

Measures of Obesity Are Associated With Vascular Stiffness in Young and Older Adults

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Abstract—Obesity has reached epidemic levels and carries a risk for cardiovascular disease. Obesity's effects on the vascular systems of young adults and African Americans have not been well characterized. The aim of this study was to assess the association between measures of obesity and aortic stiffness in 186 young adults (20 to 40 years, 50% African American) and 177 older adults (41 to 70 years, 33% African American). Aortic stiffness was measured by aortic pulse-wave velocity. The median pulse-wave velocity value was 468 cm/s for young adults and 627 cm/s for older adults ($P<0.001$). Higher body weight, body mass index, waist and hip circumferences, and waist-hip ratio were strongly correlated with higher pulse-wave velocity, independent of age, systolic blood pressure, race, and sex overall and among both age groups ($P<0.01$ for all). Even among the 20- to 30-year-olds, obese individuals (body mass index >30) had a mean pulse-wave velocity value 47 cm/s higher than did nonobese individuals ($P<0.001$). Obesity measures were among the strongest independent predictors of pulse-wave velocity overall and for both age groups. Results were consistent by race. In conclusion, excess body weight is associated with higher aortic stiffness in whites and African Americans as young as 20 to 30 years. The strength of the association, the early age at which it appears, and the prevalence of obesity among the young warn of substantially increased cardiovascular disease incidence as this cohort ages. (*Hypertension*. 2003;42:468-473.)

Key Words: arteriosclerosis ■ compliance ■ elasticity ■ insulin resistance ■ obesity ■ young adults

The prevalence of obesity in the United States has reached epidemic proportions and is continuing to increase, not only among adults but also among children and adolescents.^{1,2} According to data from the National Health and Nutrition Examination Survey for 1988 to 1994, the prevalence of overweight (body mass index [BMI] >25 kg/m²) was 11.3% among 6- to 11-year-olds, 10.5% among 12- to 19-year-olds, and 55.9% among adults, whereas in 1999 to 2000, corresponding prevalence rates had increased to 15.3%, 15.5%, and 64.5%, respectively.^{1,2} In addition, the likelihood that an obese child will remain obese into adulthood is high. In the Bogalusa Heart Study, 77% of obese children remained obese as adults an average of 17 years later.³ Excess weight has been shown to carry a risk for stroke, incident cardiovascular disease, cardiovascular mortality, and all-cause mortality among middle-aged and elderly participants in longitudinal studies.⁴⁻⁷ Thus, the increase in obesity prevalence, particularly among younger age groups, is likely to have long-term implications for cardiovascular disease in the years to come.

The age at which excess weight begins to exact its toll on the cardiovascular system is still unknown, as is the exact mechanism through which cardiovascular damage is accomplished. Obesity might adversely affect cardiovascular health

through associations with dyslipidemia,⁶ hypertension,⁶ and inflammation.^{8,9} Obesity might also exert adverse effects on the vascular system by increasing arterial stiffness, thus predisposing the individual to hypertension and premature aging of the vascular system. Excess body fat, abdominal visceral fat, and larger waist circumference have been identified as risk factors for accelerated arterial stiffening in elderly participants^{10,11} and in middle-aged white participants.¹²⁻¹⁴ The mechanism behind these associations might be the connection between excess body fat and insulin resistance.

The degree to which excess body fat is associated with vascular stiffening in younger populations is not yet clear. The purpose of this report was to assess the association between aortic pulse-wave velocity (aPWV), a measure of central artery stiffening, and measures of obesity in two biracial populations, one aged 20 to 40 years and one aged 41 to 77 years.

Methods

Study Population

aPWV was assessed in 2 age groups of participants. The first was a group of 186 participants aged 20 to 40 years recruited from a National Institute on Aging-funded study of vascular stiffness. The

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second was a group of 177 participants aged 41 to 77 years recruited from a study of ethnic differences in cardiovascular risk. Both groups of participants were originally recruited from Allegheny County, Pennsylvania, by newspaper advertisements, mailed flyers, and automatic voice messages through the University of Pittsburgh's telephone message system. Exclusion criteria for all participants included use of antihypertensive, lipid-lowering, thyroid, blood sugar-lowering, or cardiovascular medications, as well as a history of lupus or clinical cardiovascular disease. Data for both groups were collected under identical procedures detailed later. This study was approved by the University of Pittsburgh's Institutional Review Board.

