Journal of
HYPERTENSION RESEARCH
www.hypertens.org/jhr

Original Articles

J Hypertens Res (2015) 1: 47–52

The role of exercise and physical fitness in the management of hypertension

Andreas Pittaras[1,*], Charles Faselis[2], Michael Doumas[3], Peter Kokkinos[4]

[1] Mediton Medical Center, 22 El. Venizelou Str. Galatsi, Athens 11147 and Veterans Affairs Medical Center/Cardiology, 50 Irving Street NW, Washington, DC 20422 and George Washington University School of Medicine, 2121 I Street, Washington, DC.
[2] Veterans Affairs Medical Center/Cardiology, 50 Irving Street NW, Washington, DC 20422 and George Washington University School of Medicine, 2121 I Street, Washington, DC.
[3] Veterans Affairs Medical Center/Cardiology, 50 Irving Street NW, Washington, DC 20422 and George Washington University School of Medicine, 2121 I Street, Washington, DC.
[4] Veterans Affairs Medical Center, Cardiology Department, 50 Irving Street NW, Washington, DC 20422 and Georgetown University School of Medicine, 4000 Reservoir Road NW, Washington, DC. and George Washington University School of Medicine, 2121 I Street, Washington, DC.

Received: December 8, 2015; Accepted: January 31, 2015

Introduction

The association between physical activity and health was recognized as early as the 5th century BC by the Greek physician Hippocrates, who wrote:

> *"…all parts of the body, if used in moderation and exercised in labors to which each is accustomed, become thereby healthy and well developed and age slowly; but if they are unused and left idle, they become liable to disease, defective in growth and age quickly."*

With the decline of the Hellenic civilization this concept faded. For centuries, physical activity and fitness were considered largely for military purposes and associated with youth sports and athletics even through the post WWII era.

For over half a century now, a plethora of evidence has accumulated on the beneficial effect of exercise and physical fitness. Findings from well-designed large epidemiologic studies and diverse populations support a robust, inverse, and independent association between physical activity, cardiorespiratory fitness and cardiovascular (CV) and overall mortality risk. The association is independent of age, race, gender, established CV disease, or co-morbidities including hypertension [1,2]. In pre-hypertension, high-normal blood pressure and hypertension, cardiorespiratory fitness exhibits preventive, prognostic and therapeutic properties [1–4]. Thus, appropriate lifestyle interventions including increased physical activity designed to enhance cardiorespiratory fitness, are recommended by the Eight Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) and the European Society of Hypertension/European Society of Cardiology recent guidelines as initial therapy to prevent, treat, and control hypertension [5,6]. This review presents evidence regarding the preventive, prognostic and therapeutic aspects of exercise and fitness status of the individual on blood pressure (BP).

* Correspondence to: Andreas Pittaras, Mediton Medical Center, 22 El. Venizelou Str. Galatsi, Athens 11147
Phone: (210) 2138435-7 ; Fax: (210) 2138437,
Email: andreaspittaras@gmail.com

Preventive aspects of fitness on blood pressure

The age-related progressive increase in BP is accompanied by an incremental increase in CV risk evident beyond BP levels of 115/75 mmHg [7]. Evidence suggests that this increase in BP is preceded by arterial stiffness, an important and independent contributor to hypertension [8-12]. To some extent, the age-related increase in arterial stiffness and BP is inevitable (biological aging). However, a substantial portion of the pronounced increase observed in industrialized societies is pathological and more likely a consequence of lifestyle characterized by high-fat and salty diets, and physical inactivity than an inevitable outcome of aging [13–19]. Indigenous populations living a relatively traditional hunter-gatherer lifestyle exhibit only a modest and substantially lower increase in arterial stiffness and BP compared to individuals living in westernized environments [14,15]. Additionally, vascular health is improved by habitual physical activity and exercise intervention programs implemented in westernized populations [16-19] and diminished by inactivity and bed rest [18,19]. The exercise-induced increase in shear stress appears to provide the physiological stimulus for the adaptations in endothelial function and vascular remodeling observed following exercise training in healthy subjects [20].

