Επίκαιρο Άρθρο

The Role of Exercise and Physical Activity in Hypertension

Andreas Pittaras

ABSTRACT

Increased physical activity or structured exercise programs lower blood pressure (BP) and leads to Left Ventricular hypertrophy(LVH) regression. The two traditional types of exercise training are: aerobic or endurance and anaerobic or strength training. Structured aerobic exercise training programs result in an independent reduction of approximately 4 to 10 mmHg in SBP and 3 to 8 mmHg in DBP for patients with Stage 1 hypertension related to the level of initial blood pressure. On the other hand, resistance training is less efficacious than aerobic exercise in lowering resting BP. Exercise-induced changes in BP are the result of the interaction among duration of exercise sessions, intensity, frequency and the length of exercise training. Of note, changes in BP are independent of changes in body weight, body composition and dietary influences. Likewise, combination of diet and exercise may be beneficial for the entire hypertensive individual. It's therefore clear that reductions in SVR, plasma norepinephrine, and plasma renin activity are main reasons for the decrease in BP following exercise. The findings presented in this paper support that regularly performed aerobic exercise of moderate intensity, adequate duration and volume that leads to improved fitness status can be implemented to lower BP in hypertensive patients and modulate the associated hypertensive heart disease. Specifically, aerobic exercise training can prevent the development of concentric cardiac remodeling and lower LV mass in those with LVH.

Key words: Blood Pressure, Exercise blood pressure, Hypertension, Hypertensive heart disease, Heart failure, Left Ventricular Hypertrophy, Physical Activity, Physical Fitness, Stroke, Prevention

Increased physical activity or structured exercise programs have been shown to significantly lower blood pressure in individuals with mild to moderate hypertension. Some evidence also support that the lowering BP with physical activity and exercise leads to LVH regression.

Almost all of the information regarding exercise and BP control in individuals with mild to moderate hypertension has been consistently documented by a plethora of well-controlled studies. Their findings are summarized by several reviews and meta-analyses[1-12]. In general, these studies support that structured aerobic exercise training programs of moderate intensity or increased physical activity of adequate volume and intensity result in an independent reduction of approximately 4 to 10 mmHg in SBP and 3 to 8 mmHg in DBP for patients with Stage 1 hypertension. The magnitude of the reduction is likely related to the level of initial blood pressure[7-9] whereas the influences of age, or gender are not clear[8,9]. The influence of exercise intensity has also been scrutinized. Overall, the evidence that the blood pressure response to regular exercise differs according to training intensity is not convincing[9,12]. It is likely that the exercise-induced changes in BP are the result of the interaction among duration of exercise sessions, intensity, frequency and the length of exercise training. Moreover, an exercise volume threshold must be achieved before any favorable BP changes are realized. This threshold is likely to be influenced by age, gender, genetic factors and the initial fitness status of the individual.

Veterans Affairs Medical Center, Cardiology Department 50 Irving Street NW, Washington, DC 20422
George Washington University School of Medicine 2121 I Street, Washington, DC, 20052
✉ **Correspondence: Andreas Pittaras,** *MD*, Mediton Medical Center, Athens, Greece. 22 El. Venizelou Str, Galatsi, Athens, Greece, 11147
• Tel.: +6932416145 • Email: andreaspittaras@gmail.com

Information on the effects of exercise is limited in individuals with stage 2 hypertension or those with resistant hypertension. We reported that moderate-intensity aerobic exercise was well-tolerated by male veterans with stage 2 hypertension and led to significant reductions in BP just after 16 weeks of exercise training. At 32 weeks, BP reduction was more pronounced even after a 33% reduction in antihypertensive medication in the exercise group, while BP in the no-exercise group increased substantially[13]. Similar findings were observed in individuals with resistant hypertension. Moderate-intensity exercise was effective in significantly lowering 24-hour ambulatory BP[14]. The BP reduction in this study was similar to that reported by previous studies in individuals with mild to moderate hypertension[2,4,6,9,15,16].

