

# Body Fat Is Associated With Reduced Aortic Stiffness Until Middle Age

Ben Corden, Niall G. Keenan, Antonio S.M. de Marvao, Timothy J.W. Dawes, Alain DeCesare, Tamara Diamond, Giuliana Durighel, Alun D. Hughes, Stuart A. Cook, Declan P. O'Regan

**Abstract**—Obesity is a major risk factor for cardiometabolic disease, but the effect of body composition on vascular aging and arterial stiffness remains uncertain. We investigated relationships among body composition, blood pressure, age, and aortic pulse wave velocity in healthy individuals. Pulse wave velocity in the thoracic aorta, an indicator of central arterial stiffness, was measured in 221 volunteers (range, 18–72 years; mean, 40.3±13 years) who had no history of cardiovascular disease using cardiovascular MRI. In univariate analyses, age ( $r=0.78$ ;  $P<0.001$ ) and blood pressure ( $r=0.41$ ;  $P<0.001$ ) showed a strong positive association with pulse wave velocity. In multivariate analysis, after adjustment for age, sex, and mean arterial blood pressure, elevated body fat% was associated with reduced aortic stiffness until the age of 50 years, thereafter adiposity had an increasingly positive association with aortic stiffness ( $\beta=0.16$ ;  $P<0.001$ ). Body fat% was positively associated with cardiac output when age, sex, height, and absolute lean mass were adjusted for ( $\beta=0.23$ ;  $P=0.002$ ). These findings suggest that the cardiovascular system of young adults may be capable of adapting to the state of obesity and that an adverse association between body fat and aortic stiffness is only apparent in later life. (*Hypertension*. 2013;61:00-00.)

**Key Words:** aging ■ aortic stiffness ■ blood pressure ■ MRI ■ obesity

Obesity is associated with an excess of major cardiovascular events<sup>1–3</sup> and potentially represents an important modifiable risk-factor in the general population. One of the earliest manifestations of vascular aging in humans is impairment of central arterial function<sup>4–6</sup> but how adiposity modifies this process is uncertain. In older adults, there are data that indicate increasing arterial stiffness with obesity,<sup>7–9</sup> although findings have been inconsistent across studies.<sup>10–13</sup> In contrast, obese children have reduced arterial stiffness compared with their normal weight peers,<sup>14–16</sup> an effect thought to result from physiological adaptation to the hyperemic state of obesity in the young.<sup>16</sup> Taken together these contrasting data from young and old populations suggest age-related differences in the relationship between body composition and arterial stiffness, which have not been fully explored.

Pulse wave velocity (PWV) has been extensively used as a noninvasive measure of arterial stiffness and is strongly predictive of adverse cardiovascular outcomes and all-cause mortality in unselected populations.<sup>17–19</sup> Central arteries are rich in elastin that enables efficient arterial-ventricular coupling and optimal transfer of stroke volume to the circulation.<sup>20,21</sup> Elastic fibers become degraded and fragmented with age and disease, which are accelerated by additional crosslinking from advanced glycation end-products, leading to increased

stiffness of the arterial wall.<sup>22</sup> Assessment of the vascular phenotype using PWV enables subclinical vascular disease to be quantified even before the onset of systemic hypertension.<sup>23,24</sup>

Although the association between obesity and adult cardiovascular disease has been extensively studied, there are fewer data available on the subclinical effects of elevated body fat on early vascular disease in overtly healthy subjects. In this study, we aimed to investigate a population without known cardiovascular disease and assess the effect of body composition on the relationship between aging and aortic PWV.

## Methods

### Subjects

A total of 221 adult volunteers (127 women; age range, 18–72 years; mean, 40.3 years) were prospectively recruited via advertisement for a substudy of the UK GenScan (Genetic Studies of the Heart and Circulation) project. We excluded participants at screening who had known cardiovascular disease or were being treated for hypertension, diabetes mellitus, or hypercholesterolemia. Female subjects were excluded if they were pregnant or breastfeeding but were eligible if they took oral contraceptives. Standard published safety contraindications to MRI were applied<sup>25</sup> with a scanner weight limit of 100 kg. All subjects provided written informed consent for participation in the study, which was approved by the local research ethics committee.

Received March 5, 2013; first decision March 25, 2013; revision accepted March 25, 2013.

From the Robert Steiner MRI Unit, MRC Clinical Sciences Centre, Imperial College London, United Kingdom (B.C., A.S.M.d.M., T.J.W.D., T.D., G.D., S.A.C., D.P.O.R.); Department of Cardiology, Imperial College Healthcare NHS Trust, London, United Kingdom (N.G.K.); Institut National de la Santé et de la Recherche Médicale (INSERM), Paris, France (A.D.); International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College London, United Kingdom (A.D.H.); Department of Cardiology, National Heart Centre Singapore, Singapore (S.A.C.); and Cardiovascular and Metabolic Disorders Program, Duke-National University of Singapore, Singapore (S.A.C.).