Prehypertension, defined as systolic BP levels of 120–139 mmHg and/or diastolic BP of 80 to 89 mmHg [21] is frequently a precursor of hypertension [22]. The aforementioned findings suggest that cardiorespiratory fitness may attenuate the rate of progression from pre-hypertension to hypertension. This concept was investigated in 2,303 pre-hypertensive, middle-aged, male veterans followed for over 9.2 years. Higher cardiorespiratory fitness, as reflected by peak METs achieved during a standardized exercise test, was inversely associated with the rate of progression to hypertension. Compared to the individuals with the highest exercise capacity (>10 METs), the multivariate-adjusted risk for developing hypertension was 36% higher for those with an exercise capacity of 8.6–10 METs; 66% for those with 6.6–8.5 METs, and 72% higher for individuals who achieved ≤6.5 METs [23]. Similar findings have been reported by others [24], and a recent meta-analysis of thirteen prospective cohort studies confirmed an inverse, dose-response association between levels of recreational physical activity and risk for developing hypertension [3].

Collectively, these studies [13-19] support that the age-related insidious increases in arterial stiffness, systolic BP and incident hypertension are not entirely inevitable and that increased physical activity or a physically active lifestyle that leads to increased cardiorespiratory fitness can attenuate and even reverse the process [18,20].

Prognostic aspects of exercise blood pressure

Physiological rise in BP occurs during acute exercise [1]. However, in some individuals, systolic BP rises disproportionally to the workload. This disproportionate BP rise is adversely associated with end-organ damage [25]. For example, in our study of 790 middle-aged, pre-hypertensive individuals, exercise systolic BP at the workload of approximately 5 METs was the strongest predictor of left ventricular hypertrophy (LVH) [25]. Systolic BP ≥150 mmHg was the threshold for LVH. Individuals who achieved a systolic BP ≥150 mmHg had significantly greater cardiac wall thickness, left ventricular mass (LVM) index (Figure 1) and lower exercise capacity, compared to those with systolic BP <150 mmHg. Furthermore, the risk of LVH increased 4-fold for every 10-mmHg incremental rise in systolic BP beyond 150 mmHg. The resting BP in the two groups (systolic BP ≥150 mmHg and <150 mmHg) was similar. These findings suggest that the BP response to exercise may be used to identify individuals at risk for LVH.

Exercise blood pressure, fitness status and clinical significance

The exaggerated rise in BP during exercise may be modulated by the fitness status of the individual. Systolic BP of fit individuals at approximately 5 METs [25]and ambulatory BP [26] were significantly lower when compared to the BP of low-fit. Also, in a randomized controlled study of hypertensive individuals who completed 16 weeks of aerobic exercise training, systolic BP was 27 mmHg and 32 mmHg lower from pre-training values at the absolute workloads of 3 and 5 METs, respectively [27].

Evidence also suggests that the BP response to exercise or physical exertion may modulate left ventricular structure. In the aforementioned study of prehypertensive individuals [25] the exercise capacity-LVM index association was strong and inverse. The risk for LVH was 42% lower for every 1-MET increase in exercise capacity. When the cohort was stratified based on cardiorespiratory fitness, the least fit individuals exhibited higher exercise systolic BP and LVM index than the moderate and high-fit (Figure 2). Moreover, the exercise BP at the workload of approximately 5 METs was the strongest predictor of LVM, while resting BP was a substantially weaker predictor. Exercise intervention studies have also reported significant reductions in LVM index in older individuals with stage 1 and 2 hypertension [27-30].

