Published in final edited form as:

Am Heart J. 2007 November ; 154(5): 976–982.

High Aerobic Capacity Does Not Attenuate Aortic Stiffness in Hypertensive Subjects

Kenneth A. Kraft, PhD^{a,*}, Ross Arena, PhD^b, James A. Arrowood, MD^c, and Ding-Yu Fei, PhD^d

a Department of Radiology, Virginia Commonwealth University, Richmond, Virginia, USA

b Department of Physical Therapy, Virginia Commonwealth University, Richmond, Virginia, USA

c Department of Internal Medicine, Virginia Commonwealth University, Richmond, Virginia, USA

d Department of Biomedical Engineering, Virginia Commonwealth University, Richmond, Virginia, USA

Abstract

Background—It is unknown whether increased physical fitness reduces aortic stiffness in hypertensive individuals. The purpose of this cross-sectional study was to examine, in a cohort of community-dwelling subjects with no history of cardiac events, differences in the impact of aerobic capacity on aortic stiffness between normotensive and hypertensive subjects.

Methods—The study sample included 275 subjects representing a large age range (21–85 years). Of these, 61 subjects (hypertensive cohort) were either hypertensive at enrollment or were taking antihypertensive medication. The remaining 214 subjects (normotensive cohort) had no history of hypertension. The study protocol included maximal cardiopulmonary exercise testing (determination of maximal oxygen consumption or $\text{VO}_{2\text{Max}}$) and measurement of aortic wave velocity (AWV) using a novel magnetic resonance-based method.

Results—Overall, the hypertensive cohort exhibited significantly elevated AWV in comparison to a subset of normotensives matched for age, gender and aerobic fitness. Each cohort was then subdivided according to percent of predicted $\text{VO}_{2\text{Max}}$ achieved ($< 100\%$ = “unfit”; $\geq 100\%$ = “fit”). Differences between subgroups were assessed by unpaired t-test. In the normotensive cohort, AWV was significantly lower in the fit versus the unfit subgroup. However, in the hypertensive cohort, AWV was not significantly different between fit and unfit subgroups nor between treated and untreated subgroups.

Conclusion—Unlike the situation in healthy normotensive subjects, higher peak aerobic capacity is not associated with lower aortic stiffness in hypertensive individuals.

Keywords

hypertension; aortic stiffness; physical fitness; arterial compliance

*Corresponding author: Prof. K. Kraft, Department of Radiology, Post Office Box 980072, Virginia Commonwealth University, Richmond, Virginia 23298-0072. Ph. 804-828-4238, FAX 804-828-6129, E-mail: kakraft@vcu.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Elevated central arterial stiffness has been shown to be strongly associated with cardiovascular mortality and morbidity in a number of at-risk populations.¹ In particular, increased aortic stiffness has been associated with aging,² obesity,³ sedentary lifestyle,⁴ hypertension⁵ and other cardiovascular risk factors. One of the most reliable indices of central arterial stiffness is the rate of aortic propagation of the pressure or flow wave during early cardiac systole. This aortic wave velocity (AWV), a.k.a. pulse wave velocity (in meters per second) is directly proportional to vessel stiffness and inversely related to compliance. Because of its emergence as an independent predictor of mortality in multiple diseases with cardiovascular consequences, AWV has been described as an “integrated index of vascular function.”⁶

Aortic stiffening has traditionally been regarded as a relatively slow, progressive process arising from structural changes within arterial walls, such as loss/fragmentation of elastin, increased collagen deposition, and protein crosslinking via advanced glycation mechanisms.⁷ In this view, a high level of aerobic fitness is beneficial because it may slow the rate of progression of vessel stiffening.⁸ However, recent work has shown that significant reductions in aortic stiffness are achievable with short-term aerobic exercise interventions. Training regimens of only 4–12 weeks, for example, have reportedly improved arterial mechanical properties in healthy sedentary^{4,9} and obese subjects,¹⁰ as well as in heart failure¹¹ and hemodialysis patients.¹² These findings demonstrate that aortic stiffening is partially reversible and suggest that one or more acute (possibly functional) mechanisms are at play in mediating such rapid amelioration of arterial wall stiffness.

