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ORIGINAL ARTICLE

The influence of obesity and metabolic risk variables on brachial-ankle pulse wave velocity in healthy adolescents

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Measurement of brachial-ankle pulse wave velocity (baPWV) is recognized as a simple and practical method for assessing arterial stiffness. We determined whether the baPWV of adolescents is affected by obesity and its associated metabolic risk variables. A cross-sectional sample of 754 apparently healthy adolescents (383 men and 371 women), aged 15–17 years, was recruited for this study. baPWV was measured by a simple automatic oscillometric technique. Adiposity measures, blood pressure, serum lipoproteins, fasting glucose and insulin were evaluated. The baPWV of the adolescents was significantly higher in men than in women and increased with age in both genders. After being statistically adjusted for age and gender, baPWV was significantly correlated with body mass index, percent body fat, waist-to-height ratio, systolic and diastolic blood pressures, mean arterial pressure, triglycerides, high-density lipoprotein cholesterol (HDL-C), atherogenic index, glucose, insulin, and homoeostasis model assessment of insulin resistance (HOMA-IR). In the multivariate regression analysis, mean arterial pressure, atherogenic index, HOMA-IR, systolic blood pressure and age were found to be significant determinants of baPWV ($P<0.001$). An increasing number of clustered risk variables, including high values (>gender-specific top quartiles) of waist-to-height ratio, mean arterial pressure, atherogenic index and HOMA-IR showed a graded association with baPWV ($P<0.001$ for trend). These results suggest that obesity and its associated metabolic abnormalities are important factors in the increased baPWV of adolescents and that baPWV may be useful in investigating early arterial wall changes in this population.
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Keywords: brachial-ankle pulse wave velocity; arterial stiffness; adolescents; obesity; metabolic risk variables

Introduction

Increasing arterial stiffness, one of the pathological symptoms of vascular damage, is believed to play a part in the development of atherosclerotic cardiovascular diseases.[1,2] Obesity in adults is often associated with such complications as hypertension, glucose intolerance and dyslipidaemia.[3] Clustering of these metabolic disturbances contributes to the acceleration of vascular stiffening and atherosclerosis.[4] In recent decades, the prevalence of childhood obesity has been increasing in developed countries.[5,6] Some studies have shown that severe obesity in teenagers is associated with an adverse metabolic profile[7,8] and produces endothelial dysfunction and reduced arterial distensibility.[9,10] Furthermore, the early structural changes are a sign of an increased risk of developing atherosclerosis in adulthood.[11,12] These observations emphasize not only the importance of strategies to control obesity and its metabolic consequences but also the need to evaluate arterial wall properties early in life.

Arterial stiffness can be assessed by pulse wave velocity (PWV),[13] which is associated with systemic atherosclerosis at various sites in the vascular tree.[14] In recent years, brachial-ankle PWV (baPWV) has been utilized as a simple, convenient and automatic method of measuring PWV, and it is considered useful for screening arterial stiffness in primary care settings and in large populations.[15,16] Therefore, baPWV measurement may be suitable for the assessment of arterial wall properties in adolescents, although few studies have been conducted in this generation.[17–19] The purpose of this study was to determine whether baPWV is affected by obesity and its associated metabolic abnormalities and whether baPWV is applicable to the investigation of the early progression of arterial stiffness in healthy adolescents.

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Materials and methods

Study subjects

We conducted health-screening examinations of adolescents in high schools in Japan between 2002 and 2007. From the participants, a cross-sectional sample of apparently healthy adolescents (383 male and 371 female subjects aged 15–17 years) was included in the analyses of this study. The subjects had no history of hypertension, syndromal obesity, diabetes mellitus, dyslipidaemia or renal disease. Individuals who had electrocardiographic evidence of coronary disease or cardiac arrhythmia were also excluded.

Written informed consent as well as clearance for the examination data to be used were obtained from the subjects and their guardians after they had received an explanation of the study aim and procedures. The protocol was approved by the Ethics Committee of Wakayama Medical University.

Obesity and metabolic risk variables

Anthropometric measurements were made with each subject in light clothing without shoes. Weight was measured with a precalibrated digital scale and height was measured with a portable stadiometer. Body fat mass was estimated from total the body resistance, measured with a bioelectrical impedance analyzer (TBF-310, TANITA Co., Tokyo, Japan). Waist circumference was measured at the end of normal expiration at the midpoint between the iliac crest and the lower edge of the ribs in the midaxillary line using a standard non-stretchable flexible measuring tape. Waist-to-height ratio (WHR) was calculated as an index of visceral fat accumulation.

When the subject was in a supine position, brachial arterial blood pressure (BP) was measured three times in the right arm with a digital BP monitor (HEM907, OMRON Co., Tokyo, Japan). The average of the last two readings was used to derive the representative value for systolic BP (SBP) and diastolic BP (DBP). The mean arterial pressure (MAP) was calculated as $MAP = DBP + (SBP - DBP)/3$.

