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Abdominal obesity is associated with arterial stiffness in middle-aged adults

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Abstract *Background and aims:* The relation between adiposity and arterial stiffness remains controversial. We determined whether abdominal and visceral adipose tissue may be a better predictor of arterial stiffness than general obesity in middle-aged adults.
Methods and results: A total of 146 participants (76 men, 70 women; 50 years) were studied. The automatic vascular screening device (Omron VP-1000plus) was used to measure blood pressure simultaneously in the arms and ankles and to determine arterial stiffness by pulse wave velocity (PWV). Using multiple linear regressions, the relations between indicators of obesity and arterial stiffness were examined after adjustment for confounders. Both carotid-femoral PWV and brachial-ankle PWV were significantly associated with BMI (both $P < 0.05$) but not with body fat percentage. Measures of abdominal obesity, including waist circumference and visceral fat mass (via DXA), were strongly associated with PWV and remained positively associated with arterial stiffness after adjustment for age and gender. Cardiovascular fitness as assessed by maximal oxygen consumption was related to body fat percentage but not with visceral fat. More favorable cardiovascular health profile was associated with both lower visceral fat mass and PWV (both $P < 0.001$).
Conclusion: Abdominal obesity and visceral fat are associated with large artery stiffness. These findings support the importance of adiposity measures as a risk factor for arterial stiffening in middle-aged adults.

Introduction

Excess adipose tissue, in particular abdominal and visceral adipose tissue (VAT), has been closely linked to the development of the metabolic syndrome, cardiovascular disease, and diastolic dysfunction [1,2]. In contrast, excess adiposity in the extremity does not appear to increase the cardiometabolic risk as much [3]. Although the link between obesity and cardiovascular disease has been extensively studied, the underlying mechanism has not been determined. Vascular dysfunction, particularly arterial stiffening, has been suggested as a factor mediating these two pathological states [4]. However, the association between arterial stiffness and adiposity remains highly controversial even to this date [5–8]. These discordant results may be due to the methodological issues pertaining to arterial stiffness.

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Obese individuals exhibit a greater stroke volume and cardiac output simply because of the larger body size and could influence measures of arterial stiffness that rely heavily on stroke volume (e.g., systemic arterial compliance) independent of arterial distensibility. Additionally, arterial compliance measurements using ultrasonography may be limited by decreased acoustic penetration and its dependence on lumen diameter, which tends to be greater in obese individuals. Pulse wave velocity (PWV) is considered the reference-standard noninvasive method for measuring arterial stiffness [9] and an independent predictor for atherosclerosis, cardiovascular risk, and future cardiovascular disease (CVD) events [10,11].

The age of the subjects studied in previous investigations appears to be another factor that could explain discordant results. The cardiovascular system of young adults may be capable of adapting better to the state of obesity because of the higher proportion of lean mass [12]. With the expansion of VAT in older adults, an adverse association between body fat and arterial stiffness may become apparent in later life [13]. Given that arterial stiffening is a subclinical process linking between obesity, CVD risk factors, and clinical vascular disease, it is crucial to examine the associations in midlife, where targeted preventative efforts may be launched.

With this information as background, the main objective of the present study was to determine the relation between various measures of body composition and arterial stiffness as assessed by PWV in middle-aged adults. We hypothesized that abdominal obesity, such as waist circumference, android fat, and VAT, may be a better predictor of aortic stiffness than general obesity (indicated by body mass index and whole body fat percentage). Further, we aimed to investigate the extent to which the presence of cardiovascular risk factors, such as blood pressure, total cholesterol, HbA1c, and cardiorespiratory fitness is associated with arterial stiffness in midlife. To do so, the ideal cardiovascular health, a concept developed by the American Heart Association [14], was calculated by including the presence of both ideal health behaviors (nonsmoking, body mass index <25 kg/m^2, physical activity at goal levels, and pursuit of a diet consistent with current guideline recommendations) and ideal health factors (total cholesterol <200 mg/dL, blood pressure $<120/<80$ mm Hg, and fasting blood glucose <100 mg/dL).

Methods

Subjects

A total of 146 adults between the ages of 40–60 years were recruited from the community through electronic and print advertisements. Individuals with a history of coronary artery disease, neurological disease, angina pectoris, myocardial infarctions, heart failure and cardiac surgery were excluded. None of the postmenopausal women were taking hormone replacement therapy. Participants who passed the initial screen were enrolled in the study after providing written informed consent. The study was approved by the institutional review board at the University of Texas at Austin and was conducted in accordance with the declaration of Helsinki, 1975.