Among hypertensive patients, lifestyle interventions such as aerobic exercise have been recommended for reducing blood pressure.¹³ However, the efficacy of aerobic exercise as a treatment for hypertension is controversial,¹⁴ in that training-mediated blood pressure reductions are generally small in comparison to those produced by pharmacologic means or weight loss.¹⁵ Although several studies have linked higher levels of aerobic fitness with reduced central arterial stiffness in healthy subjects,⁸ exercise training studies involving hypertensive subjects have not generally demonstrated improvement in arterial compliance.^{16–18}

The negative results of these previous exercise training interventions suggest that acute mechanisms for reducing aortic stiffness may be absent in hypertension. However, a remaining unanswered question is whether habitual exercise training in hypertensive subjects can decelerate the chronic changes that promote arterial stiffening, in comparison to a more sedentary hypertensive cohort. The goal of this study, therefore, was to determine whether higher levels of aerobic fitness in community-dwelling hypertensives are manifested as a beneficial reduction of aortic stiffness in a similar fashion to that observed in normotensive cohorts.

METHODS

Study Population

A total of 275 adults (149 males, 126 females, age range 21–85 years) were recruited from the community and local running clubs. Exclusion criteria included resting systolic blood pressure (SBP) > 180 mm Hg, resting diastolic blood pressure (DBP) > 100 mm Hg, pregnancy, age < 21 years, magnetic resonance imaging (MRI) contraindications (e.g. ferromagnetic implants, claustrophobia), or a history of myocardial infarction, stroke, coronary heart disease, peripheral arterial disease, heart failure, cardiac arrhythmia or diabetes. The university Institutional Review Board approved the study, and all participants provided informed consent.

At enrollment, 214 subjects (117 males, 97 females) had no history of hypertension, with SBP < 140 and DBP < 90 mm Hg. Sixty-one subjects (32 males/29 females) had elevated blood pressure (SBP/DBP $\geq$ 140/90 mm Hg) at two clinic visits or were previously diagnosed with hypertension and taking at least one antihypertensive medication. Subjects were instructed to continue their usual medications during the study.

Anthropometric and Biochemical Testing

Height and weight were measured and used to calculate body mass index (BMI). Venous blood samples were obtained from each subject following an overnight fast. Total, HDL and LDL cholesterol, as well as triglycerides and glucose were quantified using standard methods. Brachial artery blood pressures were measured six times (three prior to exercise testing and three after the MR exam) and overall average systolic and diastolic pressures were computed. Mean arterial pressure (MAP) was calculated as $2/3(\text{DBP}) + 1/3(\text{SBP})$ for each subject.

Cardiopulmonary Exercise Testing

Physician-supervised maximal exercise tests were carried out using a modified Balke treadmill protocol. Ventilatory expired gas analysis was obtained using a metabolic cart (Vmax Spectra29, SensorMedics, Inc., Yorba Linda, CA). Oxygen, carbon dioxide and flow sensors were calibrated prior to each test. Subjects were monitored throughout the test via 12-lead electrocardiography (ECG), BP measurements at 3-minute intervals, continuous heart rate recording, and ratings of perceived exertion at regular intervals (Borg 6–20 scale). American College of Sports Medicine criteria¹⁹ were followed for test termination, and subjects were encouraged to exercise to muscular fatigue. Heart rate and BP were monitored for 5 minutes of recovery after exercise ceased. Peak respiratory exchange ratio and maximal oxygen consumption ($\text{VO}_{2\text{Max}}$) were defined by their 20-second averages during the final stage of the exercise test. Predicted $\text{VO}_{2\text{Max}}$ (based on age, sex, height and weight) was calculated²⁰ for each subject, and percent of predicted was expressed as 100 times actual $\text{VO}_{2\text{Max}}$ divided by predicted $\text{VO}_{2\text{Max}}$.

Measurement of Aortic Wave Velocity

Within one week of the exercise test, AWW was measured in the descending thoracic aorta using a clinical 1.5T MR system (Vision, Siemens Medical Solutions, Erlangen, Germany). The radiofrequency body coil was used for pulse transmission and a standard spine array surface coil was employed for signal reception. ECG leads were placed to allow synchronization of MR acquisitions to the early systolic part of the cardiac cycle. Subjects were positioned supine on the spine array coil and centered in the magnet using the xiphisternum as an anatomical landmark. Transaxial and sagittal scout images through the descending thoracic aorta were then acquired. The sagittal image was used to guide the positioning and angulation of subsequent AWW sequences as well as for positioning spatial saturation regions. Finally, cardiac-triggered AWW measurements were performed as described previously.^{21;22} Very briefly, the strategy of the measurement is to simultaneously record early systolic flow at multiple positions along the thoracic aorta. Because of the finite flow propagation rate, a distinct delay is discernible between proximal and distal aortic flow waveforms. The separation distance divided by this observed delay time yields the AWW. Because of the short acquisition times of the sequences employed (1 or 2 heartbeats), multiple independent measurements were achieved per subject. After each MR acquisition, raw data were wirelessly offloaded to a personal computer for data processing and analysis, as described previously.²³ The mean of at least five individual trials was taken as the final aortic wave velocity for each subject.

