

Correlates of Aortic Stiffness in Elderly Individuals: A Subgroup of the Cardiovascular Health Study

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Background: Arterial stiffness has been associated with aging, hypertension, and diabetes; however, little data has been published examining risk factors associated with arterial stiffness in elderly individuals.

Methods: Longitudinal associations were made between aortic stiffness and risk factors measured approximately 4 years earlier. Aortic pulse wave velocity (PWV), an established index of arterial stiffness, was measured in 356 participants (53.4% women, 25.3% African American), aged 70 to 96 years, from the Pittsburgh site of the Cardiovascular Health Study during 1996 to 1998.

Results: Mean aortic pulse wave velocity (850 cm/sec, range 365 to 1863) did not differ by ethnicity or sex. Increased aortic stiffness was positively associated with higher systolic blood pressure (SBP), age, fasting and 2-h postload glucose, fasting and 2-h insulin, triglycerides, waist circumference, body mass index, truncal fat, decreased physical activity, heart rate, and common carotid artery wall thickness ($P < .05$). After controlling for age

and SBP, the strongest predictors of aortic stiffness in men were heart rate ($P = .001$) and 2-h glucose ($P = .063$). In women, PWV was positively associated with heart rate ($P = .018$), use of antihypertensive medication ($P = .035$), waist circumference ($P = .030$), and triglycerides ($P = .081$), and was negatively associated with physical activity ($P = .111$). Results were similar when the analysis was repeated in nondiabetic individuals and in those free of clinical or subclinical cardiovascular disease in 1992 to 1993.

Conclusions: In these elderly participants, aortic stiffness was positively associated with risk factors associated with the insulin resistance syndrome, increased common carotid intima-media thickness, heart rate, and decreased physical activity measured several years earlier. Am J Hypertens 2002;15:16–23 © 2002 American Journal of Hypertension, Ltd.

Key Words: Pulse wave velocity, aging, arterial stiffness, insulin resistance, heart rate.

With each ventricular contraction, the aorta and other large arteries expand to accommodate the ejection of blood. During diastole, the elastic recoil of the distended arterial walls continues to

propel the blood through the arterial tree. With age, arterial walls stiffen, diminishing their ability to perform this important buffering function, which contributes to the development of increased pulse pressure and isolated sys-

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tolic hypertension.¹ Both isolated systolic hypertension² and increased pulse pressure³ have been shown to be independent predictors of cardiovascular events.

Stiffer arteries have been shown to be associated with age, hypertension, and diabetes in middle-aged individuals and in participants in studies that included a wide age range.^{1,4,5} However, to date, the studies of arterial stiffness have used cross-sectional or case-control designs and have not investigated these associations among elderly individuals. With the increase in the elderly population and the prevalence of isolated systolic hypertension, it is important to investigate factors associated with arterial stiffness in elderly persons. This study used longitudinal data to describe the relationship between aortic stiffness and risk factors measured approximately 4 years earlier in a large group of elderly participants.

Methods

The Cardiovascular Health Study is a longitudinal study of older adults that originally included 5201 men and women aged ≥ 65 years recruited from random samples of Medicare eligibility lists at four sites (Pittsburgh, PA; Washington County, MD; Sacramento County, CA; and Forsyth County, NC). An additional cohort of African American participants ($n = 687$) was recruited 3 years after the original cohort (1992 to 1993). The study design and methods have previously been described in detail.⁶ All surviving Cardiovascular Health Study participants from the Pittsburgh site ($n = 1210$) were invited to participate in this study of aortic stiffness, which was approved by the Cardiovascular Health Study Steering Committee and the University of Pittsburgh Biomedical Institutional Review Board. Participants with known stenosis of the right carotid artery $\geq 75\%$ ($n = 10$) were excluded to prevent adverse effects from the investigation of the carotid artery. Between March 1996 and October 1998, a consecutive sample of 371 men and women gave informed written consent to participate in the study of aortic stiffness.

