Aging, Habitual Exercise, and Dynamic Arterial Compliance

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Background—A reduction in compliance of the large-sized cardiothoracic (central) arteries is an independent risk factor for the development of cardiovascular disease with advancing age.

Methods and Results—We determined the role of habitual exercise on the age-related decrease in central arterial compliance by using both cross-sectional and interventional approaches. First, we studied 151 healthy men aged 18 to 77 years: 54 were sedentary, 45 were recreationally active, and 53 were endurance exercise–trained. Central arterial compliance (simultaneous B-mode ultrasound and arterial applanation tonometry on the common carotid artery) was lower ($P<0.05$) in middle-aged and older men than in young men in all 3 groups. There were no significant differences between sedentary and recreationally active men at any age. However, arterial compliance in the endurance-trained middle-aged and older men was 20% to 35% higher than in the 2 less active groups ($P<0.01$). As such, age-related differences in central arterial compliance were smaller in the endurance-trained men than in the sedentary and recreationally active men. Second, we studied 20 middle-aged and older (53 ± 2 years) sedentary healthy men before and after a 3-month aerobic exercise intervention (primarily walking). Regular exercise increased central arterial compliance ($P<0.01$) to levels similar to those of the middle-aged and older endurance-trained men. These effects were independent of changes in body mass, adiposity, arterial blood pressure, or maximal oxygen consumption.

Conclusions—Regular aerobic-endurance exercise attenuates age-related reductions in central arterial compliance and restores levels in previously sedentary healthy middle-aged and older men. This may be one mechanism by which habitual exercise lowers the risk of cardiovascular disease in this population. **(*Circulation*. 2000;102:1270-1275.)**

Key Words: elasticity ■ arteries ■ lifestyle ■ ultrasonics

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Arterial compliance reflects the ability of an artery to expand and recoil with cardiac pulsation and relaxation.[1] In sedentary humans, the compliance of the large-sized arteries in the cardiothoracic region (central circulation) decreases with advancing age.[1–3] These reductions are associated with several pathological states common to older adults, including isolated systolic hypertension, left ventricular hypertrophy, congestive heart failure, aortic root regurgitation, and orthostatic and postprandial hypotension.[1,4] As such, decreased central arterial compliance has been identified as an independent risk factor for future cardiovascular disease.[1,5]

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Several epidemiological studies have found that physically active men and women have a lower incidence of cardiovascular disease compared with their sedentary peers.[6,7] Although the mechanisms underlying this protective effect probably include favorable changes in blood pressure, plasma lipids and lipoproteins, and glucose-insulin metabolism,[8] an additional possibility is that regular aerobic exercise is associated with enhanced central arterial compliance, particularly in middle-aged and older adults. Previously, we reported that age-related increases in arterial stiffness are absent or attenuated in endurance exercise–trained adults.[2] However, these findings were based on cross-sectional comparisons only and were derived from "indirect" estimates of arterial compliance. Thus, no information is presently available from intervention studies or from direct measurements of arterial compliance.

Accordingly, the aim of the present study was to determine the role of regular exercise on the age-related reduction in central arterial compliance. To comprehensively address this aim, we used 2 different approaches: Protocol I (cross-sectional study) was designed to determine the potential benefit of regular physical activity in the primary prevention of age-related decreases in central arterial compliance. In this protocol, we also attempted to gain insight into a possible "dose-response" relation by examining 2 different levels of habitual exercise. Protocol II (intervention study) was designed to determine whether regular aerobic-endurance exercise could reverse the age-associated decline in central

Received March 14, 2000; revision received April 10, 2000; accepted April 10, 2000.

