

Review Article

Physical Activity in the Prevention and Management of High Blood Pressure

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Hypertension was not recognized as a menace to health until the latter part of the last century. Even until the sixties the prevailing belief among physicians was that a rise in blood pressure (BP) was an important and essential compensatory mechanism (thus essential blood pressure) to maintain adequate perfusion as an individual advanced in age. Based on that, the use of drugs to lower BP was scoffed at as “treatment of the manometer rather than of the patient”.¹ In the mid 1960s and early 1970s Dr. Edward Freis and the Veterans Administration study group proved conclusively that treatment of hypertension reduces strokes and cardiovascular complications.²⁻⁷

Hypertension is now a well established, major cardiovascular risk factor.⁸⁻¹² The relationship is direct, strong, continuous, graded, consistent and independent.¹² Mortality and morbidity double for every 20 mmHg increase in systolic BP above 115 mmHg and for every 10 mmHg increase in diastolic BP above 75 mmHg.¹³

The World Health Organization (WHO) reports that the number of people with hypertension worldwide is estimated to be as many as 1 billion, with 7.1 million deaths per year attributable to hypertension.¹⁴ The prevalence of hypertension increases with age. A higher percentage of men have high BP up to the age of 45, while

women overtake men after 54 years of age.¹⁵ For an individual with normal BP at the age of 55 years, the risk of developing hypertension during the remainder of his or her life is estimated to be 90%.¹⁶

It is also broadly accepted that even small reductions in an abnormally elevated BP result in a decrease of death from heart disease and stroke. For example, a 5 mmHg reduction in diastolic BP over a period of five years was associated with at least 34% less stroke and at least 21% less coronary heart disease (CHD). Reductions of 7.5 mmHg and 10 mmHg are associated with a 46% and 56% decrease in the incidence of stroke and a 29% and 37% decrease in the incidence of CHD, respectively.⁸

An overwhelming number of epidemiological and interventional exercise studies provide unequivocal support that increased physical activity, of adequate duration, intensity and volume, lowers BP significantly, alone or as an adjunct to pharmacological therapy.¹⁷ The purpose of this review is to assess the efficacy and safety of exercise in the management of high BP and its consequences.

Epidemiological and interventional studies

Epidemiological studies that assessed physical activity by a questionnaire, or more objectively by a treadmill test, suggested

that fitness levels are inversely associated with BP.¹⁸⁻²² Middle-aged women who were classified as having moderate and high-fitness, based on their peak exercise time during a treadmill test, had significantly lower diastolic BP (5 and 7 mmHg, respectively) when compared to women of low fitness level.²² In addition, cross-sectional and large-scale longitudinal population studies reported that the relative risk for developing hypertension in sedentary men and women with normal BP at rest is approximately 35% to 70% higher when compared to their physically active peers.²³⁻²⁵

Interventional studies confirmed the epidemiological findings. In a recent review, we reported the results of well controlled exercise interventional studies for BP control (Table 1). The average exercise-related BP reduction in these studies was 10.5 mmHg for systolic and 7.6 mmHg for diastolic BP. In the control group, the average reduction was only 3.8 mmHg and 1.3 mmHg for systolic and diastolic BP, respectively.¹⁷ Similar findings were reported by a recent meta-analysis of randomized controlled trials, involving 72 trials, 105 study groups, and 3936 hypertensive participants. The average exercise-related reduction in resting BP was 6.9 mmHg and 4.9 mmHg for systolic and diastolic BP, respectively.²⁶

Ambulatory blood pressure monitoring

The changes in BP over a 24-hour period as a result of exercise training have not been studied extensively. The few studies that utilized ambulatory BP monitoring reported favorable findings, but a substantially smaller effect than that reported by the studies assess-

ing resting BP.²⁷⁻³⁴ However, the small number of participants, the lack of a control group and the different mode of BP measurement make the interpretation of the findings difficult.