Measurements

Body composition

Body mass index (BMI) was expressed as the ratio of total body mass divided by height squared (kg/m^2). Individuals with a BMI between 18.5 and 24.9 kg/m^2 were classified as having normal or acceptable body mass. Individuals with a BMI ranging from 25 to 29.9 kg/m^2 were classified as overweight while obesity was present when BMI reached $\geq$30 kg/m^2. Waist circumference, defined as the minimal abdominal circumference between the lower edge of the rib cage and the iliac crests, was measured according to a highly standardized procedure, and National Cholesterol Education Program Adult Treatment Panel III criteria were used to estimate the prevalence of abdominal obesity ($>$88 cm in women and $>$102 cm in men) [15]. The sagittal abdominal diameter, the distance between the back surface and the top of the abdomen midway between the lower edge of the rib cage and the iliac crests, was measured with an anthropometer after a gentle expiration by the patient in a standing position. Body composition and visceral fat mass were estimated non-invasively via dual-energy X-ray absorptiometry (DXA) using a Lunar Dual Energy X-Ray Absorptiometry DPX (General Electric Medical Systems, Fairfield, Connecticut). The total body scan was analyzed to yield measures of bone, fat, and lean tissue for particular body regions (e.g., arms, legs, or trunk) [16]. For measuring android fat, a region-of-interest is automatically defined whose caudal limit is placed at the top of the iliac crest and its height is set to 20% of the distance from the top of the iliac crest to the base of the skull to define its cephalad limit. Abdominal subcutaneous fat and visceral fat are estimated within the android region. Visceral fat was computed by subtracting subcutaneous fat from the total abdominal fat in the android region. DXA has been well validated as a sensitive, relatively inexpensive tool for visceral fat measurement with results comparable to that of computed tomography [17,18], the gold standard for measuring visceral fat.

Arterial stiffness

All experiments were performed in an environmentally controlled quiet laboratory during the morning hours, and the room temperature was controlled at 22–24 C. Premenopausal women were studied in the follicular phase of the menstrual cycle. After at least 15 min of rest in the supine position, bilateral brachial and ankle blood pressure, carotid and femoral pulse pressure waveforms, and heart rate were simultaneously measured by an automated vascular testing device (VP-1000 plus; Omron Healthcare, Bannockburn, IL) [19,20] that has been validated against the manual measurement of pulse wave velocity [19]. Arterial applanation tonometry incorporating an array of 15 micropiezoresistive transducers recorded pulse

pressure waveforms from the carotid and femoral arteries. The time it takes for the pulse wave to travel between the two tonometers was automatically measured based on the foot-to-foot method. The straight distance between the carotid and femoral arterial recording sites was measured on body surface and multiplied by 0.8 in order to adjust the measured distance close to the real pulse travel distance [21]. In order to minimize the influence of body curvature affecting the distance measurements in obese subjects, a customized segmometer specifically designed for PWV studies (Rosscraft Anthropometric Calipers, Surray, Canada) was used. Subsequently, carotid-femoral pulse wave velocity (cfPWV) was calculated as pulse travel distance divided by the transit time. Additionally, brachial-ankle PWV (baPWV) was measured [22]. To do so, four limb occlusion cuffs were placed on the participant's arms and ankles to record the pulse waveform of pressure for 10 s. On the basis of the foot-to-foot interval of waveforms at the oscillometric cuffs, the pulse transit time between right arm and right ankle, and between right arm and left ankle were calculated. Then the PWV across two arterial segments was determined by dividing body distances by the time traveled over the segment (m/s).

Other measurements

A modified Bruce treadmill protocol was used to assess maximal oxygen consumption (VO_2max). This measurement is generally considered the best indicator of cardiovascular fitness and aerobic endurance because it establishes the upper limit of maximal energy production through oxidative pathways. Whole blood samples were drawn after overnight fasting and $\geq$24 h of abstinence from alcohol, caffeine, food, and exercise. Triglycerides, total and high-density lipoprotein cholesterol were determined enzymatically. Routine fasting blood glucose levels and glycosylated hemoglobin (HbA1c) were measured with standard techniques.

Statistical analyses

Outcomes were first checked for normality. Descriptive characteristics of participants were presented as means $\pm$ SD. Gender differences were assessed using the Student t-tests or Fisher's exact tests as appropriate. The unadjusted bivariate relationships were examined using Pearson product correlation coefficient analysis. To examine the independent associations between arterial stiffness and indicators of obesity (BMI, waist circumference, and visceral fat mass), multiple linear regression analyses were performed before and after adjustment for confounders such as age, gender. The models were determined to be stable and not disturbed by multi-collinearity. For detecting the outliers in outcomes and indicators the empirical rule method of 3 standard deviations from the mean was used. Subjects were divided based on the American Heart Association-proposed cardiovascular health status [13] into ideal cardiovascular health (total cholesterol $<$200 mg/dL, blood pressure $<$120/$<$80 mm Hg, and fasting blood glucose $<$100 mg/dL) or intermediate to poor cardiovascular health (multiple cardiovascular risk factors). All statistical analyses were conducted using SAS statistical software 9.3. The significance level for statistical tests were set at $\alpha = 0.05$.