Information available on the effects of resistance or strength training on resting blood pressure is limited and conflicting and suggests that resistance training is less efficacious than aerobic exercise in lowering resting BP[2,6,15-18]. The conclusions of a recent meta-analysis[17], and a review[18] (Hurley) suggest an average systolic blood pressure reduction of approximately 2-3 mm Hg as a result of resistance training. Thus, it is recommended that resistance training may serve as an adjunct to an aerobic-based exercise program for BP reduction[4,9] and implemented as part of a complete exercise program[19,20]. The reasons for this are not clearly defined. However, resistance exercise studies do not consistently support improvements in systemic vascular resistance, endothelium-dependent vasodilatation, and arterial compliance, mechanisms suspected to mediate the hypotensive effects of aerobic exercise[15].

Exercise intervention studies that recorded BP over a 24-hour period (ambulatory blood pressure) are relatively few. In general, the exercise-induced BP reductions over a 24-hour period appear less dramatic (mean 3.0-and 3.2-mm Hg reductions for systolic and diastolic blood pressure, respectively) than for BP assessed by auscultation[4,21].

Antihypertensive Mechanisms of Exercise

The underlying mechanisms responsible for the reduction in blood pressure elicited by exercise training remain elusive and controversial. Current opinion is that the effects of exercise training must be multifactorial and the collective effects of these actions result in the reduction of systemic vascular resistance (SVR), cardiac output or both[22-24]. It is generally agreed upon that the changes in blood pressure are independent of changes in body weight, body composition and dietary influences. However, it is likely that a combination of diet and exercise may be beneficial for the hypertensive individual.

A meta-analysis involving 72 trials and 3,936 individuals reported reductions in SVR, plasma norepinephrine, and plasma renin activity as the main reasons for the decrease in blood pressure following exercise[3]. A reduction in SVR is also suggested by arterial pressure changes observed in a group of hypertensive patients. Both systolic and diastolic BP were reduced significantly at absolute submaximal workloads following 16 weeks of aerobic exercise[25]. Consequently, mean arterial pressure was reduced by approximately 17-20 mm Hg. More impressive was that peak exercise systolic (219±24 mm Hg vs 199±34 mm Hg), diastolic (108±10 mm Hg vs 98±13 mm Hg) and mean arterial pressures (145 mm Hg vs 131 mm Hg) were also lower at a similar maximal heart rate (153±15 vs 153±11 bpm), but higher workloads[25]. Even if we assume that cardiac output at peak exercise did not increase despite the higher workload achieved at post exercise training, the substantially lower mean arterial pressure is likely the outcome of a substantial reduction in SVR. The exercise-induced reduction in SVR is substantiated further by findings that the impaired endothelial function observed in hypertensive patients[26,27] and older individuals with normal blood pressure is improved after just 12 weeks of moderate intensity exercise[28,29].

Exercise and Cardiac Hypertrophy

Although various neurohormones, growth factors and cytokines have been identified as contributors in the development of concentric LVH, the mechanical stress from chronically elevated BP in hypertensive states contributes significantly to the progression of LVH. Reductions in BP with most antihypertensive agents are associated with LVH regression and favorable CV prognosis.

Thus, it is reasonable to assume that exercise-related reduction in BP will lead to LV mass regression as a consequence of lower afterload[30,31]. Support for this premise is provided by several interventional studies[13,32-35]. Sixteen weeks of aerobic training in individuals with Stage 2 hypertension[13], resulted in a significant reduction in BP, cardiac wall thickness, LVM and LVM index. The degree of LVH regression was similar in magnitude to that

observed with most antihypertensive medications[36]. Similar findings were noted in a cohort of overweight hypertensive women (n=45) and men (n=37) undergoing 6 -months of exercise training or behavioral modification for weight loss versus a control group. Participants in both exercise and weight loss intervention groups exhibited significant reductions in BP and cardiac wall thickness compared to the control group[32]. Significant reductions in cardiac wall thickness and LVM index with no significant changes in chamber size were also reported in 16 patients with hypertension after 24 weeks of aerobic exercise training[34]. Similar findings were also observed in middle aged subjects with hypertension (n=11) who engaged in exercise and no changes were observed in the control group[33]. Finally, in the Hypertension and Ambulatory Recording Venetia Study (HARVEST)[35], BP decreased during a median follow up of 8.3 years in physically active individuals (n=173) and increased slightly in the sedentary group (n=281). In addition, physically active individuals were less likely to develop LVH compared to their sedentary counterparts.