In the HARVEST trial, where the ambulatory pressure was recorded in a relatively large population (n=592) of young stage 1 hypertensive males, the investigators reported that those who engaged in physical activity at least once a week during the previous two months exhibited lower 24-hour and daytime diastolic BP by about 3 mmHg compared to the inactive group.¹⁹ However, authorities agree that significant changes in BP are likely to occur when exercising most days of the week.³³ Thus, the exercise-related reduction in BP reported by the HARVEST trial is likely to be attenuated by the inclusion of those who exercised only once a week. Based on the limited data on ambulatory BP, the American College of Sports Medicine concluded that the average reduction in daytime BP was about 3/3.2 mmHg.³³

However, recent epidemiological evidence from a relatively large study suggests that the magnitude of daytime BP reduction is substantially higher than that reported by the aforementioned studies. In over 600 men and women, we reported that the daytime BP in high and moderate-fitness individuals was 8/4 mmHg lower in men and 9/5 mmHg lower in women, when compared to the BP of low-fitness individuals.³⁶ The difference in BP between the low and high-fitness individuals is similar in magnitude to the changes reported by interventional studies.^{17,37} Similar reductions were observed in nighttime and 24-hour BP.

Table 1. Summary of findings from select exercise studies involving hypertensive individuals.

Investigators	Mean age	Exercise intensity (% of maximum heart rate)	BP reduction	
			Systolic	Diastolic
Blumenthal et al ³⁰	45	70	8	6
Cononie et al ⁴⁸	70-79	50-85	10	9
Higashi et al ⁷³	52	Low	13	4
Kokkinos et al ⁴³	57	60-80	7	5
Matsusaki et al ³⁸	47	60 & 85	9	6
Motoyama et al ³⁹	68-84	Low	15	9
Seals et al ²⁷	>49	50	10	7
Seals et al ⁶¹	50-74	50	10	8
Somers et al ²⁸	-	-	9.7	6.8
Zanettini et al ²⁹	70-85	70-85	15	11.5

BP – blood pressure.

Optimal exercise intensity for blood pressure reduction

The efficacy of physical activity in the reduction of elevated BP is no longer in question; the challenge now is to verify the amount and the frequency of exercise that will produce the maximum health benefits at a relative low risk for injury. In this regard, low-to-moderate intensity exercise (approximately 60% to 85% of age-predicted maximum heart rate) is more effective in lowering BP when compared to higher intensities.³⁵ In studies designed to compare the effects of different exercise intensities, low to moderate intensity exercises were more efficacious in lowering BP than exercise of relatively higher intensities.³⁸⁻⁴¹ Support for this is also provided by a large epidemiological study, where the daytime, nighttime and 24-hour BP in the high-fitness group was similar to that of the moderate-fitness individuals.³⁶ These findings suggest that the antihypertensive effect of exercise occurs at a moderate level of physical activity, without significant additional changes beyond this level. This is clinically significant, because this level of fitness can be attained by 30-40 minutes of brisk walking, most days of the week. Such exercise intensity and volume is within the capacity of most middle aged and older individuals.³⁶

The findings of the Trial of Hypertension Prevention also suggest that moderate intensity physical activity (3.0-6.0 METs) for at least 2-3 days a week is an appropriate recommendation for the general public for the prevention of primary hypertension.⁴²

Severe hypertension and exercise

The management of patients with stage 2 hypertension or higher is challenging. It often requires a combination of medication that increases the likelihood of side effects. The incidence of other co-morbidities is also high and interferes with the patients' ability to exercise. For these reasons, physicians are more concerned about prescribing exercise in patients with stage 2 hypertension. Regarding the role of physical activity in the management of this population, two questions need to be addressed: 1) is exercise safe for individuals with stage 2 hypertension? 2) is exercise effective in lowering BP in these individuals?

We examined the effects of moderately intense exercise on BP in patients with stage 2 hypertension.⁴³ After 16 weeks of moderate-intensity exercise training, resting systolic BP was lowered by 7 mmHg and diastolic by 5 mmHg. Most importantly, BP continued to decrease as exercise training continued for an-

other 16 weeks, allowing a 33% reduction in antihypertensive medication for the entire group. BP in the non-exercising group increased slightly during the same period.