After the subjects had fasted for more than 8 h overnight, blood samples were obtained from the antecubital vein for the measurement of serum concentrations of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides, fasting plasma glucose and fasting serum insulin. The atherogenic index was calculated as a measure of dyslipidaemia using the following formula: (TC ($mmol\,l^{-1}$) −HDL-C ($mmol\,l^{-1}$))/HDL-C ($mmol\,l^{-1}$). Insulin resistance was estimated by the homoeostasis model assessment of insulin resistance (HOMA-IR) from glucose and insulin values. The calculations were performed as follows: fasting insulin ($\mu U\,ml^{-1}$) × fasting glucose ($mmol\,l^{-1}$)/22.5.

Pulse wave velocity

Brachial-ankle PWV was measured using a volume-plethysmographic apparatus (form ABI/PWV Colin Co., Komaki, Japan) with an appropriate cuff size. Before the test, each subject lay in a supine position for more than 10 min in a temperature-controlled, quiet room. Measurements obtained with this apparatus have been shown to have good reproducibility and to be highly correlated with aortic PWV measured using a catheter-tipped manometer.[15] Briefly, with this apparatus, waveform data were obtained from a volume plethysmographic sensor placed in cuffs on both brachia and both ankles, and time intervals (T) between the wave fronts of the brachia and those of the ankles were calculated. The distance (L) between the heart and sampling points was calculated automatically according to the subject's height. The baPWV was calculated using the following formula: $baPWV = L/T$ ($L = La - Lb$, where 'La' is the path length from the heart to the ankle and 'Lb' is the path length from the heart to the brachium). The mean of the right and left baPWV was used for the analysis because there was a highly significant positive correlation between the left and right baPWVs ($r = 0.94$, $P < 0.001$).

Statistical analyses

Results are expressed as mean ± s.d. unless otherwise stated. The gender-based differences in the population were compared using the t-test. The correlations of baPWV with obesity and metabolic risk variables were assessed with univariate analysis and multivariate linear regression analysis adjusted for age and gender. Furthermore, multivariate regression analyses were performed to investigate significant determinants of baPWV. The following recognized relevant factors were entered in the models as explanatory variables: body mass index, body fat mass, WHR, SBP, DBP, MAP, triglycerides, TC, HDL-C, atherogenic index, glucose, insulin and HOMA-IR. In the analyses, age and gender were forced into the models as covariates because the baPWV of adolescents may be influenced by these factors. Univariate one-way analysis of covariance was used to test the differences in baPWV among subgroups who were divided according to the presence or absence of metabolic risk variables, with age included as a covariate. The null hypothesis was rejected at $P < 0.05$ as the level of significance. All calculations were performed using the SPSS statistical package 12.0 for Windows (SPSS Software Inc., Chicago, IL, USA).

Results

The anthropometric, haemodynamic and blood biochemical characteristics by gender are shown in Table 1. There were no significant differences in mean age, triglycerides or atherogenic index between male and female subjects. Height, body mass index, waist circumference, SBP, DBP, MAP, baPWV and glucose were significantly higher in male

Table 1 Anthropometric, haemodynamic and blood biochemical characteristics of the study population

Variables	*Male subjects* (n = *383*)	*Female subjects* (n = *371*)	P-*value*
Age (years)	16.3 ± 0.8	16.2 ± 0.8	0.612
Height (cm)	170.7 ± 6.3	159.3 ± 5.8	<0.001
Body mass index (kg/m^2)	21.2 ± 2.8	20.6 ± 2.5	0.004
Body fat mass (%)	18.9 ± 5.4	25.8 ± 4.8	<0.001
Waist circumference (cm)	72.6 ± 7.5	69.1 ± 5.7	<0.001
Brachial-ankle pulse wave velocity (cm s^{-1})	1012 ± 114	963 ± 103	<0.001
Systolic blood pressure (mm Hg)	116.6 ± 10.3	106.2 ± 8.3	<0.001
Diastolic blood pressure (mm Hg)	60.7 ± 7.4	57.6 ± 6.1	<0.001
Mean arterial pressure (mm Hg)	79.3 ± 7.7	73.8 ± 6.3	<0.001
Heart rate (beat per min)	63.7 ± 9.8	65.4 ± 10.4	0.039
Triglycerides (mmol l^{-1})	0.69 ± 0.39	0.64 ± 0.29	0.097
Total cholesterol (mmol l^{-1})	4.29 ± 0.65	4.60 ± 0.70	<0.001
High-density lipoprotein cholesterol (mmol l^{-1})	1.67 ± 0.34	1.83 ± 0.39	<0.001
Atherogenic index	1.65 ± 0.58	1.58 ± 0.50	0.103
Fasting plasma glucose (mmol l^{-1})	4.90 ± 0.38	4.83 ± 0.39	0.022
Fasting serum insulin (pmol l^{-1})	50.6 ± 27.9	61.1 ± 27.8	<0.001
HOMA-IR	1.61 ± 1.00	1.91 ± 0.92	<0.001

Abbreviations: HOMA-IR, homoeostasis model assessment of insulin resistance.
Values are mean ± s.d.

subjects. In contrast, percent body fat, heart rate, TC, HDL-C, insulin and HOMA-IR were significantly higher in female subjects than in male subjects.