Variables	Systolic BP <150 mm Hg (n=430)	Systolic BP ≥150 mm Hg (n=360)
PW, mm	9.1±0.6*	10.3±1.0
IVS, mm	9.6±0.7*	10.6±1.0
LVDD, mm	47.0±2.6*	50.0±2.6
LVSD, mm	25.6±3.0	28.0±3.2*
LVM, g	152±24*	195±38
LVM index, g/m$^{2.7}$	36.6±6.3*	49.8±10.2
e-wave, m/s	0.74±0.10*	0.60±0.13
a-wave, m/s	0.55±0.08	0.66±0.12
e/a wave	1.3±0.2*	0.9±0.3
Deceleration time, s	214±16*	235±21
Exercise time, min	9.9±1.6*	8.2±2.1
METs	9±1.1*	7.7±1.6

*Difference between the groups ($P<0.001$).

Figure 1. Cardiac wall thickness (A) and LVM Index (B) for those with exercise SBP <150 mmHg and SBP ≥150 mmHg. Adapted from Kokkinos P., *et al.* [25].

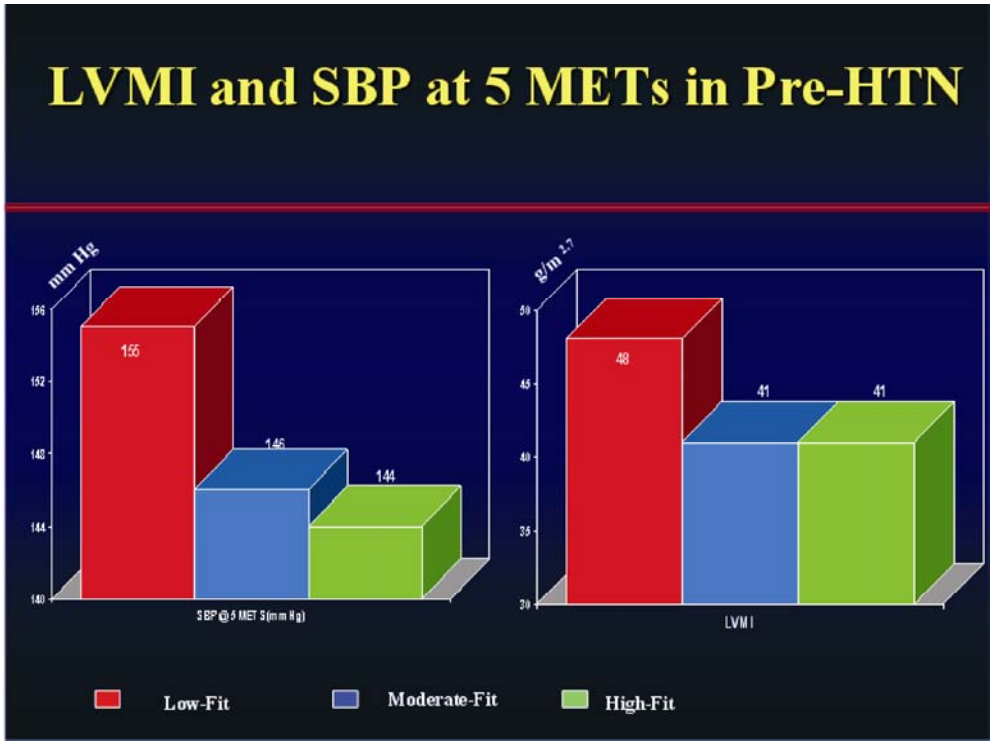

Figure 2. Systolic BP at the workload of approximately 5 METs and LVM Index according to fitness categories. Adapted from Kokkinos P., *et al.* [25].

Collectively, these findings suggest: 1) The exercise BP at the workloads of approximately 3–5 METs reflects BP during daily activities; 2) an abnormal BP response at these relatively low workloads (3–5 METs) provides the impetus for increases in LVM and progression to LVH; 3) the exaggerated BP response is attenuated by regularly performed moderate intensity exercises or increased physical activity; and 4) the lower daily BP leads to LVM regression. However, these assumptions are based on prospective epidemiologic data [25,26] and interventional exercise studies are needed to substantiate these findings.