Aortic stiffness was measured by aortic pulse wave velocity (PWV). Aortic PWV, measured by various methods, has been widely used as an index of aortic stiffness and is reproducible.⁷ Aortic PWV has also been shown to be an independent predictor of the risk of cardiovascular disease (CVD) death at 10 years (per Framingham equations)⁸ and of CVD mortality in participants with hypertension and end-stage renal disease.⁹ The method of aortic pulse wave velocity measurement used in this study^{10,11} has previously been described in detail.¹² Briefly, 20-sec data files of pulse waveforms were collected simultaneously at the carotid and femoral arteries using pencil-type Doppler probes. A single trained reader (RHM) reviewed three files per participant using software developed by the Laboratory of Cardiovascular Science, Gerontology Research Center, National Institute on Aging. For each file, the reader selected all clear waveforms for averaging into composite carotid and femoral waveforms, to deter-

mine the “foot” or upstroke of each. Fifteen participants were excluded because the sonographer was unable to obtain ≥ 10 good waveforms (10 heartbeats) for averaging. Aortic pulse wave velocity is calculated as distance/transit time (cm/sec). The transit time of the pulse wave was calculated as the foot-to-foot delay between the averaged carotid and femoral waveforms. The distance traveled by the pulse waveform was estimated by measurement over the participant’s torso. The distance from the carotid to the aortic site was subtracted from the sum of the aortic to the umbilicus and the umbilicus to the femoral site, to adjust for the opposite direction of the blood flow in that arterial branch. Reproducibility of this method in elderly individuals has been reported, with Pearson and intraclass correlation coefficients of 0.90 and 0.88, respectively, between sonographers.¹²

The mean of two automated (Dinamap) brachial blood pressure (BP) measurements taken from the participant’s right arm was used for analysis. Unless otherwise specified, all other risk factor data were collected at the 1992 to 1993 clinic visit, approximately 4 years before the PWV measurement. Fasting blood samples were collected on the morning of the clinic visit and were processed by a central blood analysis laboratory. The 2-h postchallenge insulin and glucose (2-h insulin and 2-h glucose) measures were obtained from the oral glucose tolerance test that was administered to the original cohort during their baseline clinic visit (1989 to 1990).⁶

Physical activity (excluding chores) was assessed by questionnaire and reported as kilocalories per week.⁶ Exercise intensity was categorized based on the highest intensity leisure-time physical activity over the prior 2 weeks. Internal and external carotid intima-media thickness (IMT) and arterial diameter was measured for the common carotid and internal carotid using duplex ultrasonography scans.¹³ Heart rate and major electrocardiographic abnormalities were determined using a resting 12-lead electrocardiogram. The amount of fat in the abdominal region (kg) (truncal fat) was measured using dual-energy x-ray absorptiometry (DEXA), 2 years after the rest of the risk factors were collected (1994 to 1995).

Diabetes was defined by the American Diabetes Association (ADA) criteria: fasting blood glucose ≥ 126 mg/dL (7.0 mmol/L) or self-reported use of oral hypoglycemic agents or insulin. Impaired fasting glucose was defined as fasting glucose of 110 to 125 mg/dL (6.1 to 7.0 mmol/L). World Health Organization (WHO) criteria were also used to define diabetic status as fasting glucose ≥ 140 mg/dL (7.8 mmol/L) or 2-h glucose ≥ 200 mg/dL (11.1 mmol/L), or use of insulin or oral hypoglycemic agents. Hypertension was defined as systolic blood pressure (SBP) ≥ 160 or diastolic blood pressure (DBP) ≥ 95 or self-reported history of hypertension as well as use of antihypertensive medications, and borderline hypertension was defined as SBP of 140 to 159 mm Hg or DBP of 90 to 94 mm Hg. Pulse pressure was defined as SBP – DBP. Smoking status was categorized as never, former, or current. At

entry to the Cardiovascular Health Study, lifetime smoking dose was categorized as: none, passive (lived with a regular smoker), light (1 to 13 pack-years), moderate (14 to 50 pack-years), or heavy (<50 pack-years). Clinical cardiovascular disease was defined as: confirmed history of heart disease including myocardial infarction, angina pectoris, or use of nitroglycerin; congestive heart failure; coronary bypass surgery or angioplasty; atrial fibrillation (by electrocardiography) or use of a cardiac pacemaker; history of stroke, transient ischemic attack, or carotid artery surgery; or history of intermittent claudication or peripheral vascular surgery.¹⁴ For those without clinical CVD, subclinical disease was defined as: major electrocardiographic abnormalities, increased internal or common carotid wall thickness (>80th percentile) or stenosis $\geq 25\%$, a decreased ankle-brachial BP (≤ 0.9), or positive responses to the Rose Questionnaire for angina or intermittent claudication.¹⁵