The findings of this study suggest that patients with more severe stages of hypertension can safely tolerate exercise of moderate intensity. Moreover, such exercise as an adjunct to drug therapy can lead to a better management of high BP compared to the medication therapy alone and, in some cases, a reduction in the amount of medications needed.⁴³

Aerobic versus anaerobic exercise and blood pressure

Most interventional studies examined the efficacy of aerobic exercise in lowering BP. Information regarding the efficacy of strength training in BP control is limited. This is in part due to the fact that the first studies of resistance training reported a dangerously high BP during maximum effort. More specifically, in two studies the mean peak pressure during the double leg-press for the group reached 320/250 mmHg in individuals with normal BP at rest, with pressures in one subject exceeding 480/350 mmHg.⁴⁴ Peak pressures with the single-arm curl exercise reached a mean group value of 255/190 mmHg when repetitions were continued until failure. In mildly hypertensive individuals, BP reached 345/245 mmHg during squatting.⁴⁵ In these studies the enormous increase in BP can be attributed to the lifting of a heavy weight to exhaustion and to the effect of the Valsalva maneuver.^{44,45}

However, the increased interest in resistance training because of its potential preventive and therapeutic qualities in relation to osteoporosis has led to a reexamination of the effect of resistance training on BP. Newer studies did not observe the tremendous increase in BP reported by previous studies, partly by avoiding the Valsalva effect.^{44,45} However, their findings regarding BP reduction are inconsistent. Some suggested a possible antihypertensive effect of strength training, whereas others found none.^{30,46-49} In two of the studies a small (5 mmHg), but significant reduction was observed in diastolic BP.^{46,47} In a third study the reduction of 7 mmHg for systolic and 6 mmHg for diastolic BP was comparable to the reduction in BP observed in the control group.³⁰ No changes in BP were noticed after 6 months of strength training in a group of 70-79 year old men and women, or in a group of previously sedentary middle-aged men after 20 weeks of strength training.^{48,49} A recent meta-analysis concluded that the reduction in BP as a result of resistance training is ap-

proximately 3 mmHg.⁵⁰ Based on these data, the American College of Sports Medicine concluded that studies have not been consistent in demonstrating that strength training lowers BP in hypertensive individuals. Accordingly, the American College of Sports Medicine, the European Society of Hypertension, and the European Society of Cardiology recommend that the primary type of exercise for the management of BP should be aerobic, supplemented by resistance training. High intensity isometric exercise, such as heavy weightlifting, should be avoided.^{35,51}

Physical activity and left ventricular hypertrophy

Left ventricular hypertrophy (LVH), known to be more prevalent in hypertensive individuals, is considered to be an independent risk factor for cardiovascular disease.⁵² The risk of cardiovascular morbid events, including sudden cardiac death, increases threefold in patients with LVH.⁵²

Epidemiological evidence suggests that physical activity has the potential to reduce left ventricular mass (LVM). A 12% reduction in LVM index was noticed in hypertensive individuals after 16 weeks of training.⁴³ Interestingly, the amount of the reduction was similar to the reduction achieved by medication therapy.⁵³

Whether this exercise-related left ventricular mass reduction has an effect in lowering the risk of mortality in individuals with LVH has not been extensively studied. However, in a recent study, Rodriguez et al provided evidence that physical activity has a protective role against the elevated risk of stroke associated with increased LVM.⁵⁴ In this study, the risk of stroke was similar between physically active individuals with LVH and those with normal LVM, leading to the conclusion that increased physical activity may have the potential to reduce the elevated risk of cardiovascular events associated with LVH.⁵²

Blood pressure response during exercise

A progressive rise in systolic BP is observed during exercise as the workload increases, while diastolic BP remains near resting levels and may even decrease slightly. At peak exercise systolic BP reaches approximately 200 mmHg. However, in some individuals, systolic BP rises substantially higher than 200 mmHg. This is referred to as an exaggerated BP response. Although a definitive abnormal rise threshold has not yet been established, systolic BP >200 mmHg and/or diastolic BP >110 mmHg at peak or near peak exercise has been

linked to future hypertension, heart disease and cardiovascular mortality.⁵⁵⁻⁵⁸ However, others found no relationship.⁵⁹⁻⁶⁰