The accuracy of the MR method has been previously reported both in vitro²¹ and in vivo.²⁴ A separate test-retest reliability analysis of the MR method revealed an intraclass correlation coefficient of 0.97 ($p < 0.001$) and a standard error of measurement ($\text{SEM}_{95\%}$) for AWW of

± 0.18 m/s. The Bland-Altman bias was -0.08 m/s and the limits of agreement were 0.28 and -0.44 m/s. These reproducibility benchmarks substantially surpass those reported for conventional carotid-femoral wave velocity.²⁵

Data Analysis

SPSS software (version 14.0, SPSS Inc., Chicago, IL) was employed for statistical analyses. For all statistical tests, significance was assumed at a p-value of < 0.05 .

In order to assess the degree of aortic stiffening attributable to hypertension alone, the hypertensive cohort was pairwise matched with normotensive counterparts. Because age, aerobic capacity and possibly gender are known to also influence central arterial stiffness, matching of all three parameters was attempted. Fifty-seven of sixty-one hypertensive subjects were successfully matched.

The normotensive and hypertensive cohorts were also dichotomized according to percent of predicted VO_{2Max} achieved ($< 100\%$ = “unfit”; $\geq 100\%$ = “fit”). By this criterion, in the normotensive cohort, 144 subjects were categorized as fit and 70 were deemed unfit. Likewise, in the hypertensive cohort, 30 and 31 subjects were classified as fit and unfit, respectively. Unpaired t-tests were used to evaluate group differences between unmatched and matched normotensive and hypertensive cohorts, between fit and unfit subgroups, as well as between actively treated and untreated hypertensive subgroups.

The association between aortic stiffness and aerobic capacity was further explored using Pearson correlations in the normotensive and hypertensive cohorts and various subgroups. Because aerobic capacity itself (VO_{2Max}) is highly age and gender-dependent, another parameter, termed “relative fitness” (defined as the difference between a subject’s actual and predicted VO_{2Max}) was instead correlated with AWW. The dependence of aortic wave velocity on age was also evaluated using groupwise linear regression fits to the data.

RESULTS

Table I displays a comparison of the normotensive and hypertensive cohorts. Overall, the hypertensive cohort was older and exhibited significantly higher SBP, DBP, MAP and AWW and lower VO_{2Max} ($P < 0.001$ for all). Modestly significant differences ($P < 0.05$) were also apparent in body mass index (BMI) and blood triglyceride levels. As judged by the mean peak respiratory exchange ratio (> 1.1), both cohorts put forth an excellent effort in their maximal exercise test. Table II displays the results of pairwise matching (by age, gender and VO_{2Max}) of the hypertensive subjects with normotensive counterparts. Other than blood pressure (SBP, DBP and MAP), only AWW remained significantly ($P < 0.001$) elevated among hypertensives in this matched comparison. This difference in aortic stiffness is therefore not likely a manifestation of disparities in age, aerobic capacity or tested risk factors.

Tabulated results of the comparison of fit vs. unfit subgroups are shown in Table III. Clearly, aerobic capacity (VO_{2Max}) was significantly ($P < 0.001$) higher in both the fit normotensives and hypertensives compared to their unfit peers. Aortic wave velocity, however, was only significantly different ($P < 0.05$) between fit and unfit normotensive subgroups, and was nearly identical between the fit and unfit hypertensive subgroups.

A comparison of treated and untreated hypertensive subjects is shown in Table IV, which also includes a summary of antihypertensive drug regimens. Of the 39 subjects on antihypertensive medications, 7 were taking two drugs, 2 were taking three and 1 was taking four medications. In comparison with their untreated peers, the treated hypertensives had significantly lower

SBP, DBP and MAP ($P < 0.001$); in all other respects differences were not significant. In particular, AWV was virtually identical between the treated and untreated subgroups.

Calculated Pearson correlations between AWV and “relative fitness” are displayed in Table V. Because the hypertensive cohort, overall, was older than the normotensive cohort (57.9 vs. 44.6 years, $P < 0.001$), the possibility exists that progressive aortic stiffening with age may have outweighed and therefore masked the beneficial effect of high aerobic capacity in the fit hypertensive subgroup. Therefore, in addition to the overall cohorts, correlations were computed in subgroups below and above age 50, as well as in treated and untreated hypertensives. None of the hypertensive subgroups were found to exhibit significant correlations between relative fitness and AWV, whereas all such correlations among normotensive subgroups were significant.