Results

Selected participant characteristics are summarized in Table 1. A total of 146 participants (76 men, 70 women) were included in the study. Of those, 57 subjects were obese based on BMI $\geq$30 kg/m^2, whilst 61 subjects were overweight with a BMI between 25 and 30 kg/m^2, 43 women and 34 men were classified as having abdominal obesity. Participants had a mean visceral fat mass of 1276 $\pm$ 882 g, which was significantly correlated with BMI ($r = 0.61$, $P < 0.0001$), waist circumference ($r = 0.80$, $P < 0.0001$), systolic blood pressure ($r = 0.32$, $P = 0.0003$), and HbA1c ($r = 0.24$, $P = 0.0074$).

Table 2 summarizes unadjusted correlations between adiposity measures and arterial stiffness. Both carotid-femoral and brachial-ankle PWV was significantly associated with BMI (both $P < 0.05$) but not with body fat percentage. Measures of abdominal obesity, including waist circumference and visceral fat mass, were strongly associated with both PWV measures. PWV correlated positively with cardiovascular risk factors, namely systolic blood pressure ($P < 0.0001$), fasting blood glucose ($P = 0.01$), and HbA1c ($P = 0.03$) but not with lipids. Cardiovascular fitness was associated with percent body fat and android and gynoid fat mass but not with visceral fat or arterial stiffness.

Table 3 illustrates the independent associations of various indicators of adiposity and arterial stiffness in

Table 1 Descriptive characteristics of the subjects.

Clinical characteristics	Mean $\pm$ SD
Men/women (n)	76/70
Age (years)	50 $\pm$ 6
Body mass (kg)	85 $\pm$ 19
Body mass index (kg/m^2)	29 $\pm$ 6
Waist circumference (cm)	96 $\pm$ 16
Body fat (%)	34 $\pm$ 10
Lean tissue mass (kg)	51.8 $\pm$ 11.4
Trunk fat mass (kg)	16.8 $\pm$ 8.2
Android fat mass (kg)	3.0 $\pm$ 1.7
Gynoid fat mass (kg)	5.1 $\pm$ 2.4
Total fat mass (kg)	30.1 $\pm$ 13.6
Visceral fat mass (g)	1176 $\pm$ 882
VO_2max (ml/kg/min)	29.5 $\pm$ 7
Heart rate (bpm)	62 $\pm$ 10
Systolic BP (mmHg)	122 $\pm$ 14
Diastolic BP (mmHg)	73 $\pm$ 10
Total cholesterol (mg/dl)	195 $\pm$ 41
Fasting blood glucose (mg/dl)	101 $\pm$ 31
HbA1c (%)	5.7 $\pm$ 1.1
Carotid-femoral PWV (cm/s)	1038 $\pm$ 204
Brachial-ankle PWV (cm/s)	1293 $\pm$ 206

VO_2max = maximal oxygen consumption; BP = blood pressure; HbA1c = glycosylated hemoglobin; PWV = pulse wave velocity.

Table 2 Bivariate relations between various adiposity measures and arterial stiffness.

Predictors	Carotid-femoral PWV		Brachial-ankle PWV		VO_{2max}	
	Pearson r	P-value	Pearson r	P-value	Pearson r	P-value
Body mass index	0.203	0.022	0.225	0.011	−0.193	0.066
Body fat percentage	0.169	0.058	0.103	0.248	−0.719	**<0.0001**
Waist circumference	0.369	**<0.0001**	0.260	**0.003**	−0.094	0.377
Android fat mass	0.357	**<0.0001**	0.209	**0.018**	−0.276	**0.008**
Gynoid fat mass	0.137	0.122	0.050	0.572	−0.589	**<0.0001**
Visceral fat mass	0.369	**<0.0001**	0.276	**0.002**	−0.022	0.834
Systolic blood pressure	0.546	**<0.0001**	0.526	**<0.0001**	0.071	0.503
Total cholesterol	0.101	0.262	0.103	0.253	−0.087	0.411
Fasting blood glucose	0.225	**0.011**	0.218	**0.014**	0.021	0.846
HbA1c	0.196	**0.031**	0.205	**0.024**	−0.031	0.771
VO_2max	−0.142	0.1775	−0.090	0.3914	1.000	

Bold: P values below 0.05 were considered statistically significant.
PWV = pulse wave velocity; HbA1c = glycosylated hemoglobin; VO_2max = maximal oxygen consumption.

multivariable regression analyses. BMI, waist circumference, and visceral fat mass were significantly associated with increased PWV after adjusting for age and gender (Model 2, $P < 0.05$). Visceral fat mass was significantly associated with both measures of PWV (Fig. 1). Visceral fat mass and PWV measures were significantly associated with cardiovascular health status after adjusting for age and gender (both $P < 0.001$) (Fig. 2).