The potentially detrimental exaggerated BP response during physical activity can be attenuated by moderate aerobic exercise training. Findings suggest that higher fitness levels, as indicated by peak exercise time, are inversely associated with BP at six minutes of exercise. In both normotensive and hypertensive middle-aged women peak exercise time was the strongest predictor of systolic BP response at six minutes of exercise.²²

Lower exercise BP has also been reported in postmenopausal women following eight weeks of aerobic exercise training.⁶¹ We also reported a significant reduction of approximately 20-27 mmHg in systolic and 10-14 mmHg in diastolic BP levels at maximal and submaximal workloads in hypertensive patients following 16 weeks of aerobic training. In addition, the rate-pressure product was significantly lower at sub-maximal and peak workloads, suggesting that myocardial oxygen consumption was lower at each workload. A notable observation is that the peak workload following 16 weeks of training was significantly higher. Yet peak exercise BP was lower by 20 mmHg at virtually the same peak heart rate. This suggests that the mechanism responsible for the lower BP was a reduction in peripheral resistance.⁶²

Prehypertension and left ventricular hypertrophy

In 2003 the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high BP (JNC 7) introduced a new category referred to as prehypertension, defined as systolic BP levels of 120-139 mmHg and/or diastolic BP levels of 80-89 mmHg.¹⁰ Prehypertensive individuals are at 1.5- to 2-fold higher risk for developing hypertension and major cardiovascular disease compared to those with normal BP.^{13,52,63,64}

The mechanisms involved in the increased risk are not well defined. Prehypertension may mark the beginning of a progressive increase in LVM and a decline in cardiac function that remain undetected for years. The findings of a recent study suggest that the development of LVH starts in prehypertension. In a group of 790 men and women with prehypertension, over 26% of the prehypertensive individuals had LVH, compared with 3% of those with BP <120/80 mmHg.⁶⁵ In another study, the prevalence of LVH in prehypertensive individuals was 11.4%.⁶⁶ However,

er, the average age in this population was about half the average age of the first mentioned study (26.8 versus 52 years).

The factors that influence the early increase in LVM are also not well defined. However, we reported that the prevalence of LVH was significantly higher in low-fitness than in moderate and high-fitness individuals (48.3% versus 18.7% versus 21.6%, respectively).⁶⁵ The investigators also reported that the strongest predictors of LVH were the exercise systolic BP at five METs and the change in BP from rest to the workload of five METs. In addition, they identified that a systolic BP of 150 mmHg at the exercise level of five METs was the threshold for LVH (sensitivity 86%, specificity 94%). The likelihood of LVH increased 4-fold for every 10 mmHg increment in systolic BP beyond this threshold. There was also a 42% reduction in the risk for LVH for every one MET increase in the workload.

Since previous reports suggest that high-fitness individuals exhibit a lower exercise BP, the investigators examined the fitness status of the individual and its association with exercise BP and LVH.²² When compared to high-fitness, individuals in the low-fitness category exhibited the following: 1) higher exercise BP at sub-maximal workloads; 2) greater prevalence of exercise BP above the threshold of 150 mmHg; 3) higher daytime BP;³⁶ and 4) higher prevalence of LVH.

Since the exercise workload of approximately 5 METs is similar to the workload of routine daily activities³⁷ and the exercise BP during this workload is very similar to the daytime BP, these findings suggest that low-fitness individuals exhibit higher BP during normal daily activities when compared to moderate and high-fitness individuals.³⁶ The increased hemodynamic load results in a higher myocardial workload, providing a stimulus for myocardial structural changes.

Antihypertensive mechanisms of exercise

The underlying mechanisms responsible for the reduction in BP elicited by exercise training remain elusive and controversial. The prevailing current opinion is that exercise training must act upon a number of mechanisms, resulting in the reduction of total peripheral resistance, cardiac output, or both. It is generally agreed that the changes in BP are independent of changes in body weight, body composition and dietary influences.⁵²

Reductions in cardiac output, sympathetic nerve activity, plasma norepinephrine levels, and total peripheral resistance have been reported.^{62,67,68} In a recent meta-analysis involving 72 trials, 105 study groups, and 3936 participants, the authors reported reductions in systemic vascular resistance, plasma norepinephrine, and plasma renin activity as the main reasons for the decrease in BP following exercise.²⁶ In the past two decades, several studies have shown that endothelial function is impaired in hypertensive patients.^{69,70} Improved endothelial function is another possible mediator of the hypotensive response observed with exercise training.^{71,72} An improvement in reactive hyperemia following exercise has been demonstrated in hypertensive patients.⁷³

Current recommendations

Both the American College of Sports Medicine and the European Society of Hypertension recommend physical exercise as a part of lifestyle modifications in the prevention and treatment of hypertension.^{35,51} The specific recommendations are shown in Table 2.