It is noteworthy that LVH regression related to the exercise-induced reduction in BP occurs relatively quickly within weeks. This is not surprising since several studies have shown that BP is lowered even after one bout of exercise and remains below baseline for approximately 12-24 hours[11]. Thus, engaging in aerobic activity every other day (as is customary) is likely to favorably influence BP, afterload and cardiac function. Consequently, the stimulus for cardiac hypertrophy is mitigated or removed and the impetus for LV mass regression is initiated.

In contrast to the aforementioned studies, no structural or functional cardiac changes were noted after 24 weeks of aerobic exercise and resistance training in 51 overweight and obesity individuals with an untreated baseline SBP of 130-150 mm Hg or DBP 85-99 mm Hg[36]. Similarly, no exercise-related changes in left ventricular mass were observed in 23 obese individuals with a mean baseline BP 131/84 mm Hg, despite significant reductions in BP[37]. However, the findings of these two studies should be interpreted with caution. In one studies[36], it is not clear as to how many of the participants were truly hypertensive, since the baseline BP range was 130-150 mm Hg for SBP or 85-99 mm Hg for DBP. The exercise intervention was also a mixture of both aerobic and resistance training. Moreover, based on baseline LVM index normal values (63.6 g/m^2), cardiac remodeling was absent. Thus, exercise or any other intervention cannot "fix" what is not broken. In the other study[37], a closer scrutiny of the findings revealed that the LVM index decreased by approximately 8% (baseline of 153 to 141 g/m^2 after exercise) in the exercise group, and increased by approximately 10% (baseline of 141 to 155 g/m^2 after exercise) in the control group. Cardiac wall thickness also decreased after exercise, although statistical significance was not achieved, perhaps due to relatively small number of patients studied (n=7). Collectively, the relatively limited evidence regarding the effects of aerobic exercise on cardiac remodeling supports that LVH regression is likely to occur, if the proper exercise modality is used, in populations with LVH.

Exercise Blood Pressure and LVH

A noteworthy observation is that the degree of LVH regression is disproportional to the degree of exercise-induced reduction in BP. In this regard, we noted in our hypertensive subjects that both systolic and diastolic exercise BP at submaximal and peak workloads was significantly lower following 16 weeks of aerobic exercise training[13,25]. Specifically, the exercise systolic BP at submaximal workloads of approximately 3, 4 and 5 METs was 27 mm Hg, 25 mm Hg and 32 mm Hg, respectively (average 28 mm Hg), lower after 16 weeks of exercise[25]. Consequently, the average rate-pressure product (RPP) at the same workloads was also 5,330 units lower. This is clinically significant because the metabolic demands of most daily chores fall within 3-5 METs. Based on this, it is rational to assume that the daily hemodynamic load and metabolic demands of the myocardium of these subjects would be substantially lower after 16 weeks of exercise. Moreover, we can assume that the reduced 24-hour hemodynamic load may have played a far greater role in the regression of LVH than the resting BP. This assumption is further supported by the strong association noted between the BP response at the submaximal workload of approximately 4-5 METs and LVH in 790 middle aged, individuals with prehypertension[38,39] who underwent echocardiographic studies, 24 hour ambulatory BP monitoring, and a standard exercise stress test (Bruce protocol). Specifically, moderate and high-fit individuals had significantly lower LVM index lower daytime BP and lower exercise systolic BP at the workload of

approximately 4-5 METs compared to the low-fit individuals. Individuals who achieved systolic BP ≥150 mm Hg at the exercise intensity of 4-5 METs had a significantly higher LVM index and lower exercise capacity compared to those with a SBP below this level. Furthermore, the risk of having LVH increased 4-fold for every 10 mm Hg rise in SBP beyond the threshold of 150 mm Hg at approximately 5 METs. It is important to emphasize that the resting BP in these two groups (i.e., exercise SBP<150 mm Hg and ≥150 mm Hg) was similar.