Correspondence to Declan P. O'Regan, MRC Clinical Sciences Centre, Robert Steiner MRI Unit, Faculty of Medicine, Hammersmith Hospital Campus, Imperial College London, Du Cane Rd, London W12 0NN, United Kingdom. E-mail declan.oregan@csc.mrc.ac.uk

© 2013 American Heart Association, Inc.

*Hypertension* is available at <http://hyper.ahajournals.org>

DOI: 10.1161/HYPERTENSIONAHA.113.01177

## Study Protocol

Central PWV was measured in the thoracic aorta using cardiovascular magnetic resonance. All studies were performed on a 32-channel 1.5T Philips Achieva system (Best, The Netherlands). Phase-contrast sequences were acquired at the level of the pulmonary bifurcation, perpendicular to both the ascending and the descending thoracic aorta, enabling simultaneous study of both vessels. The phase-contrast data were acquired using a retrospectively ECG-gated breath-hold sequence with a through-plane velocity-encoding gradient of 200 cm/s. The sequence parameters were as follows: field-of-view=370 mm×370 mm, repetition time=2.8 ms, echo time=1.4 ms, flip angle=15°, and voxel size=1.65 mm×1.92 mm×10 mm, with a temporal resolution of 33 ms.

For the calculation of aortic length, ECG-gated balanced steady state-free precession images were acquired through the thoracic aorta using the following parameters: field-of-view=320 mm×320 mm, repetition time=3.4 ms, echo time=1.7 ms, flip angle=60°, and voxel size=1.65 mm×1.92 mm×10 mm.

To assess left ventricular (LV) function and mass, a stack of cine balanced steady state-free precession images was acquired in the LV short axis plane from base to apex using the following parameters: field-of-view=370 mm×370 mm, repetition time=3.0 ms, echo time=1.5 ms, flip angle=60°, voxel size=2.0 mm×2.2 mm×8 mm, and 30 cardiac phases.

## Image Analysis

Aortic arch PWV was calculated from the 3-dimensional (3D) vessel length ( $D$ ) and transit time ( $\Delta t$ ) between the flow waveforms in the ascending and descending thoracic aorta. All analyses were performed using validated software (ART-FUN, Inserm, Paris).<sup>26,27</sup> The path length was defined on the anatomic images to create a 3D Bezier curve through the centerline of the aorta intersecting the plane at which flow measurements had been obtained.

Aortic PWV ( $D/\Delta t$ ) was calculated from the time-shift between the flow waveforms in the ascending and descending aorta using sigmoid curves fitted to the systolic up-slope of the normalized flow curves.<sup>27</sup> Volumetric analysis of the LV cine images was performed with CMRtools (Cardiovascular Imaging Solutions, London, United Kingdom) using semiautomated segmentation of the left ventricle with tracking of the mitral and aortic valves. LV mass and cardiac output were derived from these data. LV mass was indexed to body surface area before analysis.

## Body Composition and Blood Pressure

All measurements were performed by specially trained cardiology nurses at the study center. Height and weight were measured without shoes while wearing scrubs. Total body fat mass was measured with multi-frequency bioelectrical impedance analysis (InBody 230, BioSpace, Los Angeles, CA)<sup>28</sup> and expressed as a percentage of the participant's total body weight. Body mass index (BMI) was calculated as the total weight (kg) divided by the height (m) squared. Lean mass index (LMI) was calculated as the fat free mass (kg) divided by the height (m) squared.<sup>29</sup> Blood pressure (BP) measurement was performed after 5 minutes rest in accordance with European Society of Hypertension guidelines<sup>30</sup> using a calibrated oscillometric device (Omron M7, Omron Corporation, Kyoto, Japan) that has been validated in both normal<sup>31</sup> and obese populations.<sup>32</sup> The first of 3 measures was discarded, and the second 2 values were averaged. Mean arterial pressure (MAP) was calculated as  $[(2 \times \text{diastolic pressure}) + \text{systolic pressure}] / 3$ .

## Statistical Analysis

Data were analyzed using R, version 2.15.0.<sup>33</sup> Aortic PWV was positively skewed and so was transformed by taking logarithms for the purposes of parametric analyses. Pearson  $r$  correlation coefficients and multiple linear regression were used to assess the associations among age, sex, BP, and measures of body composition with aortic PWV, cardiac output, and LV mass. To assess for sex by body composition and age by body composition interactions, the relevant variables were first centred around their mean values to reduce errors

caused by multicollinearity and then entered into the regression model.<sup>34</sup> The Shapiro-Wilks test was used to assess the departure from normality of the residuals of the regression model using log aortic PWV as the dependent variable. Significant interactions were further analyzed using simple plots.<sup>34</sup>

## Results

Summary statistics for the main variables measured in the study are shown in Table 1.

### Univariate Associations With Aortic PWV

Table 2 summarizes correlations between log aortic PWV and age, MAP, and body composition. Age (Figure 1) and MAP showed strong positive correlations with aortic PWV; BMI showed a weak positive correlation; and body fat% and LMI did not show any significant correlation. Body fat% was positively correlated with age ( $r=0.28$ ;  $P<0.001$ ).