The extent of pre-training evaluation of the cardiovascular status must depend on the intensity of the exercise program and on the patient's symptoms and signs, total cardiovascular risk and presence of comorbidities.^{35,51} A symptom-limited exercise tread-

Table 2. Recommendations of the American College of Sports Medicine and the European Society of Hypertension concerning physical exercise for the prevention and treatment of hypertension.

Frequency	Most, preferably all, days of the week.
Intensity	Moderate intensity (60-85% of predicted maximal heart rate or 40% to <60% of VO ₂ reserve*).
Time	≥30 min of continuous or accumulated physical activity per day.
Type	Primarily endurance physical activity supplemented by resistance training.

*VO₂ reserve refers to the peak or maximal oxygen consumption (ml of O₂/kg/min) minus resting consumption (3.5 ml/kg/min)

mill test may be warranted, especially for men over 45 years old and women over 55 years who are planning an intense exercise program.^{35,51}

Conclusions

It is now well accepted that increased physical activity of appropriate intensity and duration is associated with a reduced incidence of hypertension.²³⁻²⁵ Thus, for primary prevention of hypertension an appropriate recommendation for a public health policy should include the implementation of a low to moderate intensity exercise program most, preferably all, days of the week.³⁵

Recent data suggest that structural and functional changes in the heart occur much earlier than first thought. Over 26% of pre-hypertensive individuals have LVH. The stimulus for the changes in the left ventricle appears to be an increased daily hemodynamic load resulting from relatively high BP levels during routine daily activities. This increased workload provides the stimulus for increases in LVM. The relatively high exercise BP, daytime BP, and LVM observed in low-fitness compared to moderate and high-fitness individuals suggests that low-fitness individuals exhibit higher BP during routine daily activities. Conversely, increased physical activity is associated with lower exercise BP at submaximal workloads. This suggests that increased physical activity consisting of daily brisk walks of 30-40 minutes in duration can lower BP and prevent the development of LVH.^{36,65}

The predicted reductions in mortality from stroke, CHD and all causes are substantial, even with modest reductions in systolic BP in the entire hypertensive population.¹² For individuals who are already hypertensive, the implementation of regular exercise, alone or as an adjunct to medical therapy, can improve BP control at relatively lower doses of antihypertensive pharmacological agents, and reduce adverse events. The intensity of exercise required can easily be achieved by middle aged hypertensive individuals.^{35,43}