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TABLE 1. Selected Subject Characteristics of Cross-Sectional Study

	Sedentary			Recreationally Active			Endurance Trained		
Variable	Young	Middle	Older	Young	Middle	Older	Young	Middle	Older
n	15	26	13	12	16	17	19	18	15
Age, y	28±1	50±1*	64±2*†	26±1	51±1*	65±2*†	29±1	48±1*	67±2*†
Height, cm	181±3	178±1	176±2	178±2	176±1	175±2	179±1	175±2	175±2
Body mass, kg‖	87±5	87±4	85±5	79±2	81±2	79±3	73±2	72±2	74±2
Body fat, %	22±3	26±1*	29±1*	15±1‡	22±1*	24±2*	11±1‡	16±1‡§	19±2*†‡
Systolic BP, mm Hg	112±3	113±3	115±4	112±3	118±3	115±4	110±3	108±3	118±4
Diastolic BP, mm Hg	60±2	71±2	69±2	61±2	70±2	70±2	62±2	65±1	68±2
Heart rate, bpm‖	56±2	62±2	59±2	58±2	54±2	56±2	47±1	45±1	48±2
Total cholesterol, mmol/L	4.01±0.21	4.95±0.21*	4.56±0.21	3.83±0.16	4.33±0.16	4.25±0.18	3.57±0.21	4.30±0.18*	4.43±0.18*
HDL cholesterol, mmol/L‖	1.27±0.08	1.11±0.08	1.06±0.05	1.22±0.08	1.22±0.08	1.17±0.08	1.24±0.10	1.40±0.05	1.32±0.08
Plasma insulin, μU/mL‖	5.8±0.7	7.2±0.7	7.0±0.9	5.1±0.6	5.7±0.7	5.5±0.3	4.2±0.2	4.8±0.6	4.0±0.3
Plasma glucose, mmol/L	4.9±0.1	5.2±0.3	5.5±0.2	4.9±0.1	5.3±0.1	5.1±0.1	4.8±0.2	5.2±0.1	5.0±0.2
$\dot{V}_{O_2}$max, mL · kg^{-1} · min^{-1}	41±2	33±1*	30±1*	49±3‡	42±1*‡	34±1*†	62±1‡§	52±1*‡§	38±2*†‡

Data are mean±SE. BP indicates blood pressure.

*$P<0.05$ vs young; †$P<0.05$ vs middle; ‡$P<0.05$ vs sedentary of same age group; §$P<0.05$ vs recreationally active of same age group; and ‖$P<0.05$ main effects of physical activity status.

arterial compliance. We hypothesized that regular exercise would either prevent or attenuate the age-associated reduction in dynamic central arterial compliance and at least partially restore levels in healthy middle-aged and older sedentary men.

Methods

Subjects

For protocol I, we studied a total of 151 healthy men. Subjects were grouped into consecutive 20-year age ranges starting from age 18: young (aged 18 to 37 years), middle-aged (aged 38 to 57 years), and older (aged 58 to 77 years) (Table 1). For at least the previous 2 years, subjects were either sedentary (no regular physical activity), recreationally active (light to moderate exercise ≥3 times per week), or endurance-trained (vigorous aerobic-endurance exercise ≥5 times per week and active in local road running races). For protocol II, 20 healthy middle-aged and older sedentary subjects (Table 3) were studied before and after 3 months of aerobic exercise training.

All subjects were normotensive (<140/90 mm Hg), nonobese, and free of overt chronic diseases as assessed by medical history, physical examination, and complete blood chemistry and hematological evaluation (eg, plasma glucose concentration <140 mg/dL, total cholesterol <240 mg/dL). Men aged >40 years were further evaluated by ECG at rest and, along with blood pressure, during incremental treadmill exercise performed to exhaustion.[9] Candidates who smoked in the past 4 years, were taking medications, or had significant intima-media thickening, plaque formation, and/or other characteristics of atherosclerosis were excluded.

All subjects gave their written informed consent to participate. All procedures were reviewed and approved by the Human Research Committee of the University of Colorado at Boulder.

Measurements

Before they were tested, subjects abstained from caffeine and fasted for at least 4 hours (a 12-hour overnight fast was used for determination of metabolic risk factors). Subjects were studied 20 to 24 hours after their last exercise training session to avoid the immediate (acute) effects of exercise, but they were still considered to be in their normal (ie, habitually exercising) physiological state.