The Figure displays linear regression fits of AWV vs. age for the aerobically fit and unfit normotensive subgroups as well as the corresponding result for the hypertensive cohort. Although in all cases AWV increased with age, overall the lowest AWVs were associated with the fit normotensive subjects and the highest AWVs with the hypertensive cohort. The AWV difference between the fit and unfit normotensive subjects appears to be roughly constant over the entire adult age span.

DISCUSSION

The main findings of this study are that, among community-dwelling hypertensive subjects, (1) aortic stiffness is elevated versus normotensive subjects, even after matching for age, gender and aerobic fitness, (2) unlike the situation among normotensive persons, a high degree of aerobic fitness does not reduce aortic wave velocity in comparison to less fit peers, and (3) antihypertensive medications reduce blood pressure but not aortic stiffness. These findings appear to have relevance to understanding the etiology and therapeutic approaches to treating premature aortic stiffening.

Both essential and systolic hypertension are associated with elevated aortic wave velocity, with the degree of stiffening increasing with the severity of hypertension.²⁶ Moreover, elevations in aortic stiffness have recently been shown to be predictive of progression toward hypertension over a 4-year period in subjects who were not hypertensive at baseline.²⁷ Although essential hypertension may have multiple causes, in isolated systolic hypertension, the prevalence of which increases with age, large artery stiffness is commonly assumed to be the principal causal factor.²⁸ In our study, 17 of 22 untreated as well as 37 of 39 treated hypertensive subjects had a mean DBP < 90 mm Hg, indicating that the majority of subjects in both cohorts had isolated systolic hypertension. However, it should be noted that, for ethical reasons, we did not suspend treatment during the study, so the true incidence of isolated systolic hypertension in the treated group is unknown.

The traditional view of aortic stiffening is that it occurs inexorably and largely irreversibly with age, due to structural deterioration and remodeling of the vessel lamina.²⁹ However, accumulating evidence has demonstrated that central arterial compliance can be acutely and dramatically altered via lifestyle interventions such as dietary modification, weight loss and aerobic exercise.³⁰ Among factors hypothesized to play a role in short-term modification of arterial compliance are nitric oxide availability, systemic inflammation, oxidative stress, smooth muscle tone, hormonal influences and sympathetic nervous system activation.⁷ It appears likely, therefore, that arterial stiffening is mediated through a number of processes, some of which may be acutely reversible and others which are not.

The inexorable increase in AWV with age, observed even among the fittest normotensive subjects in this study (Figure) may reflect a resistant or irreversible constituent of aortic

stiffening. Continuing this line of reasoning, the higher AWW of the unfit normotensive subjects can reasonably be ascribed to one or more reversible mechanisms of stiffening. This assumption is supported by evidence that short-term exercise interventions are effective in reducing AWW in normotensive sedentary subjects.⁹ Moreover, our data for normotensive subjects (roughly parallel lines separating the fit and unfit subgroups in the Figure) suggest that reversible components of arterial stiffening persist throughout the adult age span. Among the hypertensive subjects, however, no such effect of aerobic fitness was observed, in agreement with previous studies.^{16–18} This observation implies that the central arterial dysfunction is due to factors not amenable to modification through training.

Previous studies involving exercise training of hypertensive patients^{16–18} were conducted on generally older, untreated subjects. The present investigation differs from prior studies in that we enrolled subjects over a wide age range and we did not exclude persons on antihypertensive therapy. Although not a medication study, our data (Table IV) reveal an identical degree of aortic stiffening between treated and untreated hypertensive subjects. Because treatment clearly reduces MAP, these data imply that pressure reductions are not mediated by increased aortic distensibility. Whether MAP alone influences stiffness in hypertension is somewhat controversial, in view of published evidence that carotid isobaric stiffness is either normal³¹ or significantly increased³² in essential hypertension. Our data lend support to the latter observation; however, it should be noted that the majority of our subjects had systolic rather than essential hypertension. Secondly, our AWW measurements were localized to the descending thoracic aorta, whereas it has been reported that carotid and aortic stiffness are not highly correlated, especially in older subjects and those with other cardiovascular risk factors.³³ Lastly, since our method did not target the ascending aorta or aortic arch, it is possible that localized distensibility of these vessel segments improves with drug treatment. This possibility is supported by a report that six months of antihypertensive treatment reduced the elastic modulus of the ascending aorta, but did not significantly affect wave velocity in the descending aorta.³⁴