For statistical analyses, testing was two-sided with a statistical significance of $P \leq .05$, except for entry into the stepwise regression model, which was $P \leq .10$ because of the exploratory nature of the regression analysis. Aortic PWV, fasting triglycerides, glucose and insulin, and 2-h glucose and insulin were transformed (natural logarithm) for use in multivariate analysis. Analysis of covariance was used to evaluate differences in mean (log) PWV by category of risk factor after adjustment for age and SBP, with contrasts used for tests of linear trend. The adjusted means were back-transformed for presentation in the tables. Stepwise linear regression was used to determine the strongest independent predictors of PWV for the entire group, then stratified by sex. Candidate variables for the stepwise analysis were all those significant in the initial bivariate screening, with the addition of ethnicity and sex. To estimate the predicted change in PWV for the specified change in the risk factor, the final models were recalculated using untransformed variables. All analyses were performed using SAS software, version 6.12 (SAS Institute, Cary, NC). Conventional units were transformed to SI units after analysis.

Results

At the time of the PWV data collection, the mean age of the participants was 78.2 years (range 69.6 to 95.9 years), and the participant group was 25.3% African American and 53.4% female (Table 1). The mean time between the 1992 to 1993 clinic visit and the PWV measurement was 4.2 years (range 2.9 to 6.2 years). Aortic PWV ranged from 365 to 1863 cm/sec (mean 850, median 821). There were no significant differences in mean PWV by either ethnicity or sex. Participants included in the PWV study were similar to those from the Pittsburgh site who were alive when the PWV study began (1996 to 1997) but who were not included (data not shown.) No significant differences were found between participants and nonparticipants for BP, heart rate, lipids, body mass index (BMI),

waist circumference, current smoking status, or mean lifetime smoking dose (pack-years). However, those who did not participate in the aortic stiffness study were slightly older, more likely to use antihypertensive medications, to have clinical CVD, thicker carotid artery walls, and to have slightly lower physical activity (men only) ($P < .05$ for all).

Table 2 reports the Spearman correlations between PWV and measured risk factors, both unadjusted and adjusted for SBP. For the total group, PWV was positively associated with age, SBP, DBP, pulse pressure, heart rate, triglycerides, fasting and 2-h glucose, fasting and 2-h insulin, BMI, waist circumference, and truncal fat ($P < .05$). The pattern of associations was similar for men and women, although BMI, activity level, LDL cholesterol, and fasting triglycerides were significant only in women. Results were similar when diabetic individuals were excluded, by either ADA or WHO criteria (data not shown).

Associations between PWV and lifestyle factors, disease, and selected subclinical measures, adjusted for age and SBP, are presented in Table 3. The effects of ethnicity and sex as well as their interactions with the risk factors were tested but were not significant in any of the analysis of covariance models. Current and former users of estrogen replacement therapy had lower mean PWV than never users, but this difference was not significant (data not shown). No consistent relationship was observed between PWV and smoking, whether smoking was measured by current smoking status or lifetime smoking dose. No significant differences were found between any of the groups except for the test of trend for smoking duration for men only ($P = .046$). For the total group, higher mean PWV was also associated with prevalent coronary heart disease and with diabetes by either ADA or WHO criteria. However, no difference in mean PWV was found for prevalent cerebrovascular disease, peripheral vascular disease, or congestive heart failure, although the small number of cases (approximately 10%) provided low power to detect a difference (data not shown).