Central Arterial Compliance

The combination of ultrasound imaging of a common carotid artery with simultaneous applanation of tonometrically obtained arterial pressure from the contralateral carotid artery permits noninvasive determination of dynamic arterial compliance. Subjects were studied under quiet resting conditions while they were in the supine position. Common carotid artery diameter was measured from the images derived from an ultrasound machine (Toshiba SSH-140) equipped with a high-resolution linear-array transducer (7.5 MHz) as previously described.[10] A longitudinal image of the cephalic portion of the common carotid artery was acquired 1 to 2 cm proximal to the carotid bulb, with the transducer placed at a 90° angle to the vessel so that near and far wall interfaces were clearly discernible. These images were recorded on a Pentium computer as well as on a super VHS videocassette recorder for later offline analysis. The computer images were digitized with a video frame grabber (DT-3152, Data Translation) and were analyzed with the use of image analysis software. All image analyses were performed by the same investigator who was blinded to the group assignments or conditions of the subjects. Time points that corresponded with maximal systolic expansion of the carotid artery and basal (minimum) diastolic relaxation were selected. The distances (or the diameters) between the vessel far-wall boundary, corresponding to the interface between the lumen and intima, and the near-wall boundary, corresponding to the interface of the adventitia and media, were then measured.

The pressure waveform and amplitude were obtained from the common carotid artery with a pencil-type probe incorporating a high-fidelity strain-gauge transducer (TCB-500, Millar Instruments), as previously described in detail by our laboratory.[2,11] This tonometer has been shown to register a pressure wave with harmonic content that does not differ from that of an intra-arterially recorded wave, and the use of the tonometer on an exposed artery records a waveform identical to that recorded intra-arterially.[12] Because the baseline levels of carotid blood pressure are subjected to hold-down force, the pressure signal obtained by tonometry was calibrated by equating the carotid mean arterial and diastolic blood pressure to the brachial artery value as previously described.[13]

To characterize central arterial compliance as comprehensively as possible, 2 different measures, arterial compliance[14] and β stiffness index,[15] were calculated. The β stiffness index provides an index of arterial compliance adjusted for distending pressure.[15] To establish the day-to-day reproducibility of carotid arterial compliance mea-

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surements in our laboratory, we performed a pilot study on 9 subjects of varying age by using these methods. The coefficients of variation for the 2 trials were 2±1%, 7±3%, and 5±2% for carotid artery diameter, pulse pressure, and arterial compliance, respectively.

Body Composition

Body composition was determined by using dual-energy x-ray absorptiometry (DPX-IQ, Lunar Radiation) with subjects in the supine position.[16] Waist circumference was measured at the narrowest part of the torso and was used as a measure of total abdominal fat.[17]

Treadmill Exercise

To obtain measures of aerobic fitness, subjects performed a modified Balke incremental treadmill exercise protocol as described previously.[18] Oxygen consumption, heart rate, and ratings of perceived exertion (Borg scale) were measured throughout the protocol, and total exercise time to exhaustion was recorded.

Metabolic Risk Factors for Atherosclerosis

To determine the relations between central arterial compliance and metabolic risk factors for atherosclerosis, fasting plasma concentrations of cholesterol, glucose, and insulin were determined by the clinical laboratory affiliated with the General Clinical Research Center, as described previously.[19]

Resting Arterial Blood Pressure

Chronic levels of arterial blood pressure at rest were measured with a semiautomated device (Dinamap XL, Johnson & Johnson) over the brachial artery, as previously described.[20] Recordings were made in triplicate with subjects in the upright sitting position and conformed strictly to American Heart Association guidelines.[21]

Exercise Intervention

Subjects underwent a week of supervised orientation and thereafter performed exercise on their own. Initially, subjects walked 25 to 30 min/d, 3 to 4 d/wk at a relatively low intensity of exercise (≈60% of their individually determined maximal heart rate). As their exercise tolerance improved, the intensity and duration of walking were increased to 40 to 45 min/d, 4 to 6 d/wk, at an intensity of 70% to 75% of maximal heart rate (30% to 40% of subjects were forced to walk/jog or jog continuously to reach their target heart rate range). Subjects recorded their actual exercise as well as any additional physical activity on a daily basis. Adherence to the exercise prescription was documented through the use of heart rate monitors (Polar Heart Rate Monitor) and physical activity logs as described previously.[22]