Vascular Stiffness

As central arteries become stiffer, the velocity of the pulse wave as it travels down the aorta becomes faster.¹⁵ aPWV was measured after ≈ 30 minutes of supine rest by Doppler ultrasound of the right carotid and femoral arteries, as previously published.¹⁶ To enable adjustment for blood pressure at the time of aPWV measurement, 7 supine blood pressure measurements were taken throughout ultrasound testing with an automatic blood pressure cuff and cuff sizes appropriate to the manufacturer's recommendations. The first measure was discarded, and the remaining 6 measurements were averaged.

Associations between vascular stiffness and obesity measures were also tested with use of pressure-strain elastic modulus and carotid arterial diameter. Results were identical to those that follow for PWV. Therefore, results are presented for PWV only.

Body Weight and Weight-Distribution Measures

Two measurements of weight, waist circumference, and hip circumference were assessed with a standard scale or tape measure and averaged. BMI was calculated by dividing the participant's weight in kilograms by the square of his/her height in meters (measured with a standard stadiometer). Obesity was defined as a BMI > 30 , as defined by the World Health Organization.¹⁷

Other Covariates

Age, history of smoking (defined as ever- versus never-smoking), and highest education level achieved were assessed by questionnaire. In addition to supine blood pressure measurements, 3 consecutive, seated, heart rate and blood pressure measurements were taken at the ultrasound examination, after 5 minutes of rest, with a standard mercury sphygmomanometer and cuff sizes according to the manufacturer's recommendations. Staff members who performed the seated blood pressure measurements had been certified by a standard clinic protocol. The first measurement was discarded, and the second and third measurements were averaged. Seated blood pressure variables included systolic (SBP) and diastolic blood pressure (DBP), pulse pressure (PP, calculated as SBP-DBP), and mean arterial pressure (MAP, calculated as $DBP + 1/3[PP]$). Total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, and glucose values were determined after a 12-hour fast by standard laboratory procedures.

Statistical Analysis

SAS software, version 8.2 (SAS Institute), was used for all analyses. aPWV was not normally distributed. Therefore, nonparametric statistics were used where possible, and $1/aPWV$ was used in all regression models.

Associations between aPWV and continuous covariates were assessed with Spearman correlations, both unadjusted and adjusted for age, supine SBP, race, and sex. The Wilcoxon signed-rank test was used to compare median aPWV values by levels of categorical variables. Linear regression was used to determine the strongest predictors of aPWV and to assess age, race, and sex interaction terms. Analyses were initially performed with both age groups combined, and interactions with age were tested for obesity measures. Although none of the age interaction terms were significant, analyses were also performed after stratification by age group (20 to

40 years, 41 to 77 years), given the slightly different recruitment procedures used within each sample.

aPWV reproducibility was evaluated graphically (Bland-Altman plots)¹⁸ after replicate aPWV measurements were performed by 2 technologists, on 2 visits, ≈ 1 week apart. Bland-Altman plots revealed that all of the mean between-technologist and within-technologist observations were within 2 SDs of the difference between those observations, indicating good reproducibility.¹⁸ Similar aPWV reproducibility results have previously been demonstrated for this ultrasound laboratory.¹⁶

Results

For the 20- to 40-year-olds, the median age was 29.8 years, 50% were African American, 46% were female, and 26% were obese (Table 1). For the 41- to 77-year-olds, the median age was 60.5 years, 33% were African American, 29% were female, and 21% were obese (Table 1). A number of differences existed between the 2 age groups. Among the older age group, there were fewer African Americans and women (Table 1). Blood pressures, lipid levels, and waist circumference were also higher among the older age group (Table 1).