### Independent Predictors of Aortic PWV

We performed multiple linear regression analyses to examine the relationship between body composition and log aortic PWV after adjusting for the effects of age, sex, and BP. The residuals of the models did not depart from normality (all  $P>0.05$ ). We found no correlation between heart rate (HR) and aortic PWV. In addition, we found no significant main effect of HR when it was included in the regression models and no significant interaction between HR and age; hence, HR has not been included in the models reported below.

Two separate models were constructed for assessing obesity (BMI and body fat%), which are summarized in Table 3. In both models, age was the strongest predictor of PWV, accounting for >60% of the variance. MAP retained an independent, positive association with PWV, accounting for a modest additional 3% to 4% of the variance.

BMI and body fat% were also independent predictors of PWV. However, despite being positively associated with PWV in the univariate analysis, when the effects of age, MAP, and sex are controlled for, BMI and body fat were shown to be negatively associated with PWV. Therefore, overall, obesity was associated with lower aortic stiffness when the effects of age, sex, and MAP were taken into account.

Next, to test the hypothesis that the relationship between body composition and aortic PWV is modified by age, we performed further regression analyses with an interaction term of age by body composition included in the model. These results are summarized in Table 4 and Figure 2. The main effects of age, BP, and body composition were similar to the previous models. In addition, there was a significant interaction between body fat% and age, but not between BMI and age. Figure 2 illustrates the nature of these interactions demonstrating that body fat% has an increasingly positive association with PWV as age increases. In young adults, increased body fat% is associated with a lower PWV, whereas, in older adults, increased body fat% is associated with a higher PWV.

We also constructed models to assess the relationship between nonfat mass and aortic PWV, using LMI as a predictor. These models are summarized in Tables 3 and 4. When included alone, LMI did not show a significant independent association with PWV. However, when the age and LMI

**Table 1. Summary Statistics for the Main Variables Under Study**

Variables	Men			Women		
	Mean	SD	%	Mean	SD	%
Age, y	39.5	12.8		40.9	13.6	
Pulse wave velocity, m/s	4.9	1.6		4.8	1.8	
BMI, kg/m <sup>2</sup>	25.9	3.4		25.2	4.9	
Underweight (<18.5)			0.0			3.2
Normal (18.5–25)			42.6			54.0
Overweight (25–30)			45.7			30.2
Obese (>30)			11.7			12.7
LMI, kg/m <sup>2</sup>	20.3	1.7		17.0	1.9	
Low			16.0			12.7
Medium			53.2			48.4
High			30.9			38.9
Percentage body fat	21.0	8.1		31.2	8.7	
Low			73.4			65.9
High			26.6			34.1
Systolic BP, mm Hg	125	13.5		117	13.5	
Diastolic BP, mm Hg	81	10.0		79	8.9	
Left ventricular mass, g	134.8	26.8		95.9	18.3	
Cardiac output, L/min	6.8	1.7		5.8	1.3	

n=221 (94 men, 127 women). Low (<18.7 kg/m<sup>2</sup> in men and <14.9 kg/m<sup>2</sup> in women), medium (18.7–21 kg/m<sup>2</sup> in men and 14.9–17.2 kg/m<sup>2</sup> in women), and high (>21 kg/m<sup>2</sup> in men and >17.2 kg/m<sup>2</sup> in women). High body fat present if value >25% in men and >35% in women.<sup>29</sup> BMI indicates body mass index; BP, blood pressure; and LMI, lean mass index.

interaction term were included, LMI did show a significant, positive main effect. In addition, there was a significant interaction between LMI and age. As demonstrated in Figure 3, the significant positive relationship between LMI and aortic PWV is diminished at older ages.

Finally, to test the hypothesis that body composition has different effects on PWV in women compared with men, we performed a further set of analyses, including a sex by body composition interaction. There were no significant sex by body composition interactions for any of the models tested, suggesting that body composition has a similar effect on PWV for both men and women (all  $P>0.05$ ).

### Body Composition and Cardiac Output

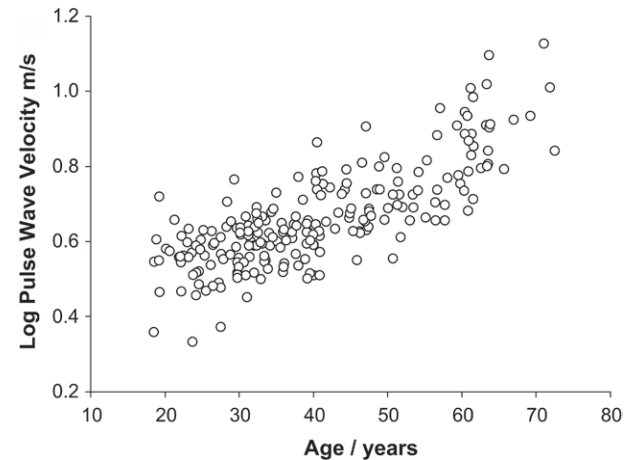
BMI was positively associated with cardiac output, both in univariate analysis ( $r=0.26$ ;  $P<0.0001$ ) and when age and sex were adjusted for ( $\beta=0.28$ ;  $P<0.0001$ ). Body fat% was not associated with cardiac output in univariate analysis ( $r=-0.11$ ;  $P=0.11$ ) but was positively associated with cardiac output