Statistical Analyses

Two-way (age×physical activity status) ANOVA was used to assess the results of protocol I. Repeated-measures ANOVA was used to examine the results of protocol II. In the case of a significant F value, a post hoc test using the Newman-Keuls method identified significant differences among mean values. Univariate regression and correlation analyses were used to analyze the relations between variables of interest. All data are reported as mean±SE. Statistical significance was set a priori at $P<0.05$ for all comparisons.

Results

Protocol I

Table 1 shows the subject characteristics for the cross-sectional study. There were no significant group differences in height or arterial blood pressure. Adiposity and total cholesterol generally increased with age, and maximal oxygen consumption decreased with age. In general, body mass, adiposity, and heart rate were lower, and HDL cholesterol and maximal oxygen consumption were higher with increasing habitual exercise levels ($P<0.05$). Carotid intima-media thickness increased with increasing age similarly in all 3 physical activity groups (data not shown).

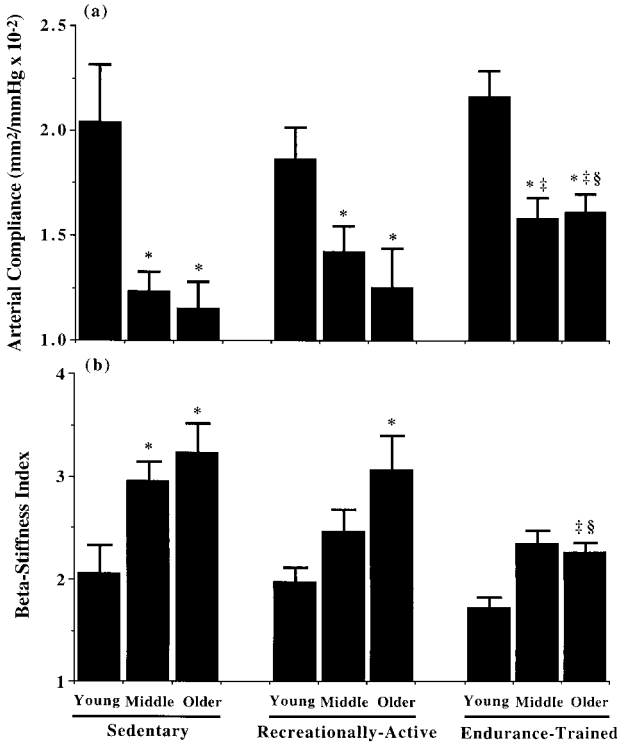


Figure 1. Arterial compliance (a) and β stiffness index (b) of subjects in cross-sectional study. *$P<0.05$ vs young within same activity group; ‡$P<0.05$ vs sedentary of same age group; and §$P<0.05$ vs recreationally active of same age group.

Within all 3 physical activity groups, central arterial compliance was lower ($P<0.05$) in the middle-aged and older men compared with the young men (Figure 1a); there were no significant differences between the middle-aged and older men. Most important, central arterial compliance in the endurance-trained middle-aged and older men was 20% to 35% higher than in their sedentary and recreationally active peers ($P<0.01$). Indeed, the differences in central arterial compliance between the young and older groups were only approximately half as great in the endurance-trained men (25%) than in the sedentary men (45%). In general, qualitatively similar results (although inverse in direction) were obtained by use of the β stiffness index (Figure 1b). There were no statistically significant differences between sedentary and recreationally active men at any age. However, mean levels of arterial compliance in the middle-aged and older recreationally active men were 10% to 17% higher than in their sedentary peers ($P>0.05$).