The clinical significance and public health impact of the exercise systolic BP-LVM relationship is two-fold. First, exercise BP may be a marker for present and future LVH and hypertension. Second, the lower exercise BP and LVM index associated with higher fitness suggest that the progression to hypertension and LVH can be attenuated by increased fitness status. Thus, exercise programs designed to improve fitness can be used to attenuate the progressive increase in arterial stiffness, BP and LVH.

Therapeutic aspects of cardiorespiratory fitness

The consensus of meta-analyses and several reviews is that structured aerobic exercise training programs or increased physical activity of moderate intensity and adequate volume result in an independent reduction of approximately 4 to 10 mmHg in systolic and 3–8 mmHg in diastolic BP for individuals with stage 1 hypertension regardless of age or gender [1,3, 31–33]. Relatively little is known on the effects of exercise in individuals with stage 2 hypertension or those with resistant hypertension. We noted significant reduction in BP in male veterans with stage 2 hypertension and LVH after 16 weeks of moderate-intensity aerobic 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 [28]. We also noted a significant reduction in cardiac wall thickness and left ventricular mass, similar to that observed with most antihypertensive medications [34]. This finding was unprecedented and clinically significant since LVH is considered an independent risk factor for mortality [35].

Similar findings were observed in individuals with resistant hypertension, defined as BP that remains above goal in spite of the concurrent use of 3 antihypertensive agents of different classes, one of which is a diuretic [36]. In this study, moderate exercise was effective in significantly lowering 24-hour ambulatory BP [37]. The reduction was similar to that reported by previous studies in individuals with mild to moderate hypertension [1,3,31-33].

Almost all of the information regarding exercise and BP is derived from aerobic exercises. Information available on the effects of resistance or strength training on resting BP is limited, conflicting and suggests that resistance training is less efficacious than aerobic exercise [1,3,31,32] in lowering resting BP [38,39]. The reasons for this are not known. 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 [33]. Thus, it is recommended that resistance training may serve as an adjunct to an aerobic-based exercise program for BP reduction [31,32] and implemented as part of a complete exercise program [40,41].

Exercise capacity and mortality risk in hypertensive and pre-hypertensive individuals

Findings from large and well-controlled epidemiologic studies support an inverse, independent and graded association between exercise capacity and mortality risk in pre-hypertensive and hypertensive individuals [42–45]. For example, in a cohort of 4,631 hypertensive veterans with multiple cardiovascular risk factors, who successfully completed a graded exercise test mortality risk was 13% lower for every 1-MET increase in exercise capacity.[43] When compared to the least-fit individuals (exercise capacity ≤5 METs), mortality risk was 34% lower for those in the next fitness category (5.1–7.0 METs) and progressively declined to over 70% for individuals with the highest exercise capacity (>10 METs). When the presence or absence of additional risk factors within fitness categories (least fit to most fit) was considered, the least-fit individuals (≤5 METs) with additional risk factors had a 47% higher mortality risk than those without risk factors. This increased risk was eliminated in the next fitness category (5.1–7.0 METs) and declined to approximately ≥50% in those with an exercise capacity >7.0 METs, regardless of CV risk factor status.

The interaction between exercise capacity, body mass index (BMI) and mortality risk was also evaluated in hypertensive veterans. Progressively lower mortality rates with increased exercise capacity were observed within each BMI category. The mortality risk reduction ranged from approximately 40% in those with an exercise capacity of 5.1-7.5 METs to 70% in those with >7.5 METs [44].