The main weakness of this study is the relatively small number of hypertensive subjects overall, and especially a dearth of young hypertensive individuals. This limitation precluded conducting analyses within narrowly defined age groups. It is therefore plausible that results in younger hypertensives might differ due to the shorter history of the disease. It is also likely that the variety of treatment regimens in our hypertensive cohort interjected additional heterogeneity into the data. Again, the small number of subjects per treatment effectively precluded conducting medication-specific analyses. On the other hand, a particular strength of the study is the excellent reproducibility of the MR-based AWW measurement method, for which sample size requirements are substantially reduced in comparison with traditional pulse wave velocity assessments.

In conclusion, notwithstanding manifold proven health benefits of increased aerobic fitness, this study shows that among hypertensive subjects, high aerobic capacity does not attenuate central arterial stiffness. These data suggest that, unlike the situation in healthy sedentary subjects and those with other cardiovascular risk factors, the pathophysiology of high blood pressure may induce stiffening of the aorta that is particularly resistant to modification through increased physical activity. In the absence of successful strategies to combat aortic stiffening in hypertension, increased vigilance and early intervention in susceptible individuals is warranted.

Acknowledgements

Grant sponsors: National Institutes of Health, Grant number: R01 HL069962; National Center for Research Resources of the National Institutes of Health, Grant number: M01 RR00065.

References

1. Safar ME, Henry O, Meaume S. Aortic pulse wave velocity: an independent marker of cardiovascular risk. *Am J Geriatr Cardiol* 2002;11:295–298. [PubMed: 12214167]
2. Mitchell GF, Parise H, Benjamin EJ, Larson MG, Keyes MJ, Vita JA, Vasan RS, Levy D. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. *Hypertension* 2004;43:1239–1245. [PubMed: 15123572]
3. Wildman RP, Mackey RH, Bostom A, Thompson T, Sutton-Tyrrell K. Measures of Obesity Are Associated With Vascular Stiffness in Young and Older Adults. *Hypertension* 2003;42:468–473. [PubMed: 12953016]
4. Tanaka H, Dinunno FA, Monahan KD, Clevenger CM, DeSouza CA, Seals DR. Aging, habitual exercise, and dynamic arterial compliance. *Circulation* 2000;102:1270–1275. [PubMed: 10982542]
5. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic Stiffness Is an Independent Predictor of All-Cause and Cardiovascular Mortality in Hypertensive Patients. *Hypertension* 2001;37:1236–1241. [PubMed: 11358934]
6. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic Pulse-Wave Velocity and Its Relationship to Mortality in Diabetes and Glucose Intolerance: An Integrated Index of Vascular Function? *Circulation* 2002;106:2085–2090. [PubMed: 12379578]
7. Ziemann SJ, Melenovsky V, Kass DA. Mechanisms, Pathophysiology, and Therapy of Arterial Stiffness. *Arterioscler Thromb Vasc Biol* 2005;25:932–943. [PubMed: 15731494]
8. Vaitkevicius PV, Fleg JL, Engel JH, O'Connor FC, Wright JG, Lakatta LE, Yin FC, Lakatta EG. Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation* 1993;88:1456–1462. [PubMed: 8403292]
9. Cameron JD, Dart AM. Exercise training increases total systemic arterial compliance in humans. *Am J Physiol* 1994;266:H693–H701. [PubMed: 8141370]
10. Balkestein EJ, Aggel-Leijssen DP, van Baak MA, Struijker-Boudier HA, Van Bortel LM. The effect of weight loss with or without exercise training on large artery compliance in healthy obese men. *J Hypertens* 1999;17:1831–1835. [PubMed: 10703876]
11. Parnell MM, Holst DP, Kaye DM. Exercise training increases arterial compliance in patients with congestive heart failure. *Clin Sci (Lond)* 2002;102:1–7. [PubMed: 11749654]
12. Mustata S, Chan C, Lai V, Miller JA. Impact of an exercise program on arterial stiffness and insulin resistance in hemodialysis patients. *J Am Soc Nephrol* 2004;15:2713–2718. [PubMed: 15466276]
13. Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003;107:3109–3116. [PubMed: 12821592]
14. Blumenthal JA, Sherwood A, Gullette EC, Babyak M, Waugh R, Georgiades A, Craighead LW, Tweedy D, Feinglos M, Appelbaum M, Hayano J, Hinderliter A. Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Arch Intern Med* 2000;160:1947–1958. [PubMed: 10888969]
15. Bacon SL, Sherwood A, Hinderliter A, Blumenthal JA. Effects of exercise, diet and weight loss on high blood pressure. *Sports Med* 2004;34:307–316. [PubMed: 15107009]
16. Ferrier KE, Waddell TK, Gatzka CD, Cameron JD, Dart AM, Kingwell BA. Aerobic exercise training does not modify large-artery compliance in isolated systolic hypertension. *Hypertension* 2001;38:222–226. [PubMed: 11509480]
17. Seals DR, Tanaka H, Clevenger CM, Monahan KD, Reiling MJ, Hiatt WR, Davy KP, DeSouza CA. Blood pressure reductions with exercise and sodium restriction in postmenopausal women with elevated systolic pressure: role of arterial stiffness. *J Am Coll Cardiol* 2001;38:506–513. [PubMed: 11499745]
18. Stewart KJ, Bacher AC, Turner KL, Fleg JL, Hees PS, Shapiro EP, Tayback M, Ouyang P. Effect of Exercise on Blood Pressure in Older Persons: A Randomized Controlled Trial. *Arch Intern Med* 2005;165:756–762. [PubMed: 15824294]