Physiological correlates of central arterial compliance for the pooled subject population are shown in Table 2. For each measure, the highest correlation was observed with maximal oxygen consumption ($r=0.44$ to 0.45, $P<0.005$). In addition, there were modest ($r=0.19$ to 0.38) but significant ($P<0.05$) correlations with measures of total and abdominal adiposity, heart rate at rest, and metabolic risk factors for atherosclerosis. As expected, central arterial compliance and the β stiffness index were inversely related ($r=-0.51$, $P<0.005$).

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TABLE 2. Selected Physiological Correlates (Pearson Correlation Coefficients) of Arterial Elasticity Measures

Variable	Arterial Compliance	β Stiffness Index
Height	NS	NS
Body mass	NS	NS
Body fat	−0.37*	0.32*
Waist circumference	−0.38*	0.24†
Systolic BP	NS	NS
Diastolic BP	−0.40*	NS
Heart rate at rest	−0.35*	0.28*
Total cholesterol	−0.29*	0.18†
HDL cholesterol	NS	NS
LDL cholesterol	−0.30*	0.23†
Plasma insulin	−0.23†	0.28*
Plasma glucose	−0.23†	0.19†
$\dot{V}o_2$max	0.44*	−0.45*

NS indicates not significant.
*$P<0.005$; †$P<0.05$.

Protocol II

All 20 middle-aged and older men completed the exercise intervention study. Subjects exercised for an average of 13.5±1.0 weeks, 5.3±0.2 d/wk, and 42±1 min/d at 73±1% of maximal heart rate. There were no significant changes in body mass, adiposity, arterial blood pressure, heart rate at rest, or plasma concentrations of cholesterol, glucose, or insulin (Table 3). Time to exhaustion during maximal treadmill exercise increased ≈20% ($P<0.01$), and heart rate and ratings of perceived exertion at the same absolute submaximal level of exercise (≈70% of baseline maximal oxygen consumption) decreased in response to exercise training ($P<0.05$); maximal oxygen consumption did not change significantly (+5%, $P>0.05$).

TABLE 3. Selected Subject Characteristics of Interventional Study

Variable	Before Intervention	After Intervention
n	20	...
Age, y	53±2	...
Height, cm	177±1	...
Body mass, kg	86.6±3.5	86.4±3.5
Body fat, %	28±1	27±2
Systolic BP, mm Hg	115±3	116±3
Diastolic BP, mm Hg	75±2	77±2
Heart rate, bpm	65±3	63±2
Total cholesterol, mmol/L	4.77±0.18	4.87±0.18
HDL cholesterol, mmol/L	1.09±0.08	1.11±0.08
LDL cholesterol, mmol/L	2.75±0.13	2.87±0.13
Plasma insulin, μU/mL	7.6±0.8	7.4±0.8
Plasma glucose, mmol/L	5.6±0.1	5.6±0.2
$\dot{V}o_2$max, mL · kg^{-1} · min^{-1}	31.2±1.3	32.6±1.5
Time to exhaustion, min	9.6±0.2	11.4±0.4*
Submaximal heart rate, bpm	141±3	132±3*
Submaximal RPE, U	12.2±0.3	10.7±0.5*

Data are mean±SE. RPE indicates rating of perceived exertion.
*$P<0.05$ vs values before intervention.

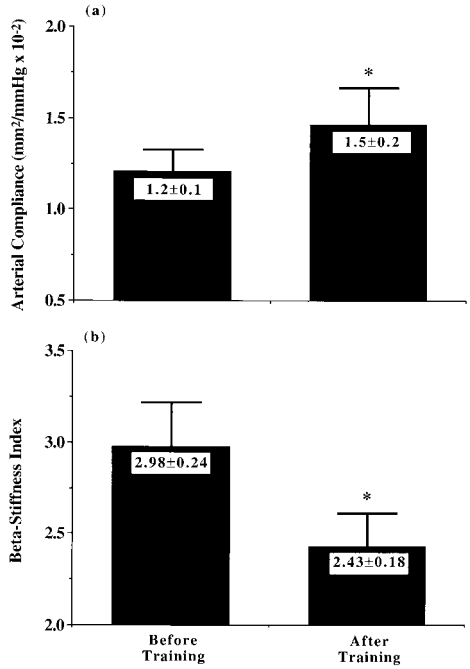


Figure 2. Arterial compliance (a) and β stiffness index (b) before and after aerobic exercise intervention. *$P<0.01$ vs before training.