Stepwise linear regression was performed using all variables significant in bivariate analysis as the candidate variables. For the total group, with age and gender forced into the model, the strongest independent predictors of PWV were SBP ($P < .001$), heart rate ($P < .001$), waist circumference ($P = .014$), hypertension medication ($P = .008$), 2-h glucose ($P = .095$), and decreased activity level ($P = .128$) with a model $R^2 = 0.26$. Table 4 shows the sex-stratified models. For men, increased heart rate ($P = .001$) and 2-h glucose ($P = .063$) were positively associated with PWV after adjustment for age and SBP. For women, after adjustment for age, increased PWV was associated with SBP, waist circumference, heart rate, antihypertensive medication ($P < .05$ for all), fasting triglycerides ($P = .081$), and decreased activity level ($P = .111$). There were no significant interactions between ethnicity and the risk factors in the models. These final models were unchanged when diabetic individuals were

Table 1. Characteristics of Cardiovascular Health Study participants from the Pittsburgh site included in this study ($n = 356$)

	Men	Women
<i>N</i>	166	190
Ethnicity (% African American)	23.6	26.8
Age (1992–1993), years	73.9 ± 4.3	73.2 ± 4.0
Age at PWV, years	78.6 ± 4.3	77.9 ± 4.1
PWV, cm/sec	865 ± 243	837 ± 241
SBP, mm Hg	129.1 ± 18.6	130.8 ± 20.3
DBP, mm Hg	73.2 ± 10.5	70.0 ± 9.5*
PP, mm Hg	55.9 ± 14.1	60.7 ± 17.1*
SBP at PWV, mm Hg	137.4 ± 18.7	136.4 ± 19.5
Heart rate, beats/min	62.3 ± 10.1	66.2 ± 9.6*
Total cholesterol, mmol/L	4.8 ± 0.9	5.4 ± 0.9*
HDL cholesterol, mmol/L	1.2 ± 0.3	1.5 ± 0.4*
LDL cholesterol, mmol/L	2.9 ± 0.8	3.2 ± 0.9*
Triglycerides, mmol/L	1.5 ± 1.0	1.6 ± 0.9
Fasting glucose, mmol/L	6.1 ± 1.7	6.0 ± 2.1
Fasting insulin, nmol/L	107.9 ± 240.4	100.6 ± 210.7
2-h Glucose, mmol/L†	7.2 ± 2.8	7.5 ± 2.6
2-h Insulin, nmol/L†	420.6 ± 304.8	516.2 ± 335.2*
Body mass index, kg/m ²	26.4 ± 3.8	27.3 ± 4.7*
Waist, cm	97.7 ± 10.5	96.7 ± 14.2
Truncal fat (kg)	11.28 ± 4.53	13.51 ± 4.73*
Activity level‡ (Kcal/wk)	1513 ± 1656	784 ± 960*
Common carotid IMT (mm)	1.11 ± 0.24	1.03 ± 0.17*
Internal carotid IMT (mm)	1.44 ± 0.58	1.30 ± 0.53*
Smoking, pack-years	22.6 ± 27.3	16.7 ± 27.9*
Current smoking (%)	9.8	9.1
Former smoking (%)	57.1	46.0*
Hypertensive§ (%)	44.2	51.1
Antihypertensive medication (%)	43.6	45.8
Diabetes-ADA (%)	16.6	14.8
Subclinical CVD (%)	44.2	40.0*
Clinical CVD¶ (%)	29.7	20.5*

PWV = pulse wave velocity; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; IMT = intima-media thickness; ADA = American Diabetes Association; CVD = cardiovascular disease.

Values are mean (SD) or percent.

* $P < .05$.

† Two hours after 75 g oral glucose tolerance test administered at baseline (1989–1990).

‡ Determined by questionnaire regarding daily activities, excluding chores.

§ Systolic BP ≥ 140 , diastolic BP ≥ 90 , or history of hypertension and use of antihypertensive medication.

|| Subclinical CVD, defined as: major electrocardiogram (ECG) abnormalities, increased internal or common carotid wall thickness (>80 th percentile) or stenosis $\geq 25\%$, a decreased ankle-brachial BP (≤ 0.9), or positive responses to the Rose Questionnaire for angina or intermittent claudication.

¶ Clinical CVD, defined as: confirmed history of heart disease including myocardial infarction, angina pectoris, or use of nitroglycerin; congestive heart failure; coronary bypass surgery or angioplasty; atrial fibrillation (by ECG) or use of a cardiac pacemaker; history of stroke, transient ischemic attack, or carotid artery surgery; or history of intermittent claudication or peripheral vascular surgery.

excluded using either the ADA or WHO definition of diabetes.

