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Sex-specific association of anthropometric measures of body composition with arterial stiffness in a healthy population

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Anthropometric measures of body composition and arterial stiffness are commonly used as indicators of cardiovascular risk. Little is known, however, about the association of the anthropometric measures with arterial stiffness, especially in a healthy, generally non-obese population.

Material/Methods: In a sample of 352 healthy subjects (200 premenopausal women), 3 arterial stiffness indices were analyzed (pulse wave velocity, augmentation index and central systolic blood pressure) in relation to 5 anthropometric measures of body composition (body mass index – BMI, body fat percentage by skinfold measurements –%BF, waist circumference – WC, waist-hip ratio – WHpR, and waist-height ratio – WHtR). Data were analyzed using correlation and regression analyses, with adjustment for the following confounders: age, blood pressures, height, heart rate, blood lipids and smoking.

Results: Most correlations between anthropometric measures and arterial stiffness indices were significant and positive in both sex groups ($r=0.14–0.40$, $P<0.05$). After adjustment for confounding effects, BMI, WC and WHtR remained significant (but inverse) predictors of arterial stiffness (β from –0.06 to –0.16; $P<0.05$) in the females, while in the males BMI was the only measure inversely predicting arterial stiffness (β from –0.09 to –0.13; $P<0.05$).

Conclusions: Measures of body composition are weak and inverse predictors of arterial stiffness and their influence is sex-dependent. BMI, WC and WHtR were key predictors of arterial stiffness in the females, while BMI was the principal predictor in the males. The associations of anthropometric measures with arterial stiffness are strongly and differently confounded by various factors that have to be taken into account when explaining results of similar studies.

key words: **anthropometric measurements • BMI • arterial stiffness • pulse wave velocity • augmentation index**

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Background

Simple anthropometric measures of body composition and fat distribution are widely accepted as being the most practical and valuable approach to diagnose excess body fat, usually classified as overweight and obesity. Excess body fat can have an adverse effect on health, leading to development of various chronic diseases, cardiovascular (CV) disease being the most typical [1–4].

The oldest and the most commonly used anthropometric measure for this purpose is the body mass index (BMI), an estimate of body fat calculated from height and weight. It distinguishes 3 categories – normal weight (<24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2) – without precise distinction between body fat and other tissues, such as musculoskeletal. Also, BMI is insensitive to the relative distribution of body fat [5]. The assessment of body fat percentage (%BF) is another measure often used, but has similar limitation as BMI. Because health risk seems to be primarily associated with abdominal fat [6–8], measures for assessment of excess abdominal fat, such as waist circumference (WC), waist-hip ratio (WHpR) and waist-height ratio (WHtR) were introduced as more specific alternatives. All these measures were shown to be associated with metabolic disorders and CV risk factors in different patterns and extent [9–14]. Some of these measures were also reported to be related to arterial stiffness, an important, independent and proven CV risk factor [15–17]. Several studies showed association of the anthropometric measures with arterial stiffness in obese population, with clear sex differences [18,19]. However, little is known about these associations in healthy and generally non-obese populations. Only a few studies have examined the association of several anthropometric measures with arterial stiffness in healthy populations close to normal weight, but their results were inconsistent [20–22]. For instance, in the study examining relation of BMI and BF content with stiffness index, augmentation index (AIx) and pulse pressure (PP), Wykretowicz et al. [20], showed that BMI was not a good predictor of arterial stiffness. On the contrary, Wildman et al. [21] found BMI together with WC and WHpR was strongly associated with pulse wave velocity (PWV), the direct marker of arterial stiffness. Further, Maher et al. [23] showed that none of the anthropometric measures was associated with AIx. In addition, none of these studies considered sex differences.

Arterial stiffness can be assessed by several approaches. A direct arterial stiffness index, PWV, considered as a 'gold standard' method, has many times been confirmed to have the strongest predictive value for CV events [15,24]. AIx is an indirect marker of arterial stiffness and a direct measure of wave reflection, also confirmed to be associated with CV risk [16,25]. Central systolic blood pressure (cSBP), an indicator of central hemodynamics, is a complementary stiffness index, also used as a predictor of CV events [26]. So far it has not been examined in relation to the anthropometric measures.

The aim of our study was assessment of sex-specific association of different anthropometric measures of body composition (BMI,%BF, WC, WHtR and WHpR) with a spectrum of arterial stiffness indices (PWV, AIx and cSBP) in healthy and generally non-obese subjects. In order to clearly distinguish the effect of each anthropometric measure, the data were complemented with a wide set of known confounders involved in the complex pathophysiology of the increased arterial stiffness, such as age, heart rate, blood pressures, blood lipids and smoking.