Discussion

The salient findings from the present study are as follows. Various measures of adiposity were significantly associated with arterial stiffness in a group of middle-aged adults. The strengths of the associations with arterial stiffness were substantially greater for abdominal obesity than general obesity indicators. Body fat percentage as assessed by DXA, a gold standard measure of whole-body adiposity, was not even associated with arterial stiffness. These results suggest that the accumulation of abdominal fat that occurs in midlife plays an important role in vascular dysfunction.

In univariate analysis, visceral fat depot was the strongest correlate of arterial stiffening. Thus, body mass, BMI, and waist size may be risk factors for arterial stiffening primarily because they are correlated with the degree of visceral adipose tissue. Our present analyses did not support a significant relationship between percentage body fat, a gold standard measure of overall obesity, and arterial stiffness on a predominantly middle-aged population. These results collectively suggest that the accumulation of abdominal fat that occurs in midlife plays an important role in vascular dysfunction, while the association between percentage body fat and arterial stiffness seems to be age-dependent. 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. We have found that android fat was positively associated with arterial stiffness whereas gynoid fat (leg fat) was not related to arterial stiffness. This suggests that regional body fat patterning indicators are differentially associated with arterial stiffness independent of total fat mass [23]. Indeed, sexual dimorphism in body size and fat distribution may contribute to differences in potential mediators of arterial stiffness such as adipocyte size, adipokines, pro-inflammatory cytokines, and lipid species, providing evidence for a possible role of adipose tissue characteristics in the sexual dimorphism of metabolic flexibility and arterial stiffness [24].

The association between arterial stiffness and adiposity remains highly controversial [5–8]. This is so even when the searches are limited to the studies using PWV. Arterial stiffness measured by PWV was greater with higher BMI in both less obese and morbidly obese middle-aged adults [25–27]. Similarly, BMI, but not VAT, were significantly

Table 3 Independent associations between indicators of obesity and arterial stiffness.

Predictor	Model	Carotid-femoral PWV		Brachial-ankle PWV	
		Standardized Beta	P-value	Standardized Beta	P-value
Body mass index	1	0.2030	**0.022**	0.2255	**0.011**
	2	0.2329	**0.005**	0.2533	**0.002**
Waist circumference	1	0.3690	**<0.0001**	0.2601	**0.003**
	2	0.3721	**<0.0001**	0.2571	**0.003**
Visceral fat mass	1	0.3687	**<0.0001**	0.2755	**0.002**
	2	0.3238	**<0.0005**	0.2328	**0.009**

Bold: P values below 0.05 were considered statistically significant.
Model 1: no adjustment.
Model 2: adjusted for age and gender (sex).