**Table 2. Pearson  $r$  Correlations With Log (Aortic Pulse Wave Velocity)**

Age	MAP	BMI	LMI	Body Fat%
0.78*	0.41*	0.13†	0.04	0.11

BMI indicates body mass index; LMI, lean mass index; and MAP, mean arterial blood pressure.

\* $P<0.0001$  and † $P=0.049$ .

**Figure 1.** Scatter plot of log pulse wave velocity and age within the cohort.

when age, sex, height, and absolute lean mass were adjusted for ( $\beta=0.23$ ;  $P=0.002$ ).

### Aortic Stiffness and LV Mass

PWV had no association with LV mass (indexed to body surface area)<sup>35</sup> in either univariate analysis ( $r=-0.11$ ;  $P=0.10$ ) or when age, sex, and MAP were adjusted for ( $\beta=0.06$ ;  $P=0.51$ ).

### Discussion

In this study of healthy adults, we found that elevated body fat is associated with reduced aortic stiffness until middle age; thereafter, adiposity has an increasingly positive association with aortic stiffness which is independent of BP. These findings suggest that an adverse association between body fat and aortic stiffness is only apparent in later life.

The negative association between obesity and vascular stiffness observed in children<sup>16</sup> and adolescents<sup>14,15</sup> and the positive association reported in older adults and the elderly<sup>7–9,12</sup> are consistent with our findings across the adult age span and

**Table 3. Multiple Linear Regression Analyses With Log (Aortic Pulse Wave Velocity) as the Dependent Variable**

Model	Variable	Standardized $\beta$ Coefficients	$P$ Value
Model 1	Age	0.76	<0.001
	Sex	-0.08	0.054
	MAP	0.16	<0.001
	BMI	-0.11	0.011
Model 2	Age	0.76	<0.001
	Sex	-0.002	0.974
	MAP	0.16	<0.001
Model 3	Body fat%	-0.14	0.008
	Age	0.74	<0.001
	Sex	-0.12	0.025
	MAP	0.14	0.003
	LMI	-0.07	0.191

$R^2$  for model 1=0.65,  $R^2$  for model 2=0.65, and  $R^2$  for model 3=0.64. BMI indicates body mass index; LMI, lean mass index; and MAP, mean arterial pressure.

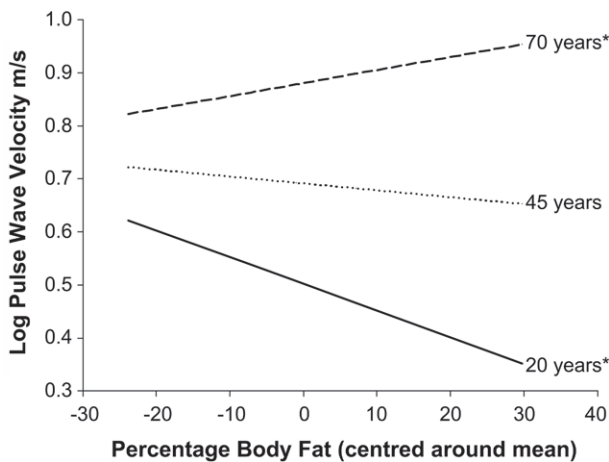


**Table 4. Multiple Linear Regression Analyses Showing the Interaction Between Age and Body Composition With Log(Aortic Pulse Wave Velocity) as the Dependent Variable**

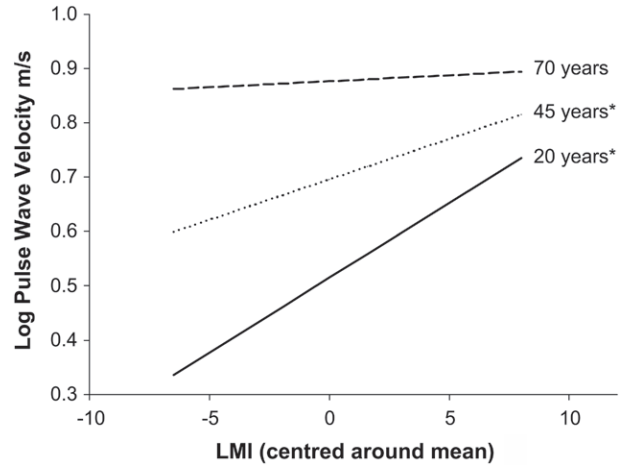
Model	Variable	Standardized $\beta$ Coefficients	P Value
Model 1	Age	0.76	<0.001
	Sex	-0.09	0.039
	MAP	0.17	<0.001
	BMI	-0.13	0.006
	Age×BMI	0.05	0.248
Model 2	Age	0.76	<0.001
	Sex	0.01	0.894
	MAP	0.16	<0.001
	Body fat%	-0.15	0.002
	Age×body fat%	0.16	<0.001
Model 3	Age	0.72	<0.001
	Sex	-0.10	0.064
	MAP	0.14	0.003
	LMI	0.32	0.022
	Age×LMI	-0.40	0.002

