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Exercise Role in the Prevention and Management of Hypertension

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ABSTRACT

Arterial hypertension is a public health problem, with increasing prevalence, worldwide. Lifestyle interventions remain the cornerstone step to reduce blood pressure levels in hypertensive individuals. Epidemiologic evidence suggests that the age-related increase in arterial stiffness and BP is more likely a consequence of lifestyle characterized by physical inactivity and inappropriate dietary habits. Increased cardiorespiratory fitness has also been associated with lower incidence of arterial hypertension. There is also an abundance of evidence supporting that structured aerobic exercise training programs of moderate intensity and adequate volume lead to significant BP reductions of approximately 4-10 mmHg and 3-8 mmHg in systolic and diastolic BP, respectively in prehypertensive and hypertensive patients regardless of age, sex, and cardiovascular risk factors. Additionally, increased physical exercise and cardiorespiratory fitness have also been associated with lower morbidity and mortality outcomes in hypertensive individuals. Available evidence on the effects of resistance or strength training on blood pressure is limited. However, most data suggest that resistance exercise is less efficacious than aerobic exercise in reducing BP levels. The mechanisms underlying these benefits are not completely elucidated. However, the reduction in systemic vascular resistance, cardiac output, and sympathetic nervous system activity are implicated in the observed benefits.

Key words: hypertension, physical activity, exercise, cardiorespiratory fitness, mortality

Introduction

Arterial hypertension is a public health problem affecting more than 1 billion patients with a prevalence of approximately 35% to 40% in the general population, worldwide[1]. The therapeutic algorithm includes a variety of pharmacological options[2,3]. However, lifestyle interventions remain the first option for the management of hypertension before drug therapy is initiated[2,3].

A plethora of evidence from large, well-conducted epidemiologic studies supports a robust, inverse, and independent association between physical activity and cardiorespiratory fitness (CRF) and BP levels and lower risk of cardiovascular morbidity and mortality in hypertensive individuals[4,5]. Thus, international guidelines strongly recommend appropriate lifestyle interventions as the first step in the management of hypertensive patients[2,3]. The purpose of this review is to summarize and critically discuss the findings from major studies of the impact of physical activity, exercise and cardiorespiratory fitness on blood pressure (BP) levels and mortality in hypertensive patients.

The preventive role of fitness on vascular health

The age-related progressive increase in BP is of multifactorial origin. Evidence suggests that increases in arterial stiffness are a major and independent contributor to hypertension[6-8]. To some

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extent, arterial stiffening is an inevitable outcome of aging. However, the pronounced increase in arterial stiffening observed in industrialized societies may be attributed to several modifiable factors, including high-fat and high-salt diets and physical inactivity[9-15]. This concept is supported by the moderate and significantly lower increase in arterial stiffness and BP observed in indigenous populations that follow a relatively traditional lifestyle characterized by high levels of physical activity necessary for their survival compared to individuals residing in westernized societies[10,11]. Furthermore, exercise intervention studies have reported improved vascular health, while diminished vascular health has been reported following inactivity and bed rest[14,15]. The impetus for the improved endothelial function and vascular remodeling following exercise training appears to be attributed to the exercise-induced increase in shear stress in healthy individuals[16].

Mechanisms underlying the benefits in blood pressure reduction from exercise training

The mechanism(s) involved in the exercise-induced favorable effects on BP remains partially decrypted. Available evidence suggests that the effects of exercise are multifactorial and collective resulting in the reduction of peripheral resistance and cardiac output at absolute workloads[4,5]. Exercise-related reductions in BP are independent of body weight, body composition and dietary habits[17]. Important alterations in sympathetic nervous system activation and systemic vascular resistance have been noted after exercise training[18]. In particular, meta-analytic data from approximately 72 trials including approximately 4,000 participants found that reductions in plasma norepinephrine, plasma renin activity, and systemic vascular resistance were the predominant causes for BP reduction after exercise training[18]. A reduction of systemic vascular resistance has been also been observed in hypertensive patients, in whom both systolic and diastolic BP were significantly reduced at absolute submaximal workloads following 16 weeks of aerobic exercise[19]. Mean BP was reduced by approximately 17-20 mmHg, while remarkable changes in peak exercise systolic, diastolic, and mean BP were noted[19]. Even if the cardiac output did not increase at peak exercise training (despite the higher workload), the mean BP reduction is likely the result of a substantial reduction in systemic vascular resistance. The benefits of exercise training in systemic vascular resistance is further supported by the improvements in endothelial function observed in hypertensive[20,21], and older normotensives after 12 weeks of moderate intensity exercise[22,23].