Regular aerobic exercise produced a 25% increase in central arterial compliance and an ≈20% reduction in the β stiffness index (both $P<0.01$, Figure 2). The level of central arterial compliance after exercise training (1.5±0.2 mm^2/mm Hg×10^{-2}) was not different from that observed in the middle-aged and older endurance-trained men studied in protocol I (1.7±0.1 mm^2/mm Hg×10^{-2}) ($P>0.05$). The individual improvements in central arterial compliance with exercise training were not associated with corresponding changes in any other subject characteristic, any factor related to the exercise stimulus, or any measure of fitness improvement.

Discussion

The main new findings of the present study were as follows. First, central arterial compliance decreases with age even in healthy physically active men, suggesting an effect of primary (intrinsic physiological) aging. Second, the magnitude of the age-related reduction in central arterial compliance is attenuated in men who regularly perform vigorous endurance exercise but not significantly so in men performing less strenuous physical activity. Third, a relatively brief (13- to 14-week) period of regular aerobic exercise can restore some of the loss of central arterial compliance in previously sedentary middle-aged and older men. Fourth, the ability of regular aerobic exercise to increase central arterial compliance in this population does not depend on changes in body weight/composition, arterial blood pressure, metabolic risk factors for atherosclerosis, or maximal aerobic capacity. To our knowledge, these findings are the first to demonstrate that

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the age-associated reduction in central arterial compliance can be favorably modified by regular aerobic-endurance exercise.

We[2] and others[23] have reported that the medium- and large-sized arteries primarily in the cardiothoracic region of middle-aged and older endurance-trained adults appear to be less stiff than those of their sedentary peers on the basis of measurements of aortic pulse wave velocity and carotid augmentation index. However, these are only indirect measures that may or may not accurately reflect population differences in the dynamic compliance of arteries in the central circulation. Moreover, although important, the cross-sectional nature of these observations precluded us from assigning the group differences to the effects of regular exercise, per se, as opposed to other lifestyle or constitutional (including genetic) influences.

The results of the present study extend considerably these prior findings. First, our cross-sectional study (protocol I) allowed us to determine the general age (young adult, middle-aged, or older adult) at which reductions in central arterial compliance are observed in sedentary healthy men as well as any possible interaction between age and habitual exercise. We found that reductions in central arterial compliance occur largely between young adulthood and middle age in both sedentary and physically active men.

Second, using direct measurements of the dynamic compliance of the carotid artery, we show that regular aerobic exercise modulates age-associated reductions in central arterial compliance. Specifically, we found that central arterial compliance was ≈40% higher in endurance-trained older men than in their sedentary peers. Because there were no significant differences among the young adult groups, this suggests that the decrease in central arterial compliance with age may be attenuated in men who habitually engage in vigorous endurance exercise.

Third, the 3-group design of our cross-sectional study also allowed us to determine that vigorous aerobic-endurance exercise appears to modulate age-related decreases in central arterial compliance, whereas less strenuous exercise may not. These findings suggest that a relatively robust endurance exercise stimulus may be necessary to clearly attenuate the age-related decrease in central arterial compliance. However, we should emphasize that although not statistically significant, mean levels of arterial compliance in our middle-aged and older recreationally active men were 10% to 17% greater than in their sedentary peers. Thus, this level of habitual physical activity may have a small, but physiologically important, effect on arterial compliance.

Finally, our follow-up intervention study (protocol II) allowed us to confirm these cross-sectional observations by demonstrating that regular aerobic-endurance exercise can increase central arterial compliance in previously sedentary middle-aged and older men. Moreover, this allowed us to examine the direct effect of exercise by determining whether the improvement in central arterial compliance depended on concomitant changes in other factors, such as arterial blood pressure or maximal oxygen consumption (ie, the capacity to transport oxygen to active skeletal muscle).