19. Balady, GJ.; Berra, K.; Lawrence, A.; Gordon, NF.; Mahler, DA.; Myers, J. ACSM's Guidelines for Exercise Testing and Prescription. 6. Lippincott Williams & Wilkins; 2000.
20. Jones, N. Clinical Exercise Testing. 4. Philadelphia: W.B. Saunders; 1997. p. 124-149.
21. Itskovich VV, Kraft KA, Fei DY. Rapid aortic wave velocity measurement with MR imaging. *Radiology* 2001;219:551–557. [PubMed: 11323487]
22. Shao X, Fei DY, Kraft KA. Rapid measurement of pulse wave velocity via multisite flow displacement. *Magn Reson Med* 2004;52:1351–1357. [PubMed: 15562479]
23. Shao X, Fei DY, Kraft KA. Computer-assisted evaluation of aortic stiffness using data acquired via magnetic resonance. *Computerized Medical Imaging and Graphics* 2004;28:353–361. [PubMed: 15294313]
24. Kraft KA, Itskovich VV, Fei DY. Rapid measurement of aortic wave velocity: in vivo evaluation. *Magn Reson Med* 2001;46:95–102. [PubMed: 11443715]
25. Sutton-Tyrrell K, Mackey RH, Holubkov R, Vaitkevicius PV, Spurgeon HA, Lakatta EG. Measurement variation of aortic pulse wave velocity in the elderly. *Am J Hypertens* 2001;14:463–468. [PubMed: 11368468]
26. Asmar R, Benetos A, Topouchian J, Laurent P, Pannier B, Brisac AM, Target R, Levy BI. Assessment of arterial distensibility by automatic pulse wave velocity measurement. Validation and clinical application studies. *Hypertension* 1995;26:485–490. [PubMed: 7649586]
27. Dernellis J, Panaretou M. Aortic stiffness is an independent predictor of progression to hypertension in nonhypertensive subjects. *Hypertension* 2005;45:426–431. [PubMed: 15710784]
28. Beltran A, McVeigh G, Morgan D, Glasser SP, Neutel JM, Weber M, Finkelstein SM, Cohn JN. Arterial compliance abnormalities in isolated systolic hypertension. *Am J Hypertens* 2001;14:1007–1011. [PubMed: 11710778]
29. Seals DR. Habitual exercise and the age-associated decline in large artery compliance. *Exerc Sport Sci Rev* 2003;31:68–72. [PubMed: 12715969]
30. Tanaka H, Safar ME. Influence of lifestyle modification on arterial stiffness and wave reflections. *American Journal of Hypertension* 2005;18:137–144. [PubMed: 15691628]
31. Bussy C, Boutouyrie P, Lacolley P, Challande P, Laurent S. Intrinsic Stiffness of the Carotid Arterial Wall Material in Essential Hypertensives. *Hypertension* 2000;35:1049–1054. [PubMed: 10818063]
32. Stewart AD, Jiang B, Millasseau SC, Ritter JM, Chowienczyk PJ. Acute Reduction of Blood Pressure by Nitroglycerin Does Not Normalize Large Artery Stiffness in Essential Hypertension. *Hypertension* 2006;48:404–410. [PubMed: 16908758]
33. Paini A, Boutouyrie P, Calvet D, Tropeano AI, Laloux B, Laurent S. Carotid and Aortic Stiffness: Determinants of Discrepancies. *Hypertension* 2006;47:371–376. [PubMed: 16446398]
34. Savolainen A, Keto P, Poutanen VP, Hekali P, Standertskjold-Nordenstam CG, Rames A, Kupari M. Effects of angiotensin-converting enzyme inhibition versus beta-adrenergic blockade on aortic stiffness in essential hypertension. *J Cardiovasc Pharmacol* 1996;27:99–104. [PubMed: 8656666]

Figure.