References

1. Freis ED. Historical Development of Antihypertensive Treatment. In: Laragh JH, Brenner BM, editors. Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York: Raven Press; 1995. p. 2741-2751.
2. Freis ED. Treatment of hypertension with chlorothiazide. *J Am Med Assoc.* 1959; 169: 105-108.
3. Freis ED. Essential hypertension. *Heart Bull.* 1959; 8: 52-54.
4. Freis ED. The value of antihypertensive therapy. *Bull N Y Acad Med.* 1969; 45: 951-962.
5. Freis ED. The Veterans Administration cooperative study on antihypertensive agents: Implications for stroke prevention. *Stroke.* 1974; 5: 76-77.
6. Freis ED, Wanko A, Wilson IM, Parrish AE. Treatment of essential hypertension with chlorothiazide (diuril); its use alone and combined with other antihypertensive agents. *J Am Med Assoc.* 1958; 166: 137-140.
7. Poblete PF, Kyle MC, Pipberger HV, Freis ED. Effect of treatment on morbidity in hypertension. Veterans Administration Cooperative Study on Antihypertensive Agents. Effect on the electrocardiogram. *Circulation.* 1973; 48: 481-490.
8. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet.* 1990; 335: 765-774.
9. Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. *Arch Intern Med.* 1993; 153: 598-615.
10. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA.* 2003; 289: 2560-2572.
11. The sixth report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. *Arch Intern Med.* 1997; 157: 2413-2446.
12. National High Blood Pressure Education Program Working Group report on primary prevention of hypertension. 1993. *Arch Intern Med.* 1993; 153: 186-208.
13. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. *Lancet.* 2001; 358: 1682-1686.
14. World Health Report 2002. Reducing risks, promoting healthy life.
15. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics—2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation.* 2007; 115: e69-171.
16. Vasan R, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA.* 2002; 287: 1003-1010.
17. Kokkinos PF, Narayan P, Papademetriou V. Exercise as hypertension therapy. *Cardiol Clin.* 2001; 19: 507-516.
18. Gibbons LW, Blair SN, Cooper KH, Smith M. Association between coronary heart disease risk factors and physical fitness in healthy adult women. *Circulation.* 1983; 67: 977-983.
19. Palatini P, Graniero G, Mormino P, et al. Relation between physical training and ambulatory blood pressure in stage I hypertensive subjects. Results of the HARVEST Trial. Hypertension and Ambulatory Recording Venetia Study. *Circulation.* 1994; 90: 2870-2876.
20. Reaven PD, Barrett-Connor E, Edelstein S. Relation between leisure-time physical activity and blood pressure in older women. *Circulation.* 1991; 83: 559-565.
21. Staessen JA, Fagard R, Amery A. Life style as a determinant of blood pressure in the general population. *Am J Hypertens.* 1994; 7: 685-694.
22. Kokkinos PF, Holland JC, Pittaras AE, Narayan P, Dotson CO, Papademetriou V. Cardiorespiratory fitness and coronary heart disease risk factor association in women. *J Am Coll Cardiol.* 1995; 26: 358-364.
23. Blair SN, Goodyear NN, Gibbons LW, Cooper KH. Physical