Exercise training and progression to hypertension

Increased CRF has also been associated with a slower rate of progression to hypertension. In a study of more than 2,300 prehypertensive, middle-aged, US veterans followed for approximately 9 years, the investigators reported an inverse and graded association between CRF and the rate of progression to hypertension. Specifically, the risk of developing hypertension increased progressively with lower exercise capacity as reflected by the peak metabolic equivalents (METs) achieved during a standardized exercise test (1 MET=3.5 ml of oxygen consumption per kg of body weight per minute). Compared to those in the individuals who achieved >10 METs (highest fitness category) the risk of developing HTN was 72%, 66%, and 36% higher in the Least-fit (≤6.5 METs), Low-Fit (6.6 to 8.5 METs) and Moderate-Fit (8.6 to 10 METs) individuals, respectively[24]. Supporting data from a meta-analysis of 13 prospective cohort studies have also showed an inverse association between levels of recreational physical activity and risk for hypertension to develop[25].

Physical activity, cardiorespiratory fitness and blood pressure levels

Findings from numerous randomized controlled trials and meta-analyses support the antihypertensive effects of mainly aerobic exercise, in patients with arterial hypertension. A reduction of approximately 4-10 mmHg and 3-8 mmHg in systolic and diastolic BP, respectively, is observed with structural aerobic exercise training program or increased physical activity of moderate intensity and adequate volume in patients with stage 1 hypertension regardless of age or sex[26-28]. In male veterans with stage 2 hypertension and left ventricular hypertrophy (LVH), we observed a significant reduction in BP after 16 weeks of moderate-intensity aerobic exercise training. At 32 weeks of exercise, BP reduction was even more pronounced, despite a 33% reduction in antihypertensive medication in the exercise group. BP in the control group (no-exercise) increased sub-

stantially[29]. Importantly, we observed significant reductions in cardiac wall thickness, and left ventricular mass index, leading to LVH regression similar to that observed with several antihypertensive medications[30].

The impact of exercise capacity on BP levels in patients with resistant hypertension has been less extensively examined. In a study of patients with resistant hypertension, 50 patients were randomized to exercise for 8-12 weeks on a treadmill or to a control group. Exercise training resulted in improved exercise capacity as indicated by increased maximal oxygen uptake and lactate curves[31]. The exercise group exhibited significant reductions in ambulatory daytime systolic and diastolic BP post-exercise training. Lower BP was also noted during exercise at absolute workloads. In another trial, approximately 30 patients with resistant hypertension were randomized to heated water exercise and no exercise control group. Heated pool exercises significantly decreased office BP by 36/12 mm Hg. In addition, significant reductions in 24-hour, daytime, and nighttime BP of 19.5/11.1 mmHg, 22.3/13.0 mmHg, and 17.4/8.5 mmHg were observed, respectively. In contrast, there was a significant increase in 24-hour, daytime, and nighttime diastolic BP of 3.0/2.1 mmHg, 4.4/3.5 mmHg, and 3.1 mmHg in the control group, respectively[32].

Of note, most studies assessing the effect of exercise on BP have implemented aerobic exercises. Available evidence on the effects of resistance or strength training on resting BP is limited, scarce, and conflicting. However, most data suggest that resistance training is less efficacious than aerobic exercise[4,5,26] in lowering resting BP[33,34].

Physical activity, exercise capacity and mortality risk

Several large and well-controlled epidemiological studies have also reported that increased CRF is associated with lower mortality risk in hypertensive patients[35-37]. In more than 4,500 veterans with multiple cardiovascular risk factors, the risk for death was 13% lower for every increase in exercise capacity by 1 MET[37]. Mortality risk was found to be reduced by 34% and 70% in patients with exercise capacity of 5.1-7.0 METs and >10 METs, respectively, compared with patients with a capacity of less than 5 METs. When the interaction between body mass index, exercise capacity and mortality risk was evaluated in hypertensive veterans, progressively lower mortality rates with increased exercise capacity were observed within each body mass index category[37]. Interestingly, when normal weight-low fit individuals were compared with overweight or obese fit individuals, a 47% and 60% lower mortality rate was found for each group of patients, respectively. Importantly, obese-moderate fit and obese-high fit patients had a 55% and 78% lower mortality rate compared with normal weight-low fit veterans, respectively[37].

Meta-analytic data from more than 95,000 patients showed that both cardiovascular and all-cause mortality were inversely related with physical activity. Hypertensive patients with any level of physical activity had a 16% to 67% reduced risk of cardiovascular mortality, whereas the inactive group had an over 2-fold increase in the risk for death[38].

Similarly, among approximately 4,500 patients with prehypertension or high-normal BP, mortality risk reduction was progressively greater in low-fit (40%), moderate-fit (58%), and high-fit (73%) individuals compared with the least-fit patients, suggesting that even low-levels of cardiorespiratory fitness could offer significant benefits. When compared based on age, the adjusted risk reduction for every 1 MET increase in exercise capacity was 18% and 12% for patients younger and older than 60 years of age, respectively[39,40].