As expected, older age and SBP were strongly associated with higher aPWV. The median aPWV was 468 cm/s among the 20- to 40-year-olds and 627 cm/s among the 41- to 77-year-olds ($P < 0.001$; Table 1). The association between aPWV and age was significant even within each of these 2 age groups (Table 2). When age was further categorized as 20 to 30 years, 31 to 40 years, 41 to 50 years, and 60+ years, the median aPWV in each category was 429, 493, 581, and 691 cm/s, respectively. PWV did not significantly differ between African Americans and whites, between men and women, or between smokers and nonsmokers in the total sample or in either the young or old age groups when the sample was stratified.

aPWV was strongly correlated with a higher BMI and body weight and larger waist circumference, hip circumference, and waist-hip ratio (WHR), independent of age, supine SBP, race, and sex. The strong associations between obesity measures and aPWV were consistent for both 20- to 40-year-olds and 41- to 77-year-olds, as documented by correlation coefficients of similar magnitude within each age group (Table 2), as well as by nonsignificant linear regression interaction terms between obesity measures and age in the full sample. Additionally, no differences were observed in the strength of these associations by race or sex, as also tested by interaction terms from linear regression or as assessed by comparison of correlation coefficients when the sample was stratified by race or sex. Higher aPWV was also associated with higher glucose values for both age groups (Table 2) and with lower education levels for 41- to 77-year-olds (median aPWV, 731 cm/s for those with less than high school education vs 614 cm/s for those with greater than high school education; $P = 0.006$).

To illustrate the effect of higher body weight on aPWV by using clinical definitions of obesity and among more specific age groupings, individuals were categorized as normal weight (BMI < 25), overweight (BMI > 25), or obese (BMI > 30), and the mean PWV, adjusted for age, supine SBP, race, and sex, was calculated for each of the 3 BMI categories for a number of age groups (Figure). Among 20- to 30-year-olds, obese

TABLE 1. Descriptive Characteristics by Age Group

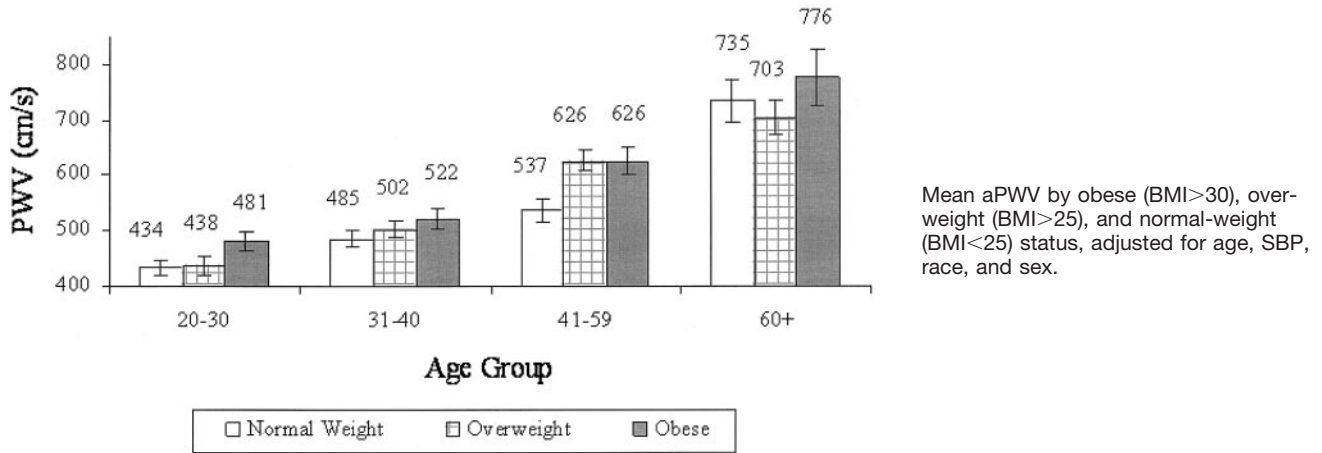
Variable Name	20–40 Years (n=186)	41–77 Years (n=177)	P
Dichotomous, n (%)			
African American	93 (50)	58 (33)	0.001
Female	101 (46)	52 (29)	0.001
≤High school education	30 (16)	38 (22)	0.19
Ever smoker	80 (43)	101 (57)	0.007
Obese (BMI≥30)	49 (26)	38 (21)	0.28
Continuous, median (range)			
PWV, cm/s	468 (256.0–858.0)	627 (393.0–2166.0)	<0.001
Supine SBP, mm Hg	126 (97.0–167.0)	140 (95.6–192.4)	<0.001
Seated SBP, mm Hg	107.0 (82.0–152.0)	128.0 (90.0–180.0)	<0.001
Seated DBP, mm Hg	70.0 (38.0–95.0)	80.0 (44.0–124.0)	<0.001
Seated PP, mm Hg	38.0 (18.0–74.0)	45.0 (22.0–90.0)	<0.001
Age, y	29.79 (20.02–39.77)	60.47 (40.05–76.67)	<0.001
Total cholesterol, mmol/L	4.6 (2.5–7.7)	5.7 (3.2–8.6)	<0.001
LDL cholesterol, mmol/L	2.6 (0.9–5.3)	3.5 (1.5–6.3)	<0.001
HDL cholesterol, mmol/L	1.3 (0.7–2.7)	1.4 (0.6–3.1)	0.56
Triglycerides, mmol/L	1.0 (0.4–6.0)	1.4 (0.4–6.3)	<0.001
Glucose, mmol/L	5.0 (3.4–6.5)	5.3 (4.0–19.3)	<0.001
Weight, kg	74.5 (44.3–141.8)	79.4 (53.3–118.6)	0.09
BMI, kg/m ²	25.79 (17.38–47.98)	26.91 (18.71–38.24)	0.23
Waist circumference, cm	81.65 (57.65–133.6)	88.35 (65.2–118.45)	<0.001
Hip circumference, cm	100.15 (81.1–149.0)	100.4 (78.65–125.75)	0.65
Waist:hip	0.82 (0.64–0.98)	0.89 (0.66–1.05)	<0.001