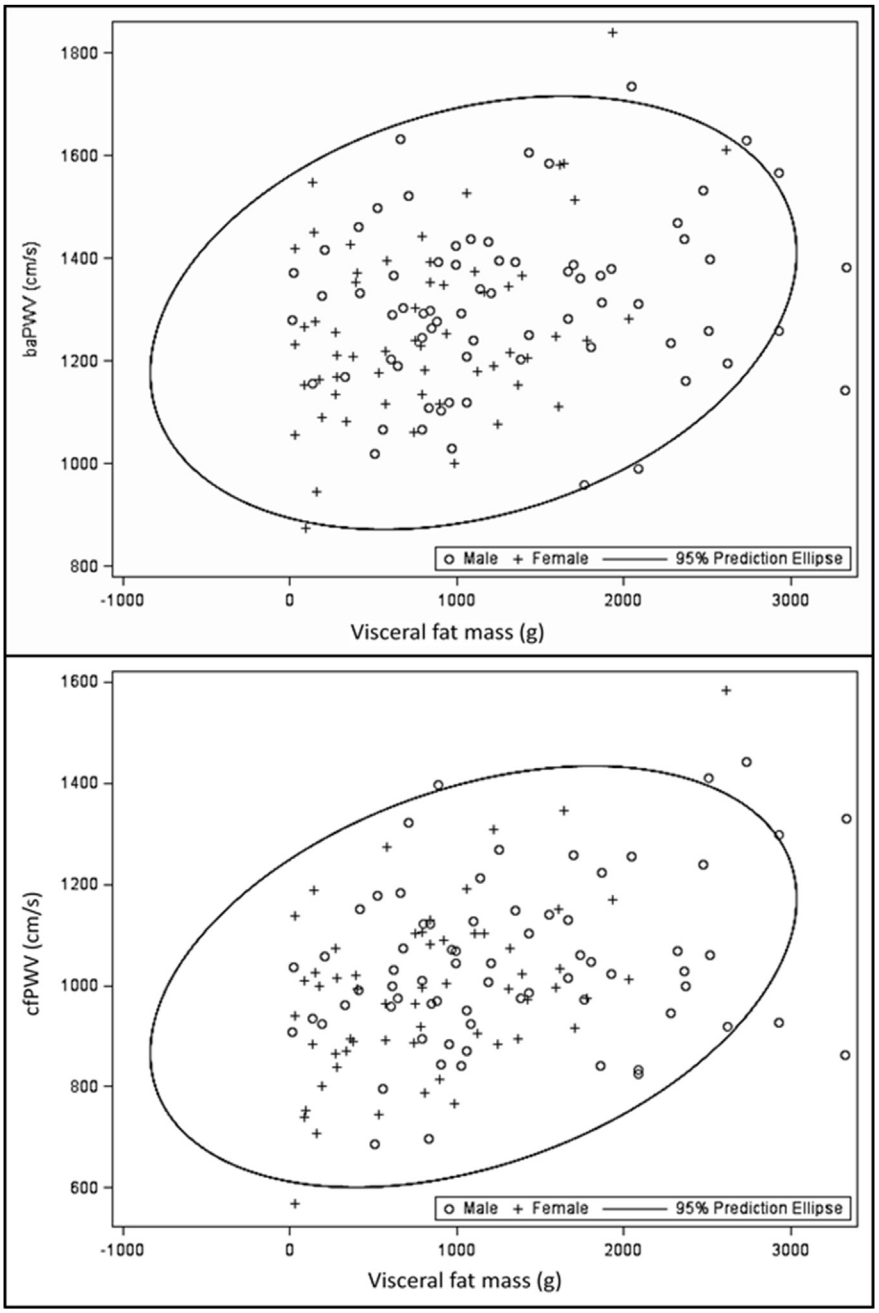

Figure 1 Correlation between visceral fat mass and arterial stiffness as assessed by carotid-femoral pulse wave velocity (cfPWV) and brachial-ankle pulse wave velocity (baPWV).

associated with PWV in 50 healthy obese patients [28]. In contrast, waist circumference, but not BMI, was significantly associated with PWV in apparently healthy middle-aged subjects [29]. We suspected that the carotid–femoral travel distance, which is an essential factor in PWV calculation, could be systematically biased in obese individuals with wider waist circumference. Indeed a recent study showed a significant overestimation of PWV with increasing central obesity in both men and women [30]. In the present study, we used a segmometer, a device specifically designed to measure the arterial travel distance in the horizontal line even in obese subjects, to measure the distance between carotid and femoral arterial recording sites. Additionally, we utilized brachial-ankle PWV, a measure of arterial stiffness that does not require a measurement of arterial travel distance, as the arterial travel distance is derived automatically from one's height via algorithm. The present results obtained with cfPWV and baPWV were highly consistent with each other and showed that arterial stiffness was more strongly associated with abdominal obesity than general obesity. Interestingly, when we used percent body fat, a gold standard measure of whole-body fatness, there was no significant association with arterial stiffness.

