [34, 36] and the INTERHEART study [33] suggest that there is insufficient evidence to recommend prophylactic use of these drugs prior to intense PA or participation in competitive sports.

Although there are various potential strategies to reduce the risk of triggering acute cardiac events, we believe that a healthy lifestyle that includes structured exercise should be included in stress reduction interventions [40], due to associated autonomic adaptations and parasympathetic predominance [41]. This strategy is readily available, beneficial for both physical and mental health, and offers gains of up to eight years in life expectancy in the most physically active population cohorts [42].

CONCLUSIONS

The effects of chronic stress and various stressors (e.g. physical, chemical, psychological) in the development of cardiovascular disease and the triggering of acute cardiac events are well documented. Regular moderate to vigorous PA, structured exercise and higher levels of RFC appear to be therapeutic in addressing risk factors that are precursors to CVD. On the other hand, studies suggest that unusual physical exertion of vigorous to high intensity may trigger acute cardiovascular events, especially in habitually sedentary individuals with known CVD. It is also reported that in some individuals, high-volume, high-intensity exercise regimens can lead, over time, to maladaptations, including increased coronary calcification and the development of AF, as depicted by an inverted J-shaped curve. Although exercise is widely recognized for its beneficial effects, from data reported in the literature it is suggested that "you might get too much of a good thing".

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