individuals demonstrated a mean adjusted PWV value 47 cm/s higher than either the normal-weight or overweight individuals (Figure). Additionally, in this youngest age group, overweight individuals demonstrated PWV values nearly

equal to their normal-weight counterparts. With increasing age group, however, the overweight individuals demonstrated higher PWV values than did the normal-weight individuals and approached the PWV levels of obese individuals (Fig-

TABLE 2. Spearman Correlations Between PWV and Covariates by Age Group: Unadjusted and Adjusted for Age, Supine SBP, Race, and Sex

Variable Name	20- to 40-Year-Olds (n=186)				41- to 77-Year-Olds (n=177)			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	r	P	r	P	r	P	r	P
Seated SBP, mm Hg	0.13	0.09	—	—	0.48	<0.001	—	—
Seated DBP, mm Hg	0.20	0.005	0.07	0.37	0.19	0.013	0.19	0.02
Seated PP, mm Hg	-0.03	0.71	-0.06	0.44	0.46	<0.001	0.13	0.10
Age, y	0.32	<0.001	—	—	0.45	<0.001	—	—
Total cholesterol, mmol/L	0.16	0.03	0.04	0.59	0.22	0.004	0.12	0.14
LDL cholesterol, mmol/L	0.18	0.01	0.09	0.23	0.16	0.04	0.09	0.24
HDL cholesterol, mmol/L	-0.14	0.06	-0.16	0.04	0.05	0.55	-0.06	0.41
Triglycerides, mmol/L	0.13	0.08	0.06	0.46	0.11	0.14	0.14	0.07
Glucose, mmol/L	0.27	<0.001	0.17	0.02	0.20	0.007	0.16	0.04
Weight, kg	0.35	<0.001	0.24	0.001	0.12	0.10	0.28	<0.001
BMI, kg/m ²	0.37	<0.001	0.21	0.004	0.18	0.02	0.26	0.001
Waist circumference, cm	0.38	<0.001	0.24	0.001	0.19	0.01	0.27	0.001
Hip circumference, cm	0.35	<0.001	0.19	0.01	0.20	0.007	0.24	0.002
Waist:hip	0.25	0.001	0.19	0.01	0.12	0.01	0.23	0.002



ure). This pattern was not consistent among the >60-year-old age group because of that group's smaller sample size.