$R^2$  for model 1=0.65,  $R^2$  for model 2=0.67, and  $R^2$  for model 3=0.65. BMI indicates body mass index; LMI, lean mass index; and MAP, mean arterial pressure.

support the hypothesis that during adulthood, the physiological relationship between obesity and vascular function alters. We also observed that both high body fat and reduced lean mass were associated with lower PWV in younger adults. Studies that have failed to show a clear relationship between body composition and aortic stiffness have typically been performed on a predominantly middle-aged population,<sup>10,36,37</sup> at which age we observed the weakest association between obesity and aortic PWV. Two previous studies have shown a positive relationship between obesity and PWV in women only,<sup>12,13</sup> but we found no sex differences in the relationship between body composition and aortic stiffness. Corresponding age-dependent effects on



**Figure 2.** Simple plots illustrating the interaction between age and body fat at 3 representative age points. Each slope's gradient represents the effect size and direction of the relationship between body fat and log (aortic pulse wave velocity [PWV]) for the age specified calculated by regression with all covariates held constant.<sup>34</sup> Slopes with a gradient significantly different from zero ( $P<0.05$ ) are starred. As age increases, body fat has an increasingly positive association with log (aortic PWV).



**Figure 3.** Simple plots illustrating the interaction between age and lean mass index (LMI) at 3 representative age points. Each slope's gradient represents the effect size and direction of the relationship between LMI and log (aortic pulse wave velocity [PWV]) for the age specified calculated by regression with all covariates held constant.<sup>34</sup> Slopes with a gradient significantly different from zero ( $P<0.05$ ) are starred. At younger ages LMI has a positive association with log (aortic PWV).

vascular elastic function have also been observed, with obese children demonstrating higher arterial elasticity<sup>38,39</sup> and obese adults having impaired elasticity.<sup>40,41</sup> An association reported between carotid-femoral pulse wave velocity and HR<sup>7,42</sup> has been attributed to fatigue failure of elastin fibers,<sup>43</sup> however in common with another MRI study, we did not observe a relationship between HR and aortic PWV.<sup>23</sup>

The physiological mechanisms linking body fat with arterial stiffness are not fully understood, although several possibilities have been proposed.<sup>44</sup> Even short-term weight gain can alter arterial stiffness, and a plausible explanation is that changes in insulin sensitivity, activation of the renin-angiotensin system, sympathetic nervous system activation, and modulation of smooth muscle tone are influential factors.<sup>45</sup> Subclinical insulin resistance and chronic hyperglycemia may also mediate vascular stiffening in older individuals through increased generation of advanced glycation end-products, and both serum carboxymethyl lysine<sup>46</sup> and glycated hemoglobin<sup>7</sup> concentration are independent predictors of PWV in the elderly. Therefore, cumulative lifetime exposure to body fat may be influential in determining age-related vascular stiffening, and persistence of excess weight beyond childhood is common especially in more severe obesity.<sup>47</sup> The cardiometabolic effects of a higher proportion of lean mass in young adults and the expansion of visceral fat depots in older adults may also influence the relationship between body composition and vascular function at different ages.<sup>48,49</sup> Overweight or obese children have a higher cardiac output and lower aortic stiffness than normal weight controls, which is thought to mitigate some of the harmful effects of obesity on the vasculature.<sup>16</sup> Our findings indicate that cardiac output is positively associated with body fat%, when age and body size are adjusted for, which indicates that cardiovascular compensation for body composition may occur in adults and in children.

What effect the reduction in PWV among children and young adults with elevated body fat has on long-term cardiovascular

risk is not known, but it has been observed that overweight children who recover their normal weight have similar outcomes to those who were never obese.<sup>50</sup> Two interventional studies have recorded a small fall in PWV after weight loss in overweight or obese middle-aged adults but whether the effect is similar in younger adults remains unknown.<sup>9,51</sup> The relationship between excess cardiovascular risk and the degree of obesity is nonlinear, and our findings indicate that the cardiovascular response to dietary interventions might be expected to vary according to age group and the proportion of body fat at baseline.<sup>52–54</sup> Further research is needed to determine in which obesity phenotypes and age groups weight loss interventions are most effective in leading to improved cardiovascular outcomes.