To determine whether the observed associations were caused by increased arterial stiffness in participants with advanced atherosclerotic cardiovascular disease, the analysis was repeated for participants who were free of any clinical or subclinical cardiovascular disease at the 1992 to 1993 visit (data not shown). For the total group, 2-h glucose and activity level were not significant but fasting insulin entered the model ($P = .056$). In men ($n = 43$), the strongest predictors were heart rate ($P = .031$) and fasting glucose ($P = .057$). In women ($n = 75$), waist circumference and heart rate were still positively associated with increased PWV ($P \leq .05$).

Discussion

In these participants aged 70 to 96 years, we found a wide range of arterial stiffness as measured by aortic PWV (365 to 1863 cm/sec.) Among these elderly men and women, arterial stiffness was positively associated with antihypertensive medication use, heart rate, fasting insulin, 2-h insulin, 2-h glucose, measures of abdominal obesity and decreased physical activity, fasting triglycerides, and common carotid wall thickness measured several years earlier. These associations were independent of age and SBP and persisted when diabetic individuals were excluded.

The association of higher PWV with antihypertensive medication use, despite adjustment for SBP, most likely

Table 2. Spearman correlations of pulse wave velocity with risk factors, unadjusted (*r*) and adjusted (*adj-r*) for systolic blood pressure, in a subgroup of the Cardiovascular Health Study

	Men		Women		Total	
	<i>r</i>	<i>adj-r</i>	<i>r</i>	<i>adj-r</i>	<i>r</i>	<i>adj-r</i>
Age of PWV	0.10	0.05	0.11	0.09	0.12*	0.08
SBP at PWV	0.30*		0.21*		0.26*	
DBP at PWV	0.11		0.13		0.13*	
Pulse pressure at PWV	0.27*		0.21*		0.24*	
Heart rate	0.34*	0.27*	0.15*	0.11	0.22*	0.17*
Total cholesterol	-0.04	-0.03	0.10	0.08	0.00	0.00
HDL cholesterol	-0.01	-0.03	-0.10	-0.11	-0.08	-0.08
LDL cholesterol	-0.05	-0.05	0.16*	0.12	0.05	0.03
Triglycerides	0.07	0.07	0.16*	0.20*	0.11*	0.14*
Fasting glucose	0.11	0.00	0.13	0.13	0.13*	0.08
Fasting insulin	0.23*	0.18*	0.18*	0.19*	0.20*	0.19*
2-h Glucose†	0.28*	0.23*	0.18*	0.19*	0.22*	0.21*
2-h Insulin†	0.28*	0.25*	0.21*	0.21*	0.22*	0.20*
Body mass index	0.12	0.03	0.21*	0.21*	0.15*	0.11*
Waist	0.17*	0.08	0.23*	0.26*	0.21*	0.19*
Activity level‡	-0.03	0.00	-0.20*	-0.18*	-0.09	-0.08
Truncal fat	0.20*	0.14	0.18*	0.18*	0.15*	0.13*

Abbreviations as in Table 1.

* $P < .05$.

† Two hours after 75 g oral glucose tolerance test administered at baseline (1989–1990).

‡ Activity level (kilocalories/week) determined by questionnaire regarding daily activities, excluding chores.

reflects the arterial damage done by long-term hypertension rather than a stiffening effect of antihypertensive medication. The associations between arterial stiffness and risk factors associated with the insulin resistance syndrome, including increased fasting insulin and glucose, 2-h insulin and glucose and central obesity, agree with those reported in cross-sectional data for younger and middle-aged participants.^{16–18} There are many mechanisms by which factors associated with the insulin resistance syndrome might promote arterial stiffness. Insulin promotes the synthesis of collagen, the stiffer form of arterial wall protein, and stimulates hyperplasia and hypertrophy of vascular smooth muscle cells.¹⁹ Hyperinsulinemia may also indirectly increase arterial stiffness by stimulating the sympathetic nervous system, which could increase heart rate, arterial smooth muscle tone, or BP.²⁰ Hyperglycemia also stimulates collagen synthesis and promotes the glycation of collagen and other extracellular matrix proteins in the arterial wall, creating advanced glycosylation end-products and increasing cross-linking between protein fibers, which has been associated with reduced arterial elasticity.^{4,19} Possibilities for intervention are suggested by studies that found that intensive glycemic control in diabetic patients reduced glycation and collagen cross-linking,²¹ and that certain drugs may be able to reverse advanced glycosylation end-product related cross-linking and decrease arterial stiffness.²²