To determine the strongest predictors of aPWV, stepwise linear regression was performed with all variables for the full sample and within each age group. For the full sample, the strongest predictors of higher aPWV were older age, higher SBP, and higher BMI ($P<0.001$ for all). For the 20- to 40-year-olds, the strongest predictors of higher aPWV were older age ($P<0.001$), higher SBP ($P<0.001$), female sex ($P=0.006$), and larger waist circumference ($P=0.03$). For the 41- to 77-year-olds, the strongest predictors were older age ($P<0.001$), higher SBP ($P<0.001$), and higher BMI ($P=0.004$). Additionally, when either waist circumference or BMI was replaced with an alternative measure of obesity, each explained similar proportions of the variance in aPWV. The strength of association between aPWV and each measure of obesity was not significantly different between the young and old groups, as assessed by an age interaction term in linear regression modeling of the full sample.

We also examined associations between aPWV and body weight or weight distribution within each race with stepwise regression. The most important predictors of higher aPWV were identical for both races: older age ($P<0.001$ for both races), higher SBP ($P<0.001$ for whites, $P=0.03$ for African Americans), and higher BMI ($P<0.01$ for both races). The strength of association between aPWV and each measure of obesity was not significantly different between African Americans and whites, as assessed by a race interaction term in linear regression modeling.

Discussion

We have found that among both young and older adults, body fat measures were among the strongest independent predictors of aortic stiffness. Median aPWV values were 40 to 90 cm/s higher for obese individuals compared with normal-weight individuals. Results were similar for both white and African American participants. These results demonstrate that excess body weight has both short- and long-term effects on the vascular system, and this might be one mechanism by which obesity is associated with cardiovascular disease. This is the first population-based study to report an effect of weight on vascular stiffness in adults as young as 20 years, and the strength of the association indicates that excess

weight begins to affect the vascular system at a very early stage of vascular aging.

Similar relations between aortic stiffness and body weight have been documented in elderly participants in both the Cardiovascular Health Study¹¹ and in the Health ABC study,¹⁰ as well as among younger hypertensives¹⁹ and individuals with a family history of hypertension²⁰. Toto-Moukouo et al¹⁹ found that obesity was associated with a 60 cm/s higher peripheral PWV in hypertensive men and a 50 cm/s higher peripheral PWV in hypertensive women compared with nonobese subjects. This increase is similar in magnitude to the 47 cm/s increase in aortic stiffness documented among the 20- to 30-year-old obese participants in the current study when compared with normal-weight individuals.

There are a number of mechanisms by which body weight might contribute to aortic stiffening, in both the short and long term. First, insulin resistance has been shown to accompany obesity.²¹ Insulin resistance likely has vascular effects through both its associated hyperinsulinemia and increased glycemia. The effects of hyperinsulinemia on the vascular system are not yet completely understood but might include promotion of sodium reabsorption,^{22,23} stimulation of the sympathetic nervous system,^{24,25} and promotion of vascular smooth muscle cell growth,²⁶ all of which might contribute to increased aortic stiffness. High levels of plasma glucose might cause glycation of the proteins in the arterial wall, and these glycosylated proteins have been associated with organ damage and atherosclerosis.²⁷ Additionally, insulin bound to its receptor has potent vasodilator effects through endothelium-derived nitric oxide release.²⁸ Endothelium-dependent vasodilation occurs in response to changes in stretch and shear on the vessel wall, maintaining favorable levels of blood pressure and low to moderate shear on the wall.²⁹ In the insulin-resistant state that occurs with obesity, the effects of bound insulin are reduced, thereby inhibiting the ability of insulin to elicit endothelium-dependent vasodilation.²⁸ Therefore, increases in blood pressure prompted by sympathetic nervous system activation would not be counteracted by vasodilation, thus increasing the possibility for injury to the vessel wall and eventually leading to vessel wall stiffening. The second mechanism by which body weight might contribute to aortic stiffening is through inflammation. Increased