There are limitations to this study. The participants were recruited by advertisement and so may not be representative of the general population. As we excluded subjects with known cardiovascular disease or associated risk factors, our cohort underrepresents individuals with diabetes mellitus when compared with the general obese population.<sup>55</sup> The study was not sufficiently powered to undertake a further subgroup analysis by ethnicity and so we do not know whether these results are applicable to all ethnic groups. Owing to limits of MR scanning tables, we were unable to study patients in excess of 100 kg, and the effect on PWV in more severely obese subjects is unknown. We assessed PWV in the proximal aorta, a technique widely used for research on obesity,<sup>9,37</sup> which has the advantage of giving precise measurements of vessel length. However, we did not assess the effect of adiposity on the less elastic abdominal aorta or the muscular peripheral vasculature.<sup>41,56</sup> We measured body composition using bioimpedance, which is a well validated method of assessing body fat;<sup>57</sup> however, dual energy x-ray absorptiometry<sup>7</sup> and whole-body MRI<sup>37</sup> may be more accurate in defining the distribution of fat.

### Perspectives

Aortic stiffness is a major subclinical biomarker for cardiovascular disease; however, the effect of body composition on aortic function across the entire adult age range is uncertain. We have shown that elevated body fat in healthy young adults is not associated with proximal aortic stiffening, and that this adverse vascular consequence of obesity may not be apparent until after middle age. This may reflect vascular adaptation to obesity in younger adults, which is lost with advancing age, or the time taken for obesity-related damage to accrue, but the mechanisms relating adiposity to vasculopathy remain to be established. Longitudinal studies are needed to fully elucidate the changing relationship between body composition and aortic stiffness as age progresses and to evaluate what effect this may have on long-term cardiovascular risk.

### Sources of Funding

The study was supported by the Medical Research Council, United Kingdom, the National Institute for Health Research (NIHR) Biomedical Research Centre based at Imperial College Healthcare National Health Service (NHS) Trust and Imperial College London, United Kingdom, and a British Heart Foundation, United Kingdom, project grant (PG/12/27/29489).

### Disclosures

None.

### References

- Jonsson S, Hedblad B, Engström G, Nilsson P, Berglund G, Janzon L. Influence of obesity on cardiovascular risk. Twenty-three-year follow-up of 22,025 men from an urban Swedish population. *Int J Obes Relat Metab Disord.* 2002;26:1046–1053.
- Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, Kannel WB, Vasan RS. Obesity and the risk of heart failure. *N Engl J Med.* 2002;347:305–313.
- Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, Hollenbeck A, Leitzmann MF. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med.* 2006;355:763–778.
- Redheuil A, Yu WC, Mousseaux E, Harouni AA, Kachenoura N, Wu CO, Bluemke D, Lima JA. Age-related changes in aortic arch geometry: relationship with proximal aortic function and left ventricular mass and remodeling. *J Am Coll Cardiol.* 2011;58:1262–1270.
- Cavalcante JL, Lima JA, Redheuil A, Al-Mallah MH. Aortic stiffness: current understanding and future directions. *J Am Coll Cardiol.* 2011;57:1511–1522.
- Shirwany NA, Zou MH. Arterial stiffness: a brief review. *Acta Pharmacol Sin.* 2010;31:1267–1276.
- Sutton-Tyrrell K, Newman A, Simonsick EM, Havlik R, Pahor M, Lakatta E, Spurgeon H, Vaitkevicius P. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. *Hypertension.* 2001;38:429–433.
- 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.
- Rider OJ, Tayal U, Francis JM, Ali MK, Robinson MR, Byrne JP, Clarke K, Neubauer S. The effect of obesity and weight loss on aortic pulse wave velocity as assessed by magnetic resonance imaging. *Obesity (Silver Spring).* 2010;18:2311–2316.
- 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.
- Oren A, Vos LE, Uiterwaal CS, Grobbee DE, Bots ML. Aortic stiffness and carotid intima-media thickness: two independent markers of subclinical vascular damage in young adults? *Eur J Clin Invest.* 2003;33:949–954.
- Zebekakis PE, Nawrot T, Thijs L, Balkstein EJ, van der Heijden-Spek J, Van Bortel LM, Struijker-Boudier HA, Safar ME, Staessen JA. Obesity is associated with increased arterial stiffness from adolescence until old age. *J Hypertens.* 2005;23:1839–1846.
- Nordstrand N, Gjevestad E, Dinh KN, Hofso D, Roislien J, Saltvedt E, Os I, Hjelmseth J. The relationship between various measures of obesity and arterial stiffness in morbidly obese patients. *BMC Cardiovasc Disord.* 2011;11:7.
- Lurbe E, Torro I, Garcia-Vicent C, Alvarez J, Fernández-Fornoso JA, Redon J. Blood pressure and obesity exert independent influences on pulse wave velocity in youth. *Hypertension.* 2012;60:550–555.
- Dangardt F, Osika W, Volkmann R, Gan LM, Friberg P. Obese children show increased intimal wall thickness and decreased pulse wave velocity. *Clin Physiol Funct Imaging.* 2008;28:287–293.
- Charakida M, Jones A, Falaschetti E, Khan T, Finer N, Sattar N, Hingorani A, Lawlor DA, Smith GD, Deanfield JE. Childhood obesity and vascular phenotypes: a population study. *J Am Coll Cardiol.* 2012;60:2643–2650.
- Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkatchalam L, Kupelian V, Simonsick EM, Havlik R, Lakatta EG, Spurgeon H, Kritchevsky S, Pahor M, Bauer D, Newman A; Health ABC Study. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. *Circulation.* 2005;111:3384–3390.
- Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, Jeppesen J. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. *Circulation.* 2006;113:664–670.
- Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA, Asmar R, Reneman RS, Hoeks AP, Breteler MM, Witteman JC. Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. *Circulation.* 2006;113:657–663.
- O'Rourke MF, Staessen JA, Vlachopoulos C, Duprez D, Plante GE. Clinical applications of arterial stiffness; definitions and reference values. *Am J Hypertens.* 2002;15:426–444.
- Chantler PD, Lakatta EG, Najjar SS. Arterial-ventricular coupling: mechanistic insights into cardiovascular performance at rest and during exercise. *J Appl Physiol.* 2008;105:1342–1351.
- Wagenseil JE, Mecham RP. Elastin in large artery stiffness and hypertension. *J Cardiovasc Transl Res.* 2012;5:264–273.