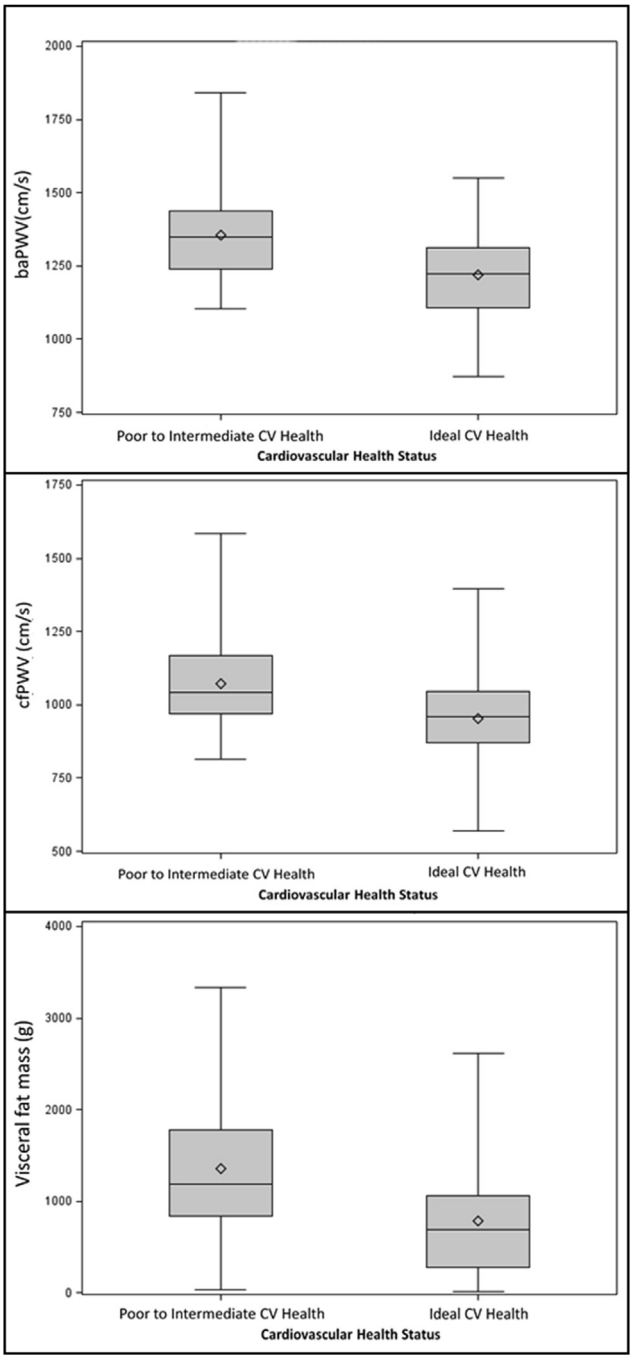

Figure 2 Independent association between visceral fat mass, arterial stiffness measures and cardiovascular health status after adjusting for age and gender.

The physiological mechanisms linking body fat with arterial stiffness are not well understood, but a plausible explanation includes changes in insulin sensitivity, activation of the renin-angiotensin system, sympathetic nervous system activation, and the subsequent increase in smooth muscle tone [31]. In the present study, PWV was correlated positively with fasting blood glucose and HbA1c, the latter being a strong independent predictor of higher cfPWV, independent of conventional cardiovascular risk factors [32]. Other potential factors include stimulation of a pro-inflammatory state, resulting in activation of oxidant enzyme systems, increased production of reactive oxygen species such as superoxide anions, and the development of oxidative stress [33]. Moreover, increased body fatness can result in elevated circulating leptin concentrations, which could mediate the positive relationship between trunk fat mass and aortic PWV as suggested in the Baltimore Longitudinal Study of Aging [34]. In addition, there is some evidence that different fat depots are metabolically distinct in their production of adipocytokines and may cause arterial stiffening [23]. Further studies are required to assess possible mediators of the association between obesity measures and arterial stiffness. Additionally, whether reductions in visceral fat obesity through lifestyle interventions are associated with the corresponding decreases in arterial stiffness should be investigated. In this context, two recent studies found that a good adherence to the therapeutic lifestyle change program can successfully modify cardiovascular and metabolic risk factors [35] and improve endothelial function in patients with abdominal obesity [36].

Habitual aerobic exercise may be a particularly effective strategy for body weight management given its favorable independent modulatory influence on age-associated arterial stiffening [37]. In the present study, higher cardiorespiratory fitness was negatively related to android and gynoid fatness. However, cardiorespiratory fitness was not related to percent body fat or visceral fat. A lack of the association may be reflecting a notion that regular exercise may not always be associated with a loss of body mass and body fatness [38]. Moreover, cardiorespiratory fitness was not related to arterial stiffness. Recent evidence indicates that aerobic exercise might not reduce arterial stiffness in patients with hypertension and/or obesity [8,39]. Additionally, aerobic exercise training may not be associated with decreased circulating levels of inflammatory factors in the absence of weight loss in obese subjects [40], suggesting that perhaps changes in body composition associated with exercise training may be required to control low-grade systemic inflammation [41]. Interestingly, low-intensity aerobic exercise interventions, which do not have any impact on cardiorespiratory fitness, may have a positive impact on arterial stiffness in obese populations [39].

Strengths of the present study include the comprehensive measures of whole-body and abdominal fatness as well as the inclusion of arterial stiffness as assessed by both cfPWV and baPWV. We used PWV in the present study, which is considered the reference-standard noninvasive method for measuring arterial stiffness and an independent predictor for atherosclerosis, cardiovascular risk and future CVD events. Additionally we included both reference standard (cfPWV) and automatic (baPWV) measures of arterial stiffness. Another novelty of the present study includes the comprehensive measures of whole-body, abdominal, and visceral fatness in healthy middle-aged adults. Moreover, we additionally assessed cardiovascular fitness (VO_{2max}), which is linked with lower whole-body adiposity but not with abdominal obesity. Furthermore, we aimed to investigate the extent to which

the presence of cardiovascular risk factors is associated with arterial stiffness in midlife with the conclusion that a better cardiovascular profile is related to both lower arterial stiffness and VAT. To our knowledge, this hypothesis has not been tested in relation to arterial stiffness and VAT, in particular using a constellation of risk factors to categorize individuals with respect to ideal cardiovascular health. It is also important to note that this study does have some limitations. The cross-sectional design of the analysis prevents inferences of causality or temporality. It should be noted that it is extremely difficult to perform intervention studies in this area as it will be considered unethical to experimentally manipulate (or increase) arterial stiffness and/or body fatness. Reductions in body fatness, on the other hand, are typically accompanied by many different changes that could reduce arterial stiffness independent on obesity. In addition, because participants with history of CVD, or excessive weight (a limitation associated with DXA) were excluded, it is possible that we may have underestimated true relations between adiposity and arterial stiffness by limiting the range of adiposity. Our results are, therefore, generalizable only to relatively healthy middle-aged individuals, where targeted preventative efforts may be launched. Additionally, the sample size is relatively small compared with large epidemiological studies.