Linear regression plots of the dependence of aortic wave velocity (AWV) on age for (1) normotensive fit group [Equation $AWV \text{ (m/s)} = 0.052 \text{ (Age)} + 3.33$], (2) normotensive unfit group [Equation $AWV \text{ (m/s)} = 0.065 \text{ (Age)} + 3.44$] and (3) hypertensive cohort [Equation $AWV \text{ (m/s)} = 0.079 \text{ (Age)} + 3.20$].

Table I
 Characteristics of normotensive and hypertensive cohorts

	Normotensive	Hypertensive
N	214	61
Male/Female	117/97	32/29
Age (years)	44.6 ± 14.6	57.9 ± 14.3 **
Body Mass Index (kg/m ²)	24.7 ± 4.3	26.3 ± 5.1 *
SBP (mm Hg)	118.8 ± 11.7	143.1 ± 16.8 **
DBP (mm Hg)	71.4 ± 8.2	81.2 ± 8.7 **
MAP (mm Hg)	87.2 ± 7.4	101.7 ± 8.2 **
Heart Rate (bpm)	64.5 ± 11.6	67.7 ± 11.3
Total Cholesterol (mg/dL)	188.9 ± 34.0	196.9 ± 35.9
HDL Cholesterol (mg/dL)	59.6 ± 17.2	60.2 ± 17.0
LDL Cholesterol (mg/dL)	112.5 ± 29.3	118.9 ± 30.6
Triglycerides (mg/dL)	104.4 ± 75.1	132.4 ± 97.0 *
Glucose (mg/dL)	89.1 ± 12.9	91.8 ± 11.5 **
VO _{2Max} (ml O ₂ ·kg ⁻¹ ·min ⁻¹)	40.9 ± 11.3	30.9 ± 11.2
Peak Respiratory Exchange Ratio	1.15 ± 0.07	1.16 ± 0.07 **
Aortic Wave Velocity (m/s)	5.9 ± 1.7	7.8 ± 1.8 **

Values are mean ± SD

* $P < 0.05$

** $P < 0.001$

Table II
Comparison of subject cohorts matched by age, gender and VO₂Max

	Normotensive	Hypertensive
N	57	57
Male/Female	32/25	32/25
Age (years)	55.6 ± 13.8	56.5 ± 13.4
Body Mass Index (kg/m ²)	25.8 ± 4.1	26.4 ± 5.2
SBP (mm Hg)	121.1 ± 9.7	142.0 ± 14.3**
DBP (mm Hg)	72.2 ± 6.7	81.8 ± 7.3**
MAP (mm Hg)	88.5 ± 6.9	101.8 ± 8.4**
Heart Rate (bpm)	65.2 ± 11.2	66.8 ± 10.9
Total Cholesterol (mg/dL)	199.7 ± 32.4	194.4 ± 34.2
HDL Cholesterol (mg/dL)	60.8 ± 18.2	60.1 ± 17.4
LDL Cholesterol (mg/dL)	121.3 ± 28.1	116.9 ± 30.0
Triglycerides (mg/dL)	106.8 ± 57.5	131.5 ± 99.1
Glucose (mg/dL)	91.8 ± 18.0	91.7 ± 11.5
VO ₂ Max (ml O ₂ ·kg ⁻¹ ·min ⁻¹)	33.6 ± 10.1	31.8 ± 11.1
Peak Respiratory Exchange Ratio	1.14 ± 0.06	1.16 ± 0.07
Aortic Wave Velocity (m/s)	6.4 ± 2.0	7.6 ± 1.8**