To explore the fitness-fatness and mortality risk relationship further, we compared between normal weight-low-fit individuals were compared to overweight or obese, but fit individuals. The mortality risk was 47% and 60% lower for the overweight-moderate-fit and overweight-high-fit individuals, respectively. Similarly, the risk was 55% lower for the obese-moderate-fit and 78% lower for the obese-high-fit individuals. These findings suggest that it is more beneficial to be fit and overweight or obese rather than normal weight and unfit. Furthermore, it appears that obese hypertensive individuals may benefit at least as much (if not more) from fitness than their overweight or normal weight counterparts.[44]

Finally, similar trends in the fitness-mortality risk association were noted in 4,478 pre-hypertensive individuals and those with high-normal BP (130–139/85–89 mmHg), independent of risk factors [45,46]. The most pronounced reduction in risk (40%) was observed in Low-Fit individuals (peak MET level 6.1–8.0) compared to the Least-Fit (peak MET level ≤6.0), suggesting that relatively low levels of cardiorespiratory fitness are necessary for exercise-related health benefits. Risk reduction was progressive greater in moderate-fit (58%) and high-fit (73%) individuals. The trends were similar, but more pronounced among younger than older individuals. For every 1-MET increase in exercise capacity the adjusted risk was 18% lower for those ≤60 years of age and 12% for individuals >60 years.

In summary, strong evidence supports that regularly performed exercise or a chronic increase in physical activity that leads to increased cardiorespiratory fitness

attenuates the age-related progressive increase in BP and prevents hypertension. In hypertensive individuals, habitual physical activity lowers BP and the risk of mortality, independent of other risk factors. Finally, some evidence suggests that increased cardiorespiratory fitness attenuates the 24-hr BP and the BP response to exercise or physical exertion, thereby lowering the risk for LVH. The dose-response association between increased cardiorespiratory fitness, BP and mortality risk reduction supports the existence of a causal mechanism(s). However, the mechanism or mechanisms are not well understood. It is likely that the favorable effects cardiorespiratory fitness, exercise and physical activity have on several biological systems and traditional risk factors are likely to share the credit.

Conflict of interest

The authors confirm that there are no conflicts of interest.