weight has been associated with low-grade inflammation.^{8,9} The presence of higher levels of circulating immune system cells possibly increases movement of these cells into the artery wall, leading to wall stiffening. Measures of inflammation have been found to be positively associated with aPWV in a population of middle-aged women with lupus.³⁰ Finally, obesity might increase aortic stiffening through the hormone leptin, which is increased with greater levels of body fat.³¹ Leptin, much like insulin, has been shown to promote smooth muscle cell proliferation³² and angiogenesis.^{33,34} Higher levels of leptin have been associated with reduced arterial distensibility in a group of 294 healthy adolescents, independent of fat mass.³⁵

Obese individuals as young as 20 to 30 years had an aPWV that was 47 cm/s higher than their nonobese counterparts. This roughly corresponds to the increase in vascular stiffness associated with a 5-year increase in age in the Baltimore Longitudinal Study of Aging.³⁶ The association between weight and vascular stiffness in individuals so young raises 2 important issues. First, given that obesity is occurring at increasingly earlier ages, our data suggest that the associated vascular consequences will be observed at earlier ages as well. For example, as this cohort ages, we will likely see a rise in the prevalence of isolated systolic hypertension among younger age groups than has been observed in the past. This does not bode well for the health of an aging population, because isolated systolic hypertension is associated with higher rates of stroke, cardiovascular events, and cognitive impairment.^{37–40} The fact that 15% of children and adolescents and nearly two thirds of adults are now considered overweight^{1,2} portends a future increase in cardiovascular disease of substantial magnitude.

The second issue raised by these data are the need for further research into how much of the effects of obesity on vascular stiffness are acute and thus, reversible. If the association between weight and vascular stiffness were present only among older adults, then one might conclude that obesity has long-term cumulative effects on the vasculature through the mechanisms identified earlier. However, the fact that the association is strong in young adults as well suggests that some of the effects of obesity on the vasculature are acute and, thus, potentially reversible. Although we did not have sufficient power to formally test these observations, this study appeared to demonstrate both short- and long-term effects of weight. Obese individuals even as young as 20 to 30 years demonstrated higher PWV values than did their normal-weight counterparts, possibly demonstrating short-term effects of weight on PWV. Overweight individuals, however, did not appear to be at much greater risk of vascular stiffening than did normal-weight individuals among the 20- to 30-year-olds, but with increasing age group, their PWV values were steadily higher. By 41 to 59 years, overweight individuals demonstrated PWV values equal to those of obese individuals, possibly demonstrating chronic or cumulative effects of weight over time. The effects of weight loss on the process of vascular stiffening need to be evaluated in a future clinical trial so that the relative contributions of acute versus chronic effects can be determined. Assuming that weight loss reverses the vascular stiffening process, a focus on early interventions

to accomplish weight loss would be wise, along with strategies for the prevention of initial weight gain.

This study has certain limitations. Although precise measures of subcutaneous and visceral adipose tissue as measured by magnetic resonance imaging (MRI) or dual energy x-ray absorptiometry (DXA) technology were not available, this study documented strong relations with aortic stiffness by using easily obtained measures such as weight and waist circumference. Previous research has indicated that among older adults, aortic stiffness is associated with visceral adipose tissue specifically.¹⁰ Future research will need to determine whether this is true for young adults as well. The PWV method involves measurement across the body, which could potentially bias the distance measurement for overweight and obese individuals. This bias was likely not operating within these data, however, given that our ultrasound laboratory has developed a technique for level measurement across the body and given that the results obtained with aPWV here were consistent for pressure-strain elastic modulus and arterial diameter, vascular stiffness techniques that do not require measurement across the body.

Perspectives

The association between excess body weight and increased vascular stiffness is present in adults as young as 20 to 30 years of age, suggesting that the vascular effects of obesity occur at a very early stage of vascular aging. Given the increasing obesity rates among young adults, these data suggest a sizeable future increase in cardiovascular disease. The degree to which vascular stiffening is reduced with weight loss should be investigated.

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