**
P < 0.001

Table III

Comparison of fit vs. unfit subgroups

	Normotensive		Hypertensive	
	Unfit	Fit	Unfit	Fit
N	70	144	31	30
Male/Female	38/32	79/65	14/17	18/12
Age (years)	42.5 ± 15.5	45.7 ± 14.2	55.6 ± 15.3	60.3 ± 13.0
Body Mass Index (kg/m ²)	27.7 ± 4.7	23.2 ± 3.1 ^{**}	29.4 ± 5.0	23.0 ± 2.7 ^{**}
SBP (mm Hg)	119.2 ± 10.0	117.8 ± 9.7	141.3 ± 14.8	143.9 ± 13.4
DBP (mm Hg)	72.1 ± 7.5	70.8 ± 7.1	82.1 ± 6.9	80.4 ± 8.1
MAP (mm Hg)	87.8 ± 7.6	86.5 ± 7.3	101.8 ± 8.0	101.6 ± 8.6
Heart Rate (bpm)	68.9 ± 10.9	62.4 ± 11.3 ^{**}	71.0 ± 11.5	64.3 ± 10.1 [*]
Total Cholesterol (mg/dL)	190.1 ± 36.5	188.3 ± 32.8	195.6 ± 36.3	198.3 ± 36.0
HDL Cholesterol (mg/dL)	52.0 ± 12.6	63.4 ± 18.0 ^{**}	55.6 ± 13.7	64.9 ± 18.9 [*]
LDL Cholesterol (mg/dL)	117.2 ± 30.4	110.2 ± 28.5	120.8 ± 31.2	117.0 ± 30.4
Triglycerides (mg/dL)	119.8 ± 53.8	96.9 ± 82.6 [*]	137.5 ± 90.2	127.1 ± 104.8
Glucose (mg/dL)	91.7 ± 14.3	87.8 ± 12.0 [*]	92.5 ± 11.0	91.2 ± 12.2
VO ₂ Max (ml O ₂ ·kg ⁻¹ ·min ⁻¹)	31.6 ± 7.3	45.4 ± 10.1 ^{**}	24.9 ± 6.1	37.2 ± 11.9 ^{**}
Pk. Resp. Exchange Ratio	1.15 ± 0.07	1.16 ± 0.06	1.15 ± 0.07	1.16 ± 0.08
Aortic Wave Velocity (m/s)	6.2 ± 2.0	5.7 ± 1.5 [*]	7.7 ± 1.9	7.9 ± 1.8

* $P < 0.05$ vs. unfit subjects in same BP category

** $P < 0.001$ vs. unfit subjects in same BP category

Table IV
Characteristics of treated and untreated hypertensive subgroups

	Treated Hypertensive	Untreated Hypertensive
N	39	22
Male/Female	17/22	15/7
Age (years)	58.6 ± 13.6	56.6 ± 15.7
Body Mass Index (kg/m ²)	26.3 ± 5.6	26.2 ± 4.4
SBP (mm Hg)	138.0 ± 14.6	150.8 ± 8.5**
DBP (mm Hg)	78.9 ± 7.0	85.4 ± 6.5**
MAP (mm Hg)	98.6 ± 7.9	107.2 ± 5.7**
Heart Rate (bpm)	68.4 ± 11.0	66.3 ± 11.8
Total Cholesterol (mg/dL)	199.6 ± 35.0	192.1 ± 37.8
HDL Cholesterol (mg/dL)	59.1 ± 16.2	62.1 ± 18.5
LDL Cholesterol (mg/dL)	121.6 ± 30.0	114.2 ± 31.8
Triglycerides (mg/dL)	142.1 ± 105.1	115.1 ± 79.9
Glucose (mg/dL)	90.8 ± 9.6	93.6 ± 14.4
VO _{2Max} (ml O ₂ ·kg ⁻¹ ·min ⁻¹)	29.4 ± 10.7	33.6 ± 11.8
Peak Respiratory Exchange Ratio	1.14 ± 0.06	1.18 ± 0.08*
Aortic Wave Velocity (m/s)	7.8 ± 1.8	7.7 ± 1.9
Treatment, N (%)		
ACE inhibitor	16 (41%)	
Diuretic	14 (36%)	
Beta-blocker	11 (28%)	
Angiotensin receptor blocker	7 (18%)	
Calcium channel blocker	5 (13%)	

ACE = angiotensin-converting enzyme

*
P < 0.05

**
P < 0.001

Table V

Correlations of AWV vs. relative fitness

Group	N	Pearson Correlation	P
Normotensive			
Overall	214	-0.216	0.001
Age < 50	135	-0.280	0.001
Age ≥ 50	79	-0.273	0.015
Hypertensive			
Overall	61	0.006	NS
Age < 50	18	-0.259	NS
Age ≥ 50	43	-0.015	NS
Treated	39	0.114	NS
Untreated	22	-0.154	NS