Material and Methods

Setting

The study was conducted at the University of Split School of Medicine, as a part of larger genetic epidemiology research program [27–29] during 2009–2010. Participants were unselected, healthy adults, >18 years of age, originating from the city of Split (Croatia) and surrounding areas. After providing a signed informed consent for participation in the study, each participant completed a detailed medical history and was subjected to thorough physical examination. Subjects with history of cardiovascular diseases (hypertension, coronary artery disease, myocardial infarction, heart failure or arrhythmia), cerebrovascular diseases, cancer, thyroid disturbances, diabetes mellitus, elevated serum glucose, triglycerides and cholesterol were excluded from the study. Also, those taking lipid-lowering, blood sugar-lowering, antihypertensive or other cardiovascular medications were excluded from the study. Postmenopausal women were also excluded since menopause has a confounding effect on arterial stiffness [30,31]. Blood sampling and anthropometric and arterial stiffness measurements were performed in the morning, after overnight fasting. Blood glucose, triglycerides, and total LDL and HDL cholesterol were measured by standard laboratory procedures. Smoking status was obtained from a questionnaire and was coded into categories: current smokers, former smokers and non-smokers.

Anthropometric measures of body composition

Height and weight were measured using a digital scale (SECA 789 Bionetics, Canada) with the precision of 0.1 cm and 0.1 kg, respectively. BMI was calculated by dividing the participant's weight (kg) by square of height (m^2). WC was measured using a tape measurer placed halfway between the lower border of the ribs and the iliac crest in a horizontal plane, and was measured to the nearest 0.1 cm. Hip circumference (HpC) was measured at the widest point over the buttocks. Waist and hip circumference were related as WHpR=WC(cm)/HpC(cm). WHtR was calculated as WC (cm)/height (cm). Percent BF was determined from measurements of skinfold thickness taken at 4 standard sites – biceps, triceps, subscapular and suprailiac – using Harpenden skinfold caliper (CMS Instruments, London, UK). Three sets of measurements were averaged for each site. Body density was calculated from the sum of the 4 skinfold measurements according to Durnin and Womersley [32], and final percentage of body fat was calculated by Siri's equation [33].

Hemodynamic measurements

All hemodynamic measurements were preformed in a temperature-controlled room, unaffected by external environmental influences, in a supine position after resting for 15 min. Arterial stiffness was measured non-invasively using Arteriograph (TensioMed Ltd., Budapest, Hungary), a recently introduced and validated device for arterial stiffness assessment [34–36]. Arteriograph uses an oscillometric principle for measurement of the aortic PWV and pulse wave analysis. Essentially, the device measures periodic pressure changes in the inflated cuff (35 mmHg above systolic pressure) induced by fluctuations in pulsatile pressure in the brachial artery beneath. The cuff was applied to the upper right arm. Simultaneously with the parameters of arterial stiffness (PWV (m/s), cAIx (%), cSBP (mmHg)), the device also recorded systolic and diastolic blood pressures (SBP and DBP, mmHg) and heart rate (min^{-1}). Mean arterial pressure (MAP) was subsequently calculated by formula: MAP=DBP+(SBP-DBP)/3. All measurements were performed by 2 well-trained investigators (DB and GG). The average values of 2 measurements that satisfied quality control, taken 5 minutes apart, were used.

Statistical analysis

The Pearson correlations and multiple regression analysis (MLR) were used to assess the associations of each anthropometric measure of body composition with a particular arterial stiffness index within each sex group of subjects. Potential confounding effects adjusted for were age, heart rate, height, SBP, DBP, smoking, total LDL and HDL cholesterol and triglycerides [37,38]. In order to avoid biased results, outliers were identified and removed from the initial dataset (N=352). In total, 7 univariate (z>3.3) and 2 overlapping extreme multivariate outliers (Mahalanobis D2, P≤0.001) were removed (N=7). Since no *a priori* hypothesis was made to determine the order of entry of the potential predictor factors (see above), a direct method for the regression analyses was used. The entering of the predictor variable was followed by removing the one with the lowest non-significant regression coefficient and by subsequent regression analysis. The procedure was repeated until all non-significant predictors were removed or until further exclusions caused a deterioration of the model according to F-test. In each case, the direct regression model was followed by backward method to check for inconsistencies. Finally, the optimal model of arterial stiffness index prediction with a particular anthropometric measure as independent variable was determined.