In our intervention study, we observed a 25% increase in arterial compliance and a 20% reduction in the β stiffness index after only 3 months of regular aerobic exercise in previously sedentary middle-aged and older men. This improvement was not associated with changes in body mass, adiposity, arterial blood pressure, plasma cholesterol, or maximal aerobic capacity, indicating a direct (primary) effect of exercise on central arterial compliance. Importantly, after exercise training, central arterial compliance was not different from that observed in the middle-aged and older endurance athletes studied in protocol I. These results suggest that relatively short-term aerobic exercise can restore some of the loss of dynamic arterial compliance in healthy middle-aged and older men. Importantly, this can be accomplished with an intensity (moderate) and type (primarily walking) of physical activity that can be performed by most, if not all, healthy men of this age.

We can only speculate on the mechanism by which regular aerobic-endurance exercise improved arterial compliance in the present study. Arterial compliance primarily is determined by the intrinsic elastic properties of the artery.[24] The elements of the arterial wall that determine its compliance are the composition of elastin and collagen (structural determinants) and the vasoconstrictor tone exerted by its smooth muscle cells (functional determinant).[24] Because biochemical changes in the elastin-collagen composition of the arterial wall are believed to occur over years, it is unlikely that short-term regular aerobic exercise increased arterial compliance by this mechanism. However, it is possible that the increased pulse pressures and mechanical distension during the exercise sessions "stretched" collagen fibers and modified their cross-linking, thereby increasing arterial compliance.[25] Arterial compliance also can be altered over a short time period, even acutely, via modulation of the sympathetic-adrenergic tone of smooth muscle cells in the arterial wall.[26,27] In this context, it is possible that regular exercise increased arterial compliance by reducing the chronic suppressive influence exerted by sympathetic-adrenergic tone either directly or by enhancing the sympathoinhibitory effect of NO.[28] Future studies will be needed to determine the physiological mechanism(s) underlying the influence of regular aerobic exercise on central arterial compliance.

Our findings have a number of potentially important clinical implications. Reductions in arterial compliance are believed to contribute significantly to the pathophysiology of age-related increases in cardiovascular diseases.[1,4] For example, reduced compliance in the central arteries has been hypothesized to be the predominant mechanism for the reduction in cardiovagal baroreflex sensitivity with aging.[4] As such, it may contribute to the increased prevalence of ventricular tachyarrhythmias and cardiac sudden death with advancing age.[29] It is possible that increased compliance in the carotid artery (and perhaps the ascending aorta) is associated with greater baroreflex sensitivity. Consistent with this, both preliminary[30] and published[31] results from our laboratory indicate that cardiovagal baroreflex sensitivity is enhanced in middle-aged and older endurance-trained adults compared with their sedentary peers. Moreover, age-related reductions in the compliance of central arteries can affect

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cardiac function by increasing the aortic impedance to ejection of left ventricular stroke volume.[24] This, in turn, may contribute to reductions in left ventricular performance and exercise capacity with age.[32] In this regard, greater central arterial compliance could contribute to the augmented left ventricular function and aerobic exercise capacity demonstrated by older endurance-trained men.[33]

In summary, the present results support the idea that regular aerobic-endurance exercise can attenuate reductions in and partially restore the loss of central arterial compliance in middle-aged and older healthy men. As such, habitual aerobic exercise may be an effective lifestyle intervention for minimizing the loss in central arterial compliance with advancing age. Greater central arterial compliance may contribute to the lower incidence of cardiovascular disease observed in middle-aged and older men who exercise regularly.

Acknowledgments

This study was supported by National Institutes of Health grants AG-00847 (Dr Tanaka), AG-16071, AG-06537, and AG-13038 (Dr Seals), and HL-03840 (Dr DeSouza); by the General Clinical Research Center (No. 5-01-RR00051); and by American Heart Association grant 9960234Z (Dr Tanaka). We thank Yoli Casas, Linda Shapiro, Jayne Semmler, and Teresa Wilson for their technical assistance in the present study.

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