The present results indicate that abdominal obesity is significantly associated with arterial stiffness in middle-aged adults, suggesting a role for central fat depots in vascular dysfunction, beyond that of generalized adiposity. Indeed a recent cross-sectional study of 120 obese subjects indicated that visceral fat cell volume may explain the correlation between central fat mass, arterial stiffness and cardiovascular risk [42]. Although a 1 m/s difference in PWV might be considered as modest with respect to arterial stiffness in an individual, every 1 m/s increase in aortic PWV at a population level represents a 14% increase in risk for total cardiovascular events, a 15% increased risk for cardiovascular mortality, and a 15% increased risk for all-cause mortality [43]. Higher cardiorespiratory fitness was not associated with visceral fat or arterial stiffness. However, having more favorable cardiovascular risk profiles was related to lower levels of visceral body fat and arterial stiffness. Since arterial stiffness is a surrogate marker between the appearance of risk factors and cardiovascular outcomes, our finding support the importance of adiposity measures as a risk factor in middle-aged adults.

Conflicts of interest

The authors declare to have no conflict of interest.

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References

[1] Nguyen-Duy TB, Nichaman MZ, Church TS, Blair SN, Ross R. Visceral fat and liver fat are independent predictors of metabolic risk factors in men. Am J Physiol Endocrinol Metab 2003;284:E1065–71.
[2] Canepa M, Strait JB, Milaneschi Y, AlGhatrif M, Ramachandran R, Makrogiannis S, et al. The relationship between visceral adiposity and left ventricular diastolic function: results from the Baltimore Longitudinal Study of Aging. Nutr Metab Cardiovasc Dis 2013;23:1263–70.
[3] Hu G, Bouchard C, Bray GA, Greenway FL, Johnson WD, Newton Jr RL, et al. Trunk versus extremity adiposity and cardiometabolic risk factors in white and African American adults. Diabetes Care 2011;34:1415–8.
[4] Bastien M, Poirier P, Lemieux I, Després JP. Overview of epidemiology and contribution of obesity to cardiovascular disease. Prog Cardiovasc Dis 2014;56:369–81.
[5] Rodrigues SL, Baldo MP, Lani L, Nogueira L, Mill JG, Sa Cunha Rd. Body mass index is not independently associated with increased aortic stiffness in a Brazilian population. Am J Hypertens 2012;25:1064–9.
[6] Wohlfahrt P, Somers VK, Cifkova R, Filipovsky J, Seidlerova J, Krajcoviechova A, et al. Relationship between measures of central and general adiposity with aortic stiffness in the general population. Atherosclerosis 2014;235:625–31.
[7] Yang F, Wang G, Wang Z, Sun M, Cao M, Zhu Z, et al. Visceral adiposity index may be a surrogate marker for the assessment of the effects of obesity on arterial stiffness. PLoS One 2014;9:e104365.
[8] Tanaka H, Safar ME. Influence of lifestyle modification on arterial stiffness and wave reflections. Am J Hypertens 2005;18:137–44.
[9] Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al., European Network for Non-invasive Investigation of Large Arteries. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J 2006;27:2588–605.
[10] Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, Hamburg NM, et al. Arterial stiffness and cardiovascular events: the Framingham Heart Study. Circulation 2010;121:505–11.
[11] Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, et al. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. Circulation 2006;113:664–70.
[12] Hull HR, Thornton J, Wang J, Pierson Jr RN, Kaleem Z, Pi-Sunyer X, et al. Fat-free mass index: changes and race/ethnic differences in adulthood. Int J Obes 2011;35:121–7.
[13] Corden B, Keenan NG, de Marvao AS, Dawes TJ, Decesare A, Diamond T, et al. Body fat is associated with reduced aortic stiffness until middle age. Hypertension 2013;61:1322–7.
[14] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al., American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 2010;121:586–613.
[15] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III) final report. Circulation 2002;106:3143–421.
[16] Mazess RB, Barden HS, Bisek JP, Hanson J. Dual-energy X-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. Am J Clin Nutr 1990;51:1106–12.
[17] Kaul S, Rothney MP, Peters DM, Wacker WK, Davis CE, Shapiro MD, et al. Dual-energy X-ray absorptiometry for quantification of visceral fat. Obesity 2012;20:1313–8.
[18] Xia Y, Ergun DL, Wacker WK, Wang X, Davis CE, Kaul S. Relationship between dual-energy X-ray absorptiometry volumetric