The effect of exercise on mortality in patients with resistant hypertension has not been adequately examined. In a study by our team, the association of cardiorespiratory fitness with all-cause mortality was assessed in around 10,000 African-Americans of which, 1,276 men had resistant hypertension. After 9.5 years of follow-up, an inverse association between all-cause death and cardiorespiratory fitness was found. Compared with the least-fit group of patients, mortality rates were lower by 21%, 36%, and 62% in the low-, moderate-, and high-fit groups, respectively. Last, an increase of 1 MET in exercise capacity was related with a mortality rate reduction of 18%[41].

Prognostic Aspects of Exercise Blood Pressure

In general, BP rises as a physiological response to acute exercise[4,5]. However, in some individuals, a disproportional increase of systolic BP to workload is observed, that is associated with target-organ damage. In our study of approximately 800 middle-aged prehypertensives we have shown that exercise

systolic BP observed at a workload of approximately 5 METs was the strongest predictor of LVH. Importantly, exercise systolic BP greater than 150 mmHg was identified as the threshold for the development of LVH. Those with SBP≥150 mmHg at the workload of 5 METs exhibited significantly higher cardiac wall thickness, left ventricular mass index, and lower exercise capacity compared to individuals with systolic BP<150 mm Hg. In addition, we observed a 4-fold higher risk in LVH for every 10 mmHg incremental increase in systolic BP above 150 mmHg[42]. These findings suggest that the systolic BP response to submaximal exercise may be an important marker to identify patients at increased risk for developing LVH.

The aforementioned findings suggest that a hemodynamic load threshold exists, reflected by the systolic blood pressure of approximately ≥150 mmHg, beyond which the cardiac muscle, as any muscle, will make the necessary adaptations to accommodate the increased demand. The level of physical activity that will elicit such response is relative to the individual's peak exercise capacity. For example, let's assume that the exercise capacity of three individuals of similar age is 7.0; 10.0 and 20.0 METs. According to our findings, systolic blood pressure ≥150 mmHg is necessary to trigger cardiac remodeling. This BP threshold will be achieved by the relatively low-fit individual (7.0 METs) at the workload of 4-5 METs. This level of physical activity typically represents approximately 60% of the peak exercise capacity of this individual. If we assume that a 60% of the peak workload is necessary to elicit a systolic blood pressure response ≥150 mmHg, for the relatively fit individuals (estimated peak exercise capacity 12 METs) this workload wil be 7.2 METs and for athletes (estimated peak exercise capacity 20 METs), 12 METs. Thus, for relatively fit individuals and athletes the workload of daily activities (4-5 METs) is not likely to elicit a systolic blood pressure response ≥150 mmHg necessary to elicit cardiac remodeling (Fig. 1). However, such blood pressure threshold is reached and well exceeded during the highly demanding exercise training endured by athletes and therefore, cardiac remodeling to accommodate the imposed demand is triggered.

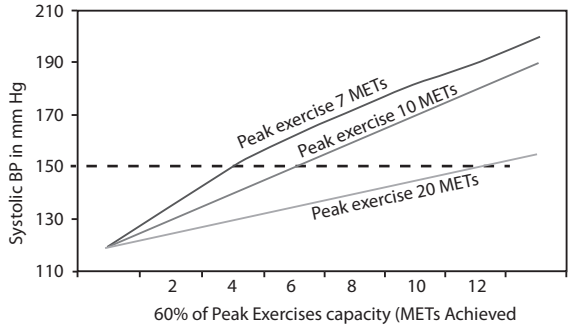

Figure 1. *Theoretical concept of exercise systolic BP threshold of 150 mmHg achieved according to fitness status. Low fit individuals achieve systolic BP of 150 mmHg (threshold) at 4 METs (within the metabolic demand for most daily activities). The same BP level is achieved at 6 METs for those with an exercise capacity of 10 METs and at 12 METs for highly individuals. Adapted from Kokkinos et al. (Reference 42 and 43)*

Conclusion

Collectively, there is strong evidence suggesting that regularly performed exercise or an increase in physical activity could attenuate the progressive age-related elevation in BP levels, thus preventing the development of hypertension. In addition, structured exercise programs and increased physical activity levels of adequate intensity, duration and frequency result in significant office and ambulatory BP reductions and LVH regression in hypertensive patients. A plethora of epidemiologic evidence also supports an inverse, and graded association between exercise capacity or CRF and risk of overall morbidity and mortality in hypertensive patients, independently of other cardiovascular risk factors. Mechanisms underlying these benefits are not completely understood. However, the favorable effects of physical activity and cardiorespiratory fitness on the sympathetic nervous and cardiovascular system, as well on other traditional risk factors are likely implicated in the observed benefits.

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