Surprisingly, in these elderly participants, decreased aortic stiffness was associated with higher activity levels (for women) and higher exercise intensity (for both sexes), similar to findings from studies which included young or middle-aged participants or a wide age range.^{11,23,24} Ad-

ditional adjustment for gender, heart rate and waist circumference or truncal fat did not change this trend, and the difference remained significant for the high intensity exercise group versus the low intensity group (data not shown).

Higher heart rates were associated with higher aortic stiffness in these elderly participants, in agreement with previous results for middle-aged participants.^{18,25} A faster heart rate might accelerate the fatigue of elastic fibers by increasing the lifetime number of repetitive stretching cycles, or by not allowing enough time for the large arteries to relax between each ventricular contraction. Increased heart rate might also indirectly increase arterial stiffness by increasing the strain on arterial walls from increased cardiac output and BP. One study found an increase in arterial stiffness when heart rate was mechanically increased by atrial pacing, but this effect might not have been independent of sympathetic nervous system stimulation caused by anxiety about the atrial pacing.²⁶

In these elderly participants, aortic stiffness was associated with thicker IMT of the common carotid artery, but not the internal carotid artery IMT. The Cardiovascular Health Study measure of the internal carotid artery, which includes the carotid bulb, is more likely to include focal atherosclerotic plaque than the common carotid artery IMT, which may be a better index of arterial wall hypertrophy.¹³ Therefore, in these elderly participants aortic stiffness was more strongly related to arterial wall hypertrophy than to atherosclerotic plaque in the carotid artery.

Age was not a significant predictor of increased aortic stiffness in this sample of elderly participants. This result

Table 3. Mean pulse wave velocity (cm/sec) by category of risk factors, adjusted for age and systolic blood pressure, in a subgroup of the Cardiovascular Health Study, 1992–1993

Variable	Category (n)	Men	Women	Total
Hypertension*	Normotensive (185)	796	755	775
	Borderline (57)	861	789	822
	Hypertensive (114)	885†	886†	886†
Antihypertensive medication	No (186)	807	761	783
	Yes (156)	856	865†	860†
Smoking status	Never (135)	830	827	828
	Former (173)	829	794	813
	Current (32)	835	789	808
Smoking duration‡	Never (124)	794	831	818
	Passive (13)	795	764	786
	Light (65)	829	759	782
	Moderate (97)	828	824	827
Exercise intensity§	Heavy (39)	930†	785	862
	Low (163)	867	837	850
	Moderate (131)	807	792	799
Diabetes—ADA	High (49)	781	733†	754†
	Normal (250)	824	786	802
	IFG (38)	795	863	824
Ankle-arm index	Diabetes (53)	866	876	873†
	Normal 0.9–1.5 (316)	819	800	809
	Abnormal <0.9 (24)	925	866	892
Major ECG abnormalities	No (233)	827	788	806
	Yes (93)	813	827	818
Cardiovascular disease	None (114)	839	809	821
	Subclinical (145)	812	786	797
	Clinical (85)	846	845	846
Coronary heart disease¶	No (285)	815	795	803
	Yes (59)	874	911†	887†
Internal carotid IMT	0.601–0.957 mm (84)	822	746	772
	0.958–1.176 mm (85)	809	843	827
	1.177–1.655 mm (87)	830	862	849
	1.656–3.655 mm (85)	847	765	810
Common carotid IMT	0.70–0.938 mm (85)	829	749	779
	0.939–1.050 mm (87)	819	803	807
	1.051–1.160 mm (85)	826	821	823
	1.161–2.300 mm (84)	838	863†	850†
CCA external diameter	6.96–8.40 mm (85)	750	770	762
	8.41–9.01 mm (87)	832	852	836
	9.02–9.64 mm (88)	827	807	816
	9.65–12.54 mm (92)	845	816	840†

IFG = impaired fasting glucose; CCA = common carotid artery; other abbreviations as in Tables 1 and 2.