The clinical significance of the BP response to submaximal workloads of approximately 4-5 METs is that it reflects daytime BP during most daily activities. This is supported by the similarity between the SBP of individuals with prehypertension (n=650) at the workload of 4-5 METs (148±12 mm Hg) and daytime ambulatory BP (144±11 mm Hg)[39]. Thus, the association between SBP during physical exertion and LVM[38,39] suggests that the daily exposure to relatively high SBP (SBP ≥150 mm Hg) provides the impetus for an increase in LVM even among those with prehypertension.

Others also reported similar findings among 49 individuals with hypertension at the exercise workload of approximately 7 METs. Systolic BP at this workload was directly and independently associated with cardiac wall thickness and LVM index. This association was stronger than with office BP and 24 hour ambulatory BP[40].

Exercise Blood Pressure and Physical Fitness

Collectively, the noteworthy findings of several studies[13,25,38,39] suggest the following: 1) the systolic BP response at the workloads of approximately 4-5 METs reflects the SBP during daily activities; 2) a systolic BP ≥150 mm Hg at this workload is associated with an increased risk for LVH; 3) daily, intermittent exposure to a systolic BP ≥150 mm Hg provides the impetus for increases in LVM and progression to LVH; and 4) increased physical fitness status achieved by regularly performed exercises of moderate intensity modulates the BP response, leading to a lower SBP at absolute submaximal and peak workloads. This is likely the outcome of favorable changes in SVR and afterload resulting from improved endothelial function. For those with existing LVH, regularly performed aerobic exercise of moderate intensity improves fitness, lowers BP at absolute workloads and the daily hemodynamic load as is reflected by lower BP.

Exercise-Induced LVH

The two traditional types of exercise training are: aerobic or endurance and anaerobic or strength training.

The acute cardiovascular responses and chronic adaptations to these two types of activities differ considerably. Acute cardiovascular responses during aerobic exercises include a substantial increase in heart rate, stroke volume, cardiac output, systolic blood pressure, oxygen consumption and a marked decrease in peripheral vascular resistance with no significant changes in diastolic BP. Cardiovascular responses to resistance training include a mild increase in cardiac output and oxygen consumption, but a substantial increase in heart rate, systolic and diastolic blood pressure and peripheral vascular resistance. Purely aerobic training leads to cardiac remodeling characterized by increases in left and right ventricular chamber dimensions and left atrial cavity size and normal systolic and diastolic function. Left ventricular wall thickness that exceeds normal upper limits is also evident in most athletes[41]. Anaerobic or strength training alone results in a mild increase in wall thickness, often disproportionate compared to cavity size, but within the accepted normal range and no changes in left ventricular chamber size. Contrary to persistent belief, strength training alone does not result always in concentric LVH[42]. It is also important to mention that most sports or daily activities are comprised of both aerobic and anaerobic types of activities. Consequently, structural and functional cardiac adaptations reflect the combined demands of the particular sport or activity. This is most evident in elite athletes participating in sports such as cycling, rowing and swimming that incorporate both aerobic and resistance components. These athletes have the most extreme increase in both LV wall thickness and cavity size. It is important to emphasize that an increase in either alone (wall thickness or LVDD) will not be physiologically desirable. LV dilatation without comparable increase in wall thickness will lead to an inappropriate increase in wall tension that is detrimental to the heart[43].