23. Redheuil A, Yu WC, Wu CO, Mousseaux E, de Cesare A, Yan R, Kachenoura N, Bluemke D, Lima JA. Reduced ascending aortic strain and distensibility: earliest manifestations of vascular aging in humans. *Hypertension*. 2010;55:319–326.
24. Kaess BM, Rong J, Larson MG, Hamburg NM, Vita JA, Levy D, Benjamin EJ, Vasan RS, Mitchell GF. Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA*. 2012;308:875–881.
25. Shellock FG. *Reference Manual for Magnetic Resonance Safety*. Salt Lake City, Utah: Amirsys; 2003.
26. Herment A, Mousseaux E, Jolivet O, DeCesare A, Frouin F, Todd-Pokropek A, Bittoun J. Improved estimation of velocity and flow rate using regularized three-point phase-contrast velocimetry. *Magn Reson Med*. 2000;44:122–128.
27. Dogui A, Redheuil A, Lefort M, DeCesare A, Kachenoura N, Herment A, Mousseaux E. Measurement of aortic arch pulse wave velocity in cardiovascular MR: comparison of transit time estimators and description of a new approach. *J Magn Reson Imaging*. 2011;33:1321–1329.
28. Rossy-Squires NE, Dieli-Conwright CM, Rossuello A, Erceg DN, McCauley S, Schroeder ET. Validity and reliability of body composition analysers in children and adults. *Br J Nutr*. 2008;100:859–865.
29. Lavie CJ, De Schutter A, Patel DA, Romero-Corral A, Artham SM, Milani RV. Body composition and survival in stable coronary heart disease: impact of lean mass index and body fat in the “obesity paradox”. *J Am Coll Cardiol*. 2012;60:1374–1380.
30. O’Brien E, Asmar R, Beilin L, et al.; European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*. 2003;21:821–848.
31. Coleman A, Steel S, Freeman P, de Greeff A, Shennan A. Validation of the Omron M7 (HEM-780-E) oscillometric blood pressure monitoring device according to the British Hypertension Society protocol. *Blood Press Monit*. 2008;13:49–54.
32. El Feghali RN, Topouchian JA, Pannier BM, El Assaad HA, Asmar RG; European Society of Hypertension. Validation of the OMRON M7 (HEM-780-E) blood pressure measuring device in a population requiring large cuff use according to the International Protocol of the European Society of Hypertension. *Blood Press Monit*. 2007;12:173–178.
33. R Development Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing; 2008.
34. Aiken LS, West SG, Reno RR. *Multiple Regression: Testing and Interpreting Interactions*. Thousand Oaks, London: SAGE; 1991.
35. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. *Nutrition*. 1989;5:303–311; discussion 312–303.
36. Nakanishi N, Suzuki K, Tatara K. Clustered features of the metabolic syndrome and the risk for increased aortic pulse wave velocity in middle-aged Japanese men. *Angiology*. 2003;54:551–559.
37. Muenkaew M, Boonyasirinant T, Krittayaphong R. Correlation between aortic stiffness and visceral fat determined by magnetic resonance imaging. *J Med Assoc Thai*. 2012;95(Suppl 2):S117–S126.
38. Tryggstad JB, Thompson DM, Copeland KC, Short KR. Obese children have higher arterial elasticity without a difference in endothelial function: the role of body composition. *Obesity (Silver Spring)*. 2012;20:165–171.
39. Chalmers LJ, Copeland KC, Hester CN, Fields DA, Gardner AW. Paradoxical increase in arterial compliance in obese pubertal children. *Angiology*. 2011;62:565–570.
40. Robinson MR, Scheuermann-Freestone M, Leeson P, Channon KM, Clarke K, Neubauer S, Wiesmann F. Uncomplicated obesity is associated with abnormal aortic function assessed by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2008;10:10.
41. Rider OJ, Holloway CJ, Emmanuel Y, Bloch E, Clarke K, Neubauer S. Increasing plasma free fatty acids in healthy subjects induces aortic distensibility changes seen in obesity. *Circ Cardiovasc Imaging*. 2012;5:367–375.
42. Johansen NB, Vistisen D, Brunner EJ, Tabák AG, Shipley MJ, Wilkinson IB, McEniery CM, Roden M, Herder C, Kivimäki M, Witte DR. Determinants of aortic stiffness: 16-year follow-up of the Whitehall II study. *PLoS One*. 2012;7:e37165.
43. Greenwald SE. Ageing of the conduit arteries. *J Pathol*. 2007;211:157–172.
44. Safar ME, Czernichow S, Blacher J. Obesity, arterial stiffness, and cardiovascular risk. *J Am Soc Nephrol*. 2006;17(Suppl 2):S109–S111.
45. Orr JS, Gentile CL, Davy BM, Davy KP. Large artery stiffening with weight gain in humans: role of visceral fat accumulation. *Hypertension*. 2008;51:1519–1524.
46. Semba RD, Najjar SS, Sun K, Lakatta EG, Ferrucci L. Serum carboxymethyllysine, an advanced glycation end product, is associated with increased aortic pulse wave velocity in adults. *Am J Hypertens*. 2009;22:74–79.
47. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obes Rev*. 2008;9:474–488.
48. Enzi G, Gasparo M, Biondetti PR, Fiore D, Semisa M, Zurlo F. Subcutaneous and visceral fat distribution according to sex, age, and overweight, evaluated by computed tomography. *Am J Clin Nutr*. 1986;44:739–746.
49. Kuk JL, Saunders TJ, Davidson LE, Ross R. Age-related changes in total and regional fat distribution. *Ageing Res Rev*. 2009;8:339–348.
50. Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, Srinivasan SR, Daniels SR, Davis PH, Chen W, Sun C, Cheung M, Viikari JS, Dwyer T, Raitakari OT. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med*. 2011;365:1876–1885.
51. Dengo AL, Dennis EA, Orr JS, Marinik EL, Ehrlich E, Davy BM, Davy KP. Arterial destiffening with weight loss in overweight and obese middle-aged and older adults. *Hypertension*. 2010;55:855–861.
52. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol*. 2009;53:1925–1932.
53. Üretsky S, Messerli FH, Bangalore S, Champion A, Cooper-Dehoff RM, Zhou Q, Pepine CJ. Obesity paradox in patients with hypertension and coronary artery disease. *Am J Med*. 2007;120:863–870.
54. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA*. 2013;309:71–82.
55. Salomaa V, Riley W, Kark JD, Nardo C, Folsom AR. Non-insulin-dependent diabetes mellitus and fasting glucose and insulin concentrations are associated with arterial stiffness indexes. The ARIC Study. Atherosclerosis Risk in Communities Study. *Circulation*. 1995;91:1432–1443.
56. Ziemann SJ, Melenovsky V, Kass DA. Mechanisms, pathophysiology, and therapy of arterial stiffness. *Arterioscler Thromb Vasc Biol*. 2005;25:932–943.
57. Kyle UG, Piccoli A, Pichard C. Body composition measurements: interpretation finally made easy for clinical use. *Curr Opin Clin Nutr Metab Care*. 2003;6:387–393.