References

1. Kokkinos P, Myers J. Exercise and physical activity: clinical outcomes and applications. *Circulation*. 2010; 122:1637-1648.
2. Charles Faselis, Michael Doumas, Andreas Pittaras, Puneet Narayan, Jonathan Myers, Apostolos Tsimploulis, Peter Kokkinos. Exercise Capacity and All-Cause Mortality in Male Veterans with Hypertension Aged ≥70 Years. *Hypertension*. 2014;64:30-35.
3. Huai P, Xun H, Heather K, Wang Y, Ma Y, Xi B. Physical activity and risk of hypertension: A Meta-analysis of prospective cohort studies. *Hypertension*. 2013; 62:1021-1026.
4. Kokubo Y. Prevention of hypertension and cardiovascular diseases. A comparison of lifestyle factors in Westerners and East Asians. *Hypertension*. 2014; 63:655-660.
5. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie T, Ogedegbe O, Smith SC., Jr, Svetkey LP, Taler SJ, Townsend RR, Wright JT, Jr, Narva AS, Ortiz E. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014; 311:507-520.
6. 2013 ESH/ESC Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC).
7. Lewington S, Clarke R, Qizilibash N, Peto R for the Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002; 360:1903-1913.
8. Kaess BM, Larson GMN, Hamburg NM, Vita JA, Levy D, Benjamin EJ, Vasan RS, Mitchell GF. Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA*. 2012; 308:875-881.
9. Mitchell GF. Arterial stiffness and hypertension. Chicken or Egg? *Hypertension*. 2014; 64:210-214.
10. Payne RA, Wilkinson IB, Webb DJ. Arterial stiffness and hypertension: Emerging concepts. *Hypertension*. 2010; 55:9-14.
11. Weisbrod RM, Shiang T, Al Sayah L, Fry JL, Bajpai S, Reinhart-King CA, Lob HE, Santhanam L, Mitchel G, Cohen RA, Seta F. Arterial stiffness precedes systolic hypertension in diet-induced obesity. *Hypertension*. 2013;62:1105-1110.
12. Wilkinson IB, McEniery CM. Arteriosclerosis: Inevitable or self-inflicted? *Hypertension*. 2012; 60:3-5.
13. Carmel M. McEniery, Yasmin, Kaisa M. Maki-Petaja, Barry J. McDonnell, Margaret Munnery, Stacey S. Hickson, Stanley S. Franklin, John R. Cockcroft, Ian B. Wilkinson, on behalf of the Anglo-Cardiff Collaboration Trial (ACCT) Investigators. The Impact of Cardiovascular Risk Factors on Aortic Stiffness and Wave Reflections Depends on Age. The Anglo-Cardiff Collaborative Trial (ACCT III) *Hypertension*. 2010; 56:591-597.
14. Gurven M, Blackwell AD, Rodriguez DE, Stieglitz J, Kaplan H. Does blood pressure inevitably rise with age? Longitudinal evidence among forager-horticulturalists. *Hypertension*. 2012; 60: 25-33.
15. Lemogoum D, Ngatchou W, Janssen C, Leeman M, Bortel LV, Boutouyrie P, Degaute JP, Van de Borne, P. Effects of hunter-gatherer subsistence mode on arterial distensibility in Cameroonian Pygmies. *Hypertension*. 2012; 60:123-128.
16. van de Laar RJ, Ferreira I, van Mechelen W, Prins MH, Twisk JW, Stehouwer CD. Lifetime vigorous but not light-to-moderate habitual physical activity impacts favorably on carotid stiffness in young adults: the Amsterdam growth and health longitudinal study. *Hypertension*. 2010;55:33-39.
17. Sacre JW, Jennings GLR, Kingwell BA. Exercise and dietary influences on arterial stiffness in cardiometabolic disease. *Hypertension*. 2014; 63:888-893.
18. Duijnhoven NTL, Green DJ, Felsenberg D, Belavy DL, Hopman MTE, Thijssen DHJ
19. Impact of bed rest on conduit artery remodeling: Effect of exercise countermeasures. *Hypertension*. 2010; 56:240-246.
20. Thijssen DHJ, Maiorana AJ, O'Driscoll G, Cable NT, Hopman MT, Green DJ. Impact of inactivity and exercise on the vasculature in humans. *J Appl Physiol*. 2010;108:845-875.
21. Tinken TM, Thijssen DHJ, Hopkins N, Dawson EA, Cable NT, Green DJ. Shear stress mediates endothelial adaptation to exercise training in humans. *Hypertension*. 2010; 55:312-318.
22. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL., Jr, Jones DW, Materson BJ, Oparil S, Wright JT, Jr., Roccella EJ. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003; 42:1206-1252.
23. Marco MD, deSimone G, Roman MJ, *et al*. Cardiovascular and Metabolic Predictors of Progression of Prehypertension into Hypertension; The Strong Heart Study. *Hypertension*. 2009;54:974-980.
24. Faselis C, Doumas M, Kokkinos JP, Panagiotakos D, Kheirbek R, Sheriff HM, Hare K, Papademetriou V, Fletcher, R, Kokkinos P. Exercise capacity and progression from prehypertension to hypertension. *Hypertension*. 2012; 60:333-338.