* Systolic BP \geq 140, diastolic BP \geq 90, or history of hypertension and use of antihypertensive medication, adjusted for age only.

† $P < .05$, from contrasts in analysis of covariance.

‡ Never, passive (lived with a regular smoker), light (1–13 pack-years), moderate (14–50 pack-years), and heavy (>50 pack-years).

§ Based on the highest intensity leisure-time physical activity over the prior 2 weeks.

|| Clinical CVD, defined as: confirmed history of heart disease including myocardial infarction, angina pectoris, or use of nitroglycerin; congestive heart failure; coronary bypass surgery or angioplasty; atrial fibrillation (by electrocardiography) or use of a cardiac pacemaker; history of stroke, transient ischemic attack, or carotid artery surgery; or history of intermittent claudication or peripheral vascular surgery. Subclinical CVD, defined as: major electrocardiographic abnormalities, increased internal or common carotid wall thickness (>80th percentile) or stenosis \geq 25%, a decreased ankle-brachial BP (\leq 0.9), or positive responses to the Rose Questionnaire for angina or intermittent claudication.

¶ History of myocardial infarction, angina, bypass surgery, or angioplasty.

is not surprising, as this study included a limited age range (interquartile range 75.2 to 80.3 years). We observed no consistent effect of smoking on arterial stiffness in these elderly participants; however, our ability to detect an association between smoking and PWV was limited by the small number of current smokers and the potential for survivor bias. In younger participants, reports of an association between smoking status and arterial stiffness have

been inconsistent.^{18,27,28} Reports of a relationship between arterial stiffness and cholesterol have also been inconsistent in younger participants.^{10,18,29} We found no relationship between PWV and total or LDL cholesterol, except for a weak correlation with LDL cholesterol for women, which may be a chance finding.

There were several limitations of this study. Although this study examined the association of PWV with risk

Table 4. Predicted difference in pulse wave velocity (cm/sec) by change in risk factor, adjusted for other variables in the model by multiple linear regression in a subgroup of the Cardiovascular Health Study

Gender	Risk Factor (amount)*	PWV Change (cm/sec)†	SE	P Value‡
Men (n = 166)	Age at PWV (1 y)	4.2	5.9	0.727
	Systolic BP (18.7 mm Hg)	48.4	21.8	0.026
	Heart rate (10.6 beats/min)	62.8	23.8	0.001
	2-h Glucose (2.8 mmol/L)	23.2	23.2	0.063
	Model R ² ‡ = 0.32			
Women (n = 190)	Age at PWV (1 y)	4.4	4.0	0.415
	Systolic BP (19.5 mm Hg)	54.3	16.7	0.005
	Waist circumf. (14.2 cm)	35.9	17.0	0.030
	Heart rate (10.6 beats/min)	8.4	18.6	0.018
	Antihypertensive meds (yes)	71.0	33.6	0.035
	Triglycerides (0.94 mmol/L)	17.5	16.4	0.081
	Activity level (960 kcal)	-27.3	18.0	0.111
	Model R ² ‡ = 0.21			

Abbreviations as in Tables 1–3.

* Amount of change for continuous variables is 1 SD.

† Predicted change estimated using regression coefficients from multiple linear regression model with untransformed variables.

‡ P values and R² from model with log-transformed variables (PWV, 2-h glucose, and triglycerides).

factors measured several years earlier, the time sequence cannot be determined because we have no baseline measure of PWV, and elevated PWV most likely develops over many years. Our ability to detect racial differences was limited by the small numbers of African American participants. Finally, these results must be interpreted with the understanding that they are affected by survivorship bias in this group of relatively healthy older adults. A prospective study with a longer follow-up period is needed to confirm these results.

Although arterial stiffness increases with age and hypertension, we found a wide range of arterial stiffness in this elderly group that was not accounted for by differences in age or SBP. Clearly, the arteries of some elderly participants have aged much more successfully than those of others. We also found that many variables associated with increased stiffness in younger populations continue to be risk factors in this older population. Interventions, such as exercise or medication to improve insulin sensitivity, or to reduce advanced glycosylation end-product formation, cross-linking, or collagen deposition, may be beneficial in reducing arterial stiffness even in elderly individuals.

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