## Novelty and Significance

### What Is New?

- In a healthy adult population, elevated body fat is associated with reduced aortic stiffness until middle age, after which adiposity is associated with progressive arterial dysfunction.
- Cardiac output, adjusted for body size and age, is positively associated with body fat%.

### What Is Relevant?

- During adulthood, the physiological relationship between obesity and vascular function fundamentally alters, which may reflect the

cumulative effect of exposure to obesity and a loss of physiological adaptation.

### Summary

- The cardiovascular system of young adults may be capable of adapting to the state of obesity, and an adverse effect of body fat on aortic stiffness is only apparent in later life.



## Body Fat Is Associated With Reduced Aortic Stiffness Until Middle Age

Ben Corden, Niall G. Keenan, Antonio S.M. de Marvao, Timothy J.W. Dawes, Alain DeCesare, Tamara Diamond, Giuliana Durighel, Alun D. Hughes, Stuart A. Cook and Declan P. O'Regan

*Hypertension*. published online April 22, 2013;

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2013 American Heart Association, Inc. All rights reserved.

Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://hyper.ahajournals.org/content/early/2013/04/22/HYPERTENSIONAHA.113.01177>

**Permissions:** Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Hypertension* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

**Reprints:** Information about reprints can be found online at:  
<http://www.lww.com/reprints>

**Subscriptions:** Information about subscribing to *Hypertension* is online at:  
<http://hyper.ahajournals.org/subscriptions/>