All statistical tests were two-tailed, with statistical significance defined as P<0.05. Normal distributions were evaluated with determination of skewness and histograms as well as with one-sample Kolmogorov-Smirnov test. Independent sample t-tests as well as χ^2 tests were used for quantitative and qualitative variables, respectively, when evaluating the differences between sexes. All other statistical calculations were performed using SPSS software, version 13 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 352 healthy subjects were included in the study. There were 152 (43.2%) men and 200 (56.8%) premenopausal women. In both sexes, body composition, hemodynamic and biochemical parameters were within the range expected for normally distributed population (Table 1). Women had significantly lower cSBP and greater AIx values, while there was no difference in PWV between sexes. All measures of body composition, except%BF, were lower in women. Our population sample was predominantly non-obese – according to BMI, 52% of subjects had normal body weight, 38% were overweight and 10% were obese. Mean (±SD) BMI was 23.95±3.60 in the female and 25.84±3.77 in the male subjects.

The analysis revealed several differences between the females and the males. In the female group univariate analysis showed that most correlations between measures of body composition and arterial stiffness indices were positive and mainly significant (Table 2, bold column). However, application of a MLR analysis revealed quite different results. In general, after adjustment for known risk factors, multivariate models detected 3 measures of body composition (BMI, WC and WHtR) as weak and inverse predictors of PWV and AIx (Table 2). In the cSBP models, only BMI remained a significant inverse predictor. As independent predictors, the 3 measures of body composition (BMI, WC and WHtR), explained only several percentages of arterial stiffness variance (sr^2=0.003–0.02). Other measures, such as%BF and WHpR, were not significant predictors of arterial stiffness in the female group.

In the male group, similar to the females, correlations between measures of body composition and arterial stiffness indices, determined by univariate analysis, were positive and mainly significant (Table 3, bold column). Again, after application of the MLR and adjustment for known confounders, most of these univariate associations disappeared (Table 3). In contrast to females, BMI was the only common and inverse predictor of arterial stiffness indices, PWV and cSBP. Similar to the female group, measures of body composition as independent predictors explained only several percent of arterial stiffness variance (sr^2=0.005–0.02). Measures such as%BF and WHpR were not significant predictors in the male group.

Finally, relative to the male models, female models in general explained 10% to 15% less variance, and differed in some predictors (Tables 2 and 3).

Discussion

The results of this study show that in the sample of healthy and generally non-obese subjects the positive univariate associations of anthropometric measures of body composition with arterial stiffness indices were not consistent, as their significance and strength depended on sex but also on the measure of body composition and arterial stiffness index. In addition, MLR analysis revealed that these associations were strongly confounded by the arterial stiffness risk factors such as age, blood pressures, height, heart rate, blood lipids and/or smoking. After removal of their confounding effects, the body composition measures turned out to be weak and inverse predictors of arterial stiffness, and their influence was sex-dependent. Namely, BMI, WC and WHtR were key predictors of arterial stiffness in the females, while BMI was the principal predictor in the males.

These key findings of our study seemingly contradict the results of several other studies that showed stronger and positive association of anthropometric measures with the arterial stiffness indices. In fact, our results indicate a possible explanation for discrepancies among these studies, as they did not completely distinguish the influence of other risk factors on

Table 1. General characteristic (body composition, hemodynamic and biochemical parameters) in sample of 352 healthy participants presented by their gender differences.

Variable; Mean ±SD	Men (n=152)	Women (n=200)	P
Age	38.93±13.67	37.22±9.58	0.633
Height (cm)	182.41±6.39	169.70±6.13	<0.001
Weight (kg)	89.26±13.32	69.06±11.33	<0.001
Smoking status; n (%)			
Current smokers	44 (28.9)	60 (30.00)	χ^2=2.316, df=2, P=0.314
Former smokers	37 (24.3)	38 (19.00)	
Non-smokers	71 (46.7)	102 (51.00)	
Glucose (mmol/L)	5.21±0.58	4.47±0.45	<0.001
Total cholesterol (mmol/L)	5.06±0.78	4.94±0.78	0.340
LDL cholesterol (mmol/L)	3.31±0.67	3.11±0.70	<0.001
HDL cholesterol (mmol/L)	1.17±0.21	1.42±0.27	<0.001
Triglycerides (mmol/L)	1.26±0.61	0.90±0.38	0.036
Hemodynamic variables			
Mean arterial pressure (mmHg)	91.7±8.6	81.56±7.95	<0.001
Central augmentation index$_{75}$* (%)	15.62±11.49	18.65±10.07	<0.001
Pulse wave velocity (m/s)	6.97±1.45	6.94±1.37	0.842
Central systolic blood pressure (mmHg)	114.95±12.55	106.45±11.43	<0.001
Pulse pressure (mmHg)	50.30±9.57	42.08±5.25	<0.001
Heart rate (min^{-1})	84.26±13.32	71.06±11.36	<0.001
Anthropometric measures of body composition and fat distribution			
Body mass index (BMI), (kg/m^2)	25.84±3.77	23.95±3.60	<0.001
Percent of body fat (%BF)	21.04±4.89	29.46±4.72	<0.001
Waist circumference (WC), (cm)	94.24±11.75	82.34±8.98	<0.001
Waist-hip ratio (WHpR)	0.90±0.13	0.79±0.12	<0.001
Waist-height ratio (WHtR)	0.52±0.06	0.48±0.05	<0.001