- fitness and incidence of hypertension in healthy normotensive men and women. *JAMA*. 1984; 252: 487-490.
24. Haapanen N, Miilupanlo S, Vuory I, Oja P, Pasanen P. Association of leisure time physical activity with the risk of coronary heart disease, hypertension and diabetes in middle-aged men and women. *Int J Epidemiol*. 1997; 26: 739-747.
 25. Paffenbarger RS, Wing AL, Hyde RT, Jung DL. Physical activity and incidence of hypertension in college alumni. *Am J Epidemiol*. 1983; 117: 245-257.
 26. Cornelissen VA, Fagard RH. Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*. 2005; 46: 667-675.
 27. Seals DR, Silverman HG, Reiling MJ, Davy KP. Effect of regular aerobic exercise on elevated blood pressure in postmenopausal women. *Am J Cardiol*. 1997; 80: 49-55.
 28. Somers VK, Conway J, Johnston J, Sleight P. Effects of endurance training on baroreflex sensitivity and blood pressure in borderline hypertension. *Lancet*. 1991; 337: 1363-1368.
 29. Zanettini R, Bettiga D, Agostoni O, et al. Exercise training in mild hypertension: effects on blood pressure, left ventricular mass and coagulation factor VII and fibrinogen. *Cardiology*. 1997; 88: 468-473.
 30. Blumenthal JA, Siegel WC, Appelbaum M. Failure of exercise to reduce blood pressure in patients with mild hypertension. Results of a randomized controlled trial. *JAMA*. 1991; 266: 2098-2104.
 31. Cooper AR, Moore LA, McKenna J, Riddoch CJ. What is the magnitude of blood pressure response to a programme of moderate intensity exercise? Randomised controlled trial among sedentary adults with unmedicated hypertension. *Br J Gen Pract*. 2000; 50: 958-962.
 32. Cox KL, Puddey IB, Morton AR, et al. Exercise and weight control in sedentary overweight men: effects on clinic and ambulatory blood pressure. *J Hypertens*. 1996; 14: 779-790.
 33. Jessup JV, Lowenthal DT, Pollock ML, Turner T. The effects of endurance exercise training on ambulatory blood pressure in normotensive older adults. *Geriatr Nephrol Urol*. 1998; 8: 103-109.
 34. Marceau M, Kouame N, Lacourciere Y, Cleroux J. Effects of different training intensities on 24-hour blood pressure in hypertensive subjects. *Circulation*. 1993; 88: 2803-2811.
 35. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc*. 2004; 36: 533-553.
 36. Kokkinos P, Pittaras A, Manolis A, et al. Exercise capacity and 24-h blood pressure in prehypertensive men and women. *Am J Hypertens*. 2006; 19: 251-258.
 37. Kokkinos PF, Papademetriou V. Exercise and hypertension. *Coron Artery Dis*. 2000; 11: 99-102.
 38. Matsusaki M, Ikeda M, Tashiro E, et al. Influence of workload on the antihypertensive effect of exercise. *Clin Exp Pharmacol Physiol*. 1992; 19: 471-479.
 39. Motoyama M, Sunami Y, Kinoshita F, et al. Blood pressure lowering effect of low intensity aerobic training in elderly hypertensive patients. *Med Sci Sports Exerc*. 1998; 30: 818-823.
 40. Hagberg JM, Montain SJ, Martin WH 3rd, Ehsani AA. Effect of exercise training in 60- to 69-year-old persons with essential hypertension. *Am J Cardiol*. 1989; 64: 348-353.
 41. Pescatello LS, Fargo AE, Leach CN Jr, Scherzer HH. Short-term effect of dynamic exercise on arterial blood pressure. *Circulation*. 1991; 83: 1557-1561.
 42. Borhani NO. Significance of physical activity for prevention and control of hypertension. *J Hum Hypertens*. 1996; 10 (Suppl 2): S7-11.
 43. Kokkinos PF, Narayan P, Collieran JA, et al. Effects of regular exercise on blood pressure and left ventricular hypertrophy in African-American men with severe hypertension. *N Engl J Med*. 1995; 333: 1462-1467.
 44. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. *J Appl Physiol*. 1985; 58: 785-790.
 45. Palatini P, Mos L, Munari L, et al. Blood pressure changes during heavy-resistance exercise. *J Hypertens Suppl*. 1989; 7: S72-73.
 46. Harris KA, Holly RG. Physiological response to circuit weight training in borderline hypertensive subjects. *Med Sci Sports Exerc*. 1987; 19: 246-252.
 47. Hurley BF, Hagberg JM, Goldberg AP, et al. Resistive training can reduce coronary risk factors without altering VO₂max or percent body fat. *Med Sci Sports Exerc*. 1988; 20: 150-154.
 48. Cononie CC, Graves JE, Pollock ML, Phillips MI, Summers C, Hagberg JM. Effect of exercise training on blood pressure in 70- to 79-yr-old men and women. *Med Sci Sports Exerc*. 1991; 23: 505-511.
 49. Smutok MA, Reece C, Kokkinos PF, et al. Aerobic versus strength training for risk factor intervention in middle-aged men at high risk for coronary heart disease. *Metabolism*. 1993; 42: 177-184.
 50. Kelley GA, Kelley KA, Tran ZV. Aerobic exercise and resting blood pressure: a meta-analytic review of randomized, controlled trials. *Prev Cardiol*. 2001; 4: 73-80.
 51. Mancia G, De Backer G, Dominiczak A, et al. 2007 European Guidelines for the management of arterial hypertension. *Eur Heart J*. 2007; 28: 1462-1536.
 52. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med*. 1990; 322: 1561-1566.
 53. Dahlof B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients. A metaanalysis of 109 treatment studies. *Am J Hypertens*. 1992; 5: 95-110.
 54. Rodriguez CJ, Sacco RL, Sciaccia RR, Boden-Albala B, Homma S, DiTullio MR. Physical activity attenuates the effect of increased left ventricular mass on the risk of ischemic stroke: The Northern Manhattan Stroke Study. *J Am Coll Cardiol*. 2002; 39: 1482-1488.
 55. Miyai N, Arita M, Miyashita K, Morioka I, Shiraishi T, Nishio I. Blood pressure response to heart rate during exercise test and risk of future hypertension. *Hypertension*. 2002; 39: 761-766.
 56. Singh JP, Larson MG, Manolio TA, et al. Blood pressure response during treadmill testing as a risk factor for new-onset hypertension. The Framingham heart study. *Circulation*. 1999; 99: 1831-1836.
 57. Filipovsky J, Ducimetiere P, Safar ME. Prognostic significance of exercise blood pressure and heart rate in middle-aged men. *Hypertension*. 1992; 20: 333-339.
 58. Mundal R, Kjeldsen SE, Sandvik L, Erikssen G, Thaulow E, Erikssen J. Exercise blood pressure predicts cardiovascular mortality in middle-aged men. *Hypertension*. 1994; 24: 56-62.
 59. Fagard RH, Pardaens K, Staessen JA, Thijs L. Prognostic value of invasive hemodynamic measurements at rest and during exercise in hypertensive men. *Hypertension*. 1996; 28: 31-36.
 60. Manolio TA, Burke GL, Savage PJ, Sidney S, Gardin JM,