25. Chase NL, Sui X, Lee D, Blair SN. The association of cardiorespiratory fitness and physical activity with incidence of hypertension in men. *Am J Hypertens*. 2009;22:417-424.
26. Kokkinos P, 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.
27. Kokkinos P, Pittaras A, Manolis A, Panagiotakos D, Narayan P, Manjoros D, Amdur R, Singh S. Exercise capacity and 24-hr blood pressure in pre-hypertensive men and women. *Am J Hypertens*.2006;19:251-258.
28. 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 hypertension treated with indapamide, verapamil and enalapril. *Am J Cardiol*. 1997;79:1424-1426.
29. Kokkinos PF, Narayan P, Colleran J, Pittaras A, Notargiacomo A, Reda D, Papademetriou V. 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.
30. Turner MJ, Spina RJ, Kohrt WM, Ehsani AA. Effect of endurance exercise training on left ventricular size and remodeling in older adults with hypertension. *J Gerontol A Biol Sci Med Sci*. 2000; 55:M245-251.
31. Hinderliter A, Sherwood A, Gullette EC, Babyak M, Waugh R, Georgiades A, Blumenthal JA. Reduction of left ventricular hypertrophy after exercise and weight loss in overweight patients with mild hypertension. *Arch Intern Med*. 2002;162:1333-1339
32. Pescatello LS, Franklin B, 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.
33. Cornelissen VA, Smart NA (2013) Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc*. 2013; 2:e004473 30.
34. Brook RD, Appel LJ, Rubenfire M, Ogedegbe G, Bisognano JD, Elliott WJ, Fuchs FD, Hughes JW, Lackland DT, Staffileno BA, Townsend RR, Rajagopalan S. Beyond Medications and Diet: Alternative Approaches to Lowering Blood Pressure. A Scientific Statement From the American Heart Association on behalf of the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research, Council on Cardiovascular and Stroke Nursing, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity and Metabolism. *Hypertension*. 2013;61:1360-1383.
35. Dahlof B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients: a metaanalysis of 109 treatment studies. *Am J Hepertens*. 1992;5:95-110.
36. 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.
37. Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, Toto RD, White A, Cushman WC, White, W, Sica D, Ferdinand, K, Giles TD, MD, Falkner B, Carey RM. Resistant hypertension: diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Hypertension*. 2008; 51:1403-1419.
38. Dimeo F. Pagonas N, Seibert F, Arndt R, Zidek W, Westhoff, TM. Aerobic exercise reduces blood pressure in resistant hypertension. *Hypertension*. 2012; 60:653-658.
39. Cornelissen VA, Fagard RH, Coeckelberghs E, Vanhees L. Impact of resistance training on blood pressure and other cardiovascular risk factors: a meta-analysis of randomized, controlled trials. *Hypertension*. 2011; 58:950-958.
40. Kelley GA, Kelley KS. Progressive resistance exercise and resting blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2000; 35:838-843.
41. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, Macera CA, Castaneda-Sceppa C. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116:1094-1105.
42. Williams MA, Haskell WL, Ades PA, Amsterdam EA, Bittner V, Franklin BA, Gulanick M, Laing ST, Stewart KJ. Resistance exercise in individuals with and without cardiovascular disease: 2007 update: a Scientific Statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2007;116:572-584.
43. Myers J, Prakash M, Froelicher V, Do D, Partington S, and Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *The New England Journal of Medicine*. 2002;346:793-801.
44. Kokkinos P, Manolis A, Pittaras A, Doumas M, Giannelou A, Panagiotakos DB, Faselis C, Narayan P, Singh S, Myers J. Exercise capacity and mortality in hypertensive men with and without additional risk factors. *Hypertension*. 2009;53:494-499.
45. Faselis C, Doumas M, Panagiotakos D, Kheirbek R, Korshak L, Manolis A, Pittaras A, Tsioufis C, Papademetriou V, Fletcher RD, Kokkinos P. Body mass index, exercise capacity, and mortality risk in male veterans with hypertension. *American Journal of Hypertension*. 2012; 25:444-450.
46. Kokkinos P, Myers J., Doumas M, Faselis C, Manolis A, Pittaras A, Kokkinos JP, Singh S, Fletcher RD. Exercise Capacity and All-Cause Mortality in Pre-Hypertensive Men. *American Journal of Hypertension*. 2009; 22:735-741.
47. Kokkinos P, Doumas M, Myers J, Faselis C, Manolis A, Pittaras A, Kokkinos JP, Papademetriou V, Singh S, Fletcher RD. Exercise Capacity and All-cause Mortality in males with High-Normal Blood Pressure. *Blood Pressure*. 2009;18;261-267.