* Corrected for heart rate 75/min.

arterial stiffness. Namely, these studies used univariate correlations [20] or did not include all confounding factors within the best-fitted models of prediction [21,23], thus their data interpretation might be insufficient because confounding effects were not removed. Actually, the initial steps in our analysis also showed similar results until we applied MLR. We therefore strongly suggest all further studies in this area to adopt a more critical approach when distinguishing body composition measures effects on arterial stiffness. Generally, the inverse association of anthropometric measures and arterial stiffness might appear to be surprising, but similar results were obtained by several other authors as well [38,39]. It was suggested that a decrease in peripheral resistance due to hyperinsulinemia [40] or low-grade inflammation [41], that is actually accompanied with excess body fat, could lead to decreased wave reflection and consequently decreased arterial stiffness values. This implies that the observed association was probably due to changes in peripheral resistance instead of direct changes in arterial stiffness.

Despite the BMI theoretical limitation (it does not show relative fat distribution), it was the most strongly associated with arterial stiffness in both the female and male populations. It had similar predictive value in the females as 2 central anthropometric measures, WC and WHtR, while it was the only measure predicting stiffness in the males. BMI has been in use for decades and its predictive value as a health risk factor has been well-investigated and confirmed [42].

Table 2. Anthropometric measures of body composition as independent predictors of different arterial stiffness indices after adjustment for possible confounders (age, systolic and diastolic blood pressure, height, heart rate, total, LDL and HDL cholesterol, triglycerides and smoking status) in **women** population.

Arterial stiffness index	Measure of body composition	Multivariate					Univariate	
		β coefficient	P	sr2	Other independent predictors within model	R2	Zero-order correlation (r)	P
PWV	BMI	–0.14	0.034	0.02	age, DBP	0.34	**0.22**	0.006
	WC	–0.16	0.019	0.02		0.35	0.11	0.176
	WHtR	–0.13	0.041	0.01		0.34	**0.22**	0.006
	WHpR	–	–	–		–	0.07	0.347
	%BF	–	–	–		–	**0.18**	0.020
cAIx	BMI	–0.13	0.020	0.01	age, DBP, height, LDL cholesterol	0.65	**0.38**	<0.0001
	WC	–0.11	0.046	0.01		0.64	**0.25**	0.001
	WHtR	–0.11	0.043	0.01		0.64	**0.38**	<0.0001
	WHpR	–	–	–		–	**0.17**	0.036
	%BF	–	–	–		–	**0.27**	0.001
cSBP	BMI	–0.06	0.021	0.003	SBP, DBP, age, heart rate, height, LDL cholesterol	0.90	**0.40**	<0.0001
	WC	–	–	–		–	**0.25**	0.001
	WHtR	–	–	–		–	**0.35**	<0.0001
	WHpR	–	–	–		–	**0.15**	0.046
	%BF	–	–	–		–	**0.14**	0.001

Data for anthropometric measures, showed as nonsignificant predictors in MLR, are not shown. PWV – pulse wave velocity; cAIx – central augmentation index; cSBP – central systolic blood pressure; PP – pulse pressure; BMI – body mass index; WHtR – waist-height ratio; WC – waist circumference; WHpR – waist-hip ratio;%BF – percentage of body fat; DBP – diastolic blood pressure; SBP – systolic blood pressure.

Table 3. Anthropometric measures of body composition as independent predictors of different arterial stiffness indices after adjustment for possible confounders (age, systolic and diastolic blood pressure, height, heart rate, total, LDL and HDL cholesterol, triglycerides and smoking status) in **men** population.