- Oberman A. Exercise blood pressure response and 5-year risk of elevated blood pressure in a cohort of young adults: the CARDIA study. *Am J Hypertens.* 1994; 7: 234-241.
61. Seals DR, Reiling MJ. Effect of regular exercise on 24-hour arterial pressure in older hypertensive humans. *Hypertension.* 1991; 18: 583-592.
 62. Kokkinos PF, Narayan P, Fletcher RD, Tsagadopoulos D, Papademetriou V. Effects of aerobic training on exaggerated blood pressure response to exercise in African-Americans with severe systemic hypertension treated with indapamide +/- verapamil +/- enalapril. *Am J Cardiol.* 1997; 79: 1424-1426.
 63. Liszka HA, Mainous AG 3rd, King DE, Everett CJ, Egan BM. Prehypertension and cardiovascular morbidity. *Ann Fam Med.* 2005; 3: 294-299.
 64. Qureshi AI, Suri MF, Kirmani JF, Divani AA. Prevalence and trends of prehypertension and hypertension in United States: National Health and Nutrition Examination Surveys 1976 to 2000. *Med Sci Monit.* 2005; 11: CR403-409.
 65. Kokkinos PF, Pittaras A, Narayan P, Faselis C, Singh S, Manolis A. Exercise capacity and blood pressure associations with left ventricular mass in prehypertensive individuals. *Hypertension.* 2007; 49: 55-61.
 66. Drukteinis JS, Roman MJ, Fabsitz RR, et al. Cardiac and systemic hemodynamic characteristics of hypertension and prehypertension in adolescents and young adults: the Strong Heart Study. *Circulation.* 2007; 115: 221-227.
 67. Cleroux J, Kouame N, Nadeau A, Coulombe D, Lacourciere Y. Aftereffects of exercise on regional and systemic hemodynamics in hypertension. *Hypertension.* 1992; 19: 183-191.
 68. Floras JS, Sinkey CA, Aylward PE, Seals DR, Thoren PN, Mark AL. Postexercise hypotension and sympathoinhibition in borderline hypertensive men. *Hypertension.* 1989; 14: 28-35.
 69. Linder L, Kiowski W, Buhler FR, Luscher TF. Indirect evidence for release of endothelium-derived relaxing factor in human forearm circulation in vivo. Blunted response in essential hypertension. *Circulation.* 1990; 81: 1762-1767.
 70. Panza JA, Quyyumi AA, Brush JE, Epstein SE. Abnormal endothelium-dependent vascular relaxation in patients with essential hypertension. *N Engl J Med.* 1990; 323: 22-27.
 71. DeSouza CA, Shapiro LF, Clevenger CM, et al. Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation.* 2000; 102: 1351-1357.
 72. Higashi Y, Sasaki S, Kurisu S, et al. Regular aerobic exercise augments endothelium-dependent vascular relaxation in normotensive as well as hypertensive subjects: role of endothelium-derived nitric oxide. *Circulation.* 1999; 100: 1194-1202.
 73. Higashi Y, Sasaki S, Sasaki N, et al. Daily aerobic exercise improves reactive hyperemia in patients with essential hypertension. *Hypertension.* 1999; 33: 591-597.