In general, chronic cardiac adaptations resulting from vigorous, chronic exercise as seen in athletes are considered normal physiologic responses to the hemodynamic demand of the particular sport or

physical activity. They are not associated with diastolic dysfunction, arrhythmias or adverse prognosis, manifestation observed in hypertension-induced LVH and regress quickly when training is discontinued[43]. Less known are the long-term effects of, rigorous exercise such as that demanded by competitive sports (basketball, soccer, etc.) and even non-competitive activities (long distance running, cycling, weight training, etc.) on cardiac structure and function in individuals with hypertension-induced LVH. However, from the available information, we can deduce that high-intensity activities are likely to impose an excessive demand on the cardiovascular system and perpetuate further maladaptations. Therefore, such activities should be avoided. Instead, the recommendations of most medical societies of low-to-moderate intensity aerobic exercise (brisk walk) of approximately 30 minutes per day, most if not all days of the week should be encouraged by health care providers. Such exercise is safe for almost all ages and populations with co-morbidities and has been shown to have a favorable effect on the traditional and novel cardiovascular risk factors[44], and it is likely to lead to LVH regression.

Exercise, Hypertension, LVH and Related Cardiovascular Events

Exercise capacity was the strongest predictor of all-cause mortality in several epidemiological studies in pre-hypertensive, those with high-normal BP and in hypertensive men, including elderly hypertensive men[48-51]. Exercise training studies addressing the efficacy of exercise in lowering the risk of mortality in individuals with hypertensive LVH have not been conducted. However, evidence from epidemiologic studies supports that physical activity and increased fitness status provides protection against cardiovascular events in individuals with hypertensive LVH.

In The Northern Manhattan Stroke Study[45] the risk of stroke in sedentary individuals with elevated LVM was 3.5 times greater when compared to sedentary individuals with normal LVM. Individuals with elevated LVM (presence of LVH), engaging in light intensity activities such as walking, had a similar risk of ischemic stroke to those with normal LVM. This is an important observation, since it suggests that the risk of stroke associated with increased LVM may be potentially attenuated by nonpharmacologic means such as moderate levels of physical activity.

It has been long known that LVH provokes arrhythmias, including atrial fibrillation (AF).

More recently findings support that moderate exercise has no adverse effect on AF[46] or lowers the risk of AF[47]. The risk was inversely associated with fitness assessed by an exercise stress test in 6,390 middle-aged and older male veterans. For every 1-MET increase in exercise capacity, the AF risk was 21% lower (hazard ratio, 0.79, 95% CI, 0.76-0.82, $p<0.001$). When the cohort was stratified according to peak METs achieved, AF risk was 23% lower for the Low-Fit; 46% for Moderate-Fit and 64% for High-Fit individuals compared to the Least-Fit[47].

Considerable evidence supports that concentric LVH is a common precursor of heart failure[48-52]. There is no direct evidence that increased fitness will attenuate the rate of progression form concentric LVH to heart failure. However, prospective epidemiologic evidence supports an association between low fitness with a higher prevalence of concentric remodeling and diastolic dysfunction. This suggests that the exercise-related favorable and long-term effects on cardiac remodeling and diastolic function may attenuate the rate of progression to heart failure[53,54]. Increased in heart failure was also noted in those engaging in low and very high volume exercise, a U-shape association. However, at least 20 minutes of cycling or walking per day was associated with the largest reduction in AF risk[55].

Clinical Implications and Conclusions

The findings presented in this chapter support that regularly performed aerobic exercise of moderate intensity, adequate duration and volume that leads to improved fitness status can be implemented to lower blood pressure in hypertensive patients and modulate the associated hypertensive heart disease. Specifically, aerobic exercise training can prevent the development of concentric cardiac remodeling and lower LV mass in those with LVH[13,32-36]. Exercise has been shown to lower the risk of stroke and all cause death even in the presence of LVH and cardiac arrhythmias. It is noteworthy that the aforementioned health benefits are achievable at a fitness level represented by an exercise capacity >5 METs. This has a significant clinical and public health impact because this level of fitness is achievable by a brisk walk of 20-40 minute, most days of the week, an activity level attainable by most middle-aged and older individuals. Since walking requires virtually no instructions, has a rela-

tively low cost, carries a low risk of injury, and can be easily implemented in large populations, it represents the ideal form of exercise for hypertensive individuals at any age. The effects of exercise have a favorable effect on a cardiovascular risk factors, are additive to pharmacologic therapies and independent of body weight reduction and dietary factors. Thus, increased physical activity of moderate intensity should be an important component of any antihypertensive regimen and should be promoted by all health care providers.

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