Stiffness index	Measure of body composition	Multivariate					Univariate	
		β coefficient	P	sr2	Other independent predictors within model	R2	Zero-order correlation (r)	P
PWV	BMI	–0.13	0.032	0.02	age, SBP, smoking	0.55	**0.19**	0.031
	WC	–	–	–		–	**0.32**	<0.0001
	WHtR	–	–	–		–	**0.38**	<0.0001
	WHpR	–	–	–		–	**0.21**	0.016
	%BF	–	–	–		–	0.17	0.847
cAIx	BMI	–	–	–	age, height, heart rate, DBP	–	**0.14**	0.042
	WC	–	–	–		–	**0.19**	0.023
	WHtR	–	–	–		–	**0.37**	<0.0001
	WHpR	–	–	–		–	0.14	0.105
	%BF	–	–	–		–	0.10	0.258
cSBP	BMI	–0.09	0.005	0.005	SBP, age, DBP, height, heart rate, HDL cholesterol	0.90	**0.21**	0.014
	WC	–	–	–		–	**0.29**	<0.0001
	WHtR	–	–	–		–	**0.37**	<0.0001
	WHpR	–	–	–		–	**0.19**	0.026
	%BF	–	–	–		–	0.05	0.539

Data for anthropometric measures, showed as nonsignificant predictors in MLR, are not shown. PWV – pulse wave velocity; cAIx – central augmentation index; cSBP – central systolic blood pressure; PP – pulse pressure; BMI – body mass index; WHtR – waist-height ratio; WC – waist circumference; WHpR – waist-hip ratio;%BF – percentage of body fat; DBP – diastolic blood pressure; SBP – systolic blood pressure.

Although it has been also increasingly criticized, our results indicate that it is still a valuable predictor.

Another parameter, WC, measures both abdominal subcutaneous and intra-abdominal amount of fat, and it has also been confirmed as a predictors of obesity-related health risk [9]. The weakness of the measure is that it does not take into account a person's stature. Two people with the same WC can have different amounts of fat depending on their height [43]. Therefore, a correction of WC with height was proposed. We found that the "corrected" measure, WHtR, was as good a parameter as WC in the females, indicating their equal usefulness in practice. This is in line with the study of Nordstrand at al, who also showed WHtR and WC to be predictors of arterial stiffness in obese females [18].

Lack of association of the skinfold assessed%BF with arterial stiffness could be explained by the fact that it depends on the amount of peripheral subcutaneous fat, regardless of the amount of visceral fat. Difficulties in estimation of the fat amount and the use of standardized estimation formula, which were not validated in the investigated population, are likely reasons that%BF turned out to be an insignificant predictor. Finally, subcutaneous fat is considered to be a cardiovascular protective [44,45].

The possible reason why another measure, WHpR, was not predicting arterial stiffness may be that hip circumference reflects different aspects of body composition, including muscle mass, fat mass and skeletal frame [46]. Thus, a reduction in weight usually results in a reduction of both waist and hip circumferences, and this will not necessarily result in changes in waist-hip ratio [47]. In addition, several studies showed that hip circumference is even negatively associated with health risk [48,49]. This may partially explain why WHpR varies from weak to strong depending on population sample.

WC and WHtR were the only measures predicting arterial stiffness in the female, but not in the male group. This sex difference in association of anthropometric measures with arterial stiffness was also found by other authors, who showed that greater number of anthropometric measures were associated with arterial stiffness in women (both non-obese and obese) compared to men [18,50]. In addition, our study also showed that different arterial stiffness indices were influenced by various confounding factors. Underlining mechanisms explaining the described differences are yet to be examined.

The limitations of this study include the cross-sectional nature of the study design, without a possibility for longitudinal follow-up. Further, the estimates of percentage of body fat mass could have been a possible source of bias, since they were based on the anthropometric measurements of skinfold thickness and not other methods such as bioelectrical impedance or dual energy X-ray absorptiometry [51].

Conclusions

The association of anthropometric measures of body composition and arterial stiffness in healthy, generally non-obese subjects suggests that BMI, WC and WHtR are predictors of arterial stiffness in the females and BMI in the males. The associations of anthropometric measures with arterial stiffness confounded by different factors (age, blood pressures, height, heart rate, blood lipids, smoking) indicate the necessity for thorough regression analysis in similar studies.

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Conflict of interest

We declare no direct or indirect financial interest in the results of this study.

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