assessment and X-ray computed tomography-derived single-slice measurement of visceral fat. J Clin Densitom 2014;17:78–83.
[19] Cortez-Cooper MY, Supak JA, Tanaka H. A new device for automatic measurements of arterial stiffness and ankle-brachial index. Am J Cardiol 2003;91:1519–22.
[20] Tanaka H, Munakata M, Kawano Y, Ohishi M, Shoji T, Sugawara J, et al. Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness. J Hypertens 2009;27:2022–7.
[21] Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, et al., Artery Society, European Society of Hypertension Working Group on Vascular Structure and Function, European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens 2012;30:445–8.
[22] Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, et al. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. Hypertens Res 2002;25:359–64.
[23] Lee M, Choh AC, Demerath EW, Towne B, Siervogel RM, Czerwinski SA. Associations between trunk, leg and total body adiposity with arterial stiffness. Am J Hypertens 2012;25:1131–7.
[24] Sparks LM, Pasarica M, Sereda O, deJonge L, Thomas S, Loggins H, et al. Effect of adipose tissue on the sexual dimorphism in metabolic flexibility. Metabolism 2009;58:1564–71.
[25] Nordstrand N, Gjevestad E, Dinh KN, Hofsø D, Røislien J, Saltvedt E, et al. The relationship between various measures of obesity and arterial stiffness in morbidly obese patients. BMC Cardiovasc Disord 2011;11:7.
[26] Zebekakis PE, Nawrot T, Thijs L, Balkestein EJ, van der Heijden-Spek J, Van Bortel LM, et al. Obesity is associated with increased arterial stiffness from adolescence until old age. J Hypertens 2005;23:1839–46.
[27] 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;42:468–73.
[28] Rider OJ, Tayal U, Francis JM, Ali MK, Robinson MR, Byrne JP, et al. The effect of obesity and weight loss on aortic pulse wave velocity as assessed by magnetic resonance imaging. Obesity 2010;18:2311–6.
[29] Czernichow S, Bertrais S, Oppert JM, Galan P, Blacher J, Ducimetière P, et al. Body composition and fat repartition in relation to structure and function of large arteries in middle-aged adults (the SU.VI.MAX study). Int J Obes 2005;29:826–32.
[30] Canepa M, Alghatrif M, Pestelli G, Kankaria R, Makrogiannis S, Strait JB, et al. Impact of central obesity on the estimation of carotid-femoral pulse wave velocity. Am J Hypertens 2014;27:1209–17.
[31] Safar ME, Czernichow S, Blacher J. Obesity, arterial stiffness, and cardiovascular risk. J Am Soc Nephrol 2006;17:S109–11.
[32] Liang J, Zhou N, Teng F, Zou C, Xue Y, Yang M, et al. Hemoglobin A1c levels and aortic arterial stiffness: the Cardiometabolic Risk in Chinese (CRC) study. PLoS One 2012;7:e38485.
[33] Seals DR, Gates PE. Stiffening our resolve against adult weight gain. Hypertension 2005;45:175–7.
[34] Windham BG, Griswold ME, Farasat SM, Ling SM, Carlson O, Egan JM, et al. Influence of leptin, adiponectin, and resistin on the association between abdominal adiposity and arterial stiffness. Am J Hypertens 2010;23:501–7.
[35] Voeghtly LM, Neatrour DM, Decewicz DJ, Burke A, Haberkorn MJ, Lechak F, et al. Cardiometabolic risk reduction in an intensive cardiovascular health program. Nutr Metab Cardiovasc Dis 2013;23:662–9.
[36] Ferré R, Plana N, Merino J, Aragonès G, Girona J, Heras M, et al. Effects of therapeutic lifestyle changes on peripheral artery tonometry in patients with abdominal obesity. Nutr Metab Cardiovasc Dis 2012;22:95–102.
[37] Seals DR, Desouza CA, Donato AJ, Tanaka H. Habitual exercise and arterial aging. J Appl Physiol 2008;105:1323–32.
[38] Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. Prog Cardiovasc Dis 2014;56:441–7.
[39] Montero D, Roberts CK, Vinet A. Effect of aerobic exercise training on arterial stiffness in obese populations: a systematic review and meta-analysis. Sports Med 2014;44:833–43.
[40] Marcell TJ, McAuley KA, Traustadóttir T, Reaven PD. Exercise training is not associated with improved levels of C-reactive protein or adiponectin. Metabolism 2005;54:533–41.
[41] Strasser B, Arvandi M, Siebert U. Resistance training, visceral obesity and inflammatory response: a review of the evidence. Obes Rev 2012;13:578–91.
[42] Arner P, Bäckdahl J, Hemmingsson P, Stenvinkel P, Eriksson-Hogling D, Näslund E, et al. Regional variations in the relationship between arterial stiffness and adipocyte volume or number in obese subjects. Int J Obes 2014. http://dx.doi.org/10.1038/ijo.2014.118 [Epub ahead of print].
[43] Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 2010;55:1318–27.