In male subjects, the mean values of baPWV at 15, 16 and 17 years were 979 ± 121, 1002 ± 105 and 1052 ± 102 cm s^{-1}, respectively. In female subjects, the mean values were 934 ± 97, 951 ± 96 and 980 ± 94 cm s^{-1}, respectively. A significant difference in baPWV was observed between genders in all age groups ($P<0.01$).

The correlations of baPWV with adiposity measures and metabolic risk variables by univariate regression analyses are shown in Table 2. In both male and female subjects, all variables except TC or glucose were significantly associated with baPWV. However, the magnitude of the correlation with baPWV differed between genders. After age and gender were adjusted for, baPWV was significantly correlated with body mass index, percent body fat, WHR, SBP, DBP, MAP, triglycerides, HDL-C, atherogenic index, glucose, insulin and HOMA-IR.

The results of stepwise multiple linear regression analysis investigating significant determinants of baPWV in each component of metabolic syndrome criteria are shown in Table 3. In the regression model, using adiposity indices of this study as explanatory variables, body fat mass and WHR, but not body mass index were significant determinants of baPWV. Among the parameters of BP, both MAP and SBP were selected in the model. However, the standardized regression coefficient for MAP was much greater than that for SBP. The atherogenic index and triglycerides were the lipoprotein parameters that determined baPWV. A stronger association was found in the atherogenic index, one of the measures of dyslipidaemia. Similarly, HOMA-IR, an estimation of insulin resistance, was selected, instead of glucose and insulin, as the best predictor of baPWV in the model.

Table 2 Correlation coefficients of brachial-ankle PWV with variables by univariate regression analysis

Variables	*Male subjects* (n = *383*)	*Female subjects* (n = *371*)	*Study subjects*[a] (n = *754*)
Age	0.182*	0.124*	—
BMI	0.329**	0.243**	0.278**
Body fat mass	0.340**	0.327**	0.387**
WHR	0.347**	0.283**	0.307**
SBP	0.594**	0.495**	0.610**
DBP	0.523**	0.504**	0.508**
MAP	0.597**	0.542**	0.594**
TG	0.266**	0.239**	0.244**
TC	0.099	0.021	0.050
HDL-C	−0.265**	−0.244**	−0.255**
AI	0.339**	0.319**	0.318**
GLU	0.251**	0.040	0.147**
IRI	0.333**	0.262**	0.302**
HOMA-IR	0.352**	0.258**	0.311**

Abbreviations: AI, atherogenic index; BMI, body mass index; DBP, diastolic blood pressure; GLU, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homoeostasis model assessment of insulin resistance; IRI, fasting serum insulin; MAP, mean arterial pressure; PWV, pulse wave velocity; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WHR, waist-to-height ratio.
[a]Correlation coefficients are adjusted for age and gender.
*$P<0.05$, **$P<0.001$.

The selected parameters in each component of metabolic syndrome together with age and gender were used to examine the independent associations with baPWV (Table 4). In the multivariate regression model, the MAP, atherogenic index, HOMA-IR, SBP and age were found to be factors that were independently associated with baPWV. Other variables, such as body fat mass, WHR, triglycerides and gender were not selected as significant determinants.

On the basis of the results of the multivariate analysis, we used WHR, MAP, atherogenic index

Table 3 Associations of brachial-ankle PWV with the parameters in each component of metabolic syndrome by stepwise multivariate regression analysis

Variables[a]	*Regression coefficient*	*s.e.*	*β*	t	P-*value*
Adiposity index ($R^2 = 0.170$, $P < 0.001$)					
Body fat mass	4.357	1.226	0.243	3.553	<0.001
WHR	418.651	154.027	0.153	2.718	0.007
Age	14.944	4.837	0.111	3.090	0.002
Gender[b]	82.696	11.121	0.372	7.436	<0.001
Blood pressure ($R^2 = 0.364$, $P < 0.001$)					
MAP	6.470	0.914	0.447	7.077	<0.001
SBP	1.493	0.693	0.146	2.156	0.031
Age	13.771	3.246	0.114	4.243	<0.001
Gender[b]	−0.163	6.990	−0.001	−0.023	0.981
Lipid profile ($R^2 = 0.172$, $P < 0.001$)					
AI	52.624	8.218	0.260	6.403	<0.001
TG	39.716	13.106	0.123	3.030	0.003
Age	15.742	4.823	0.117	3.264	0.001
Gender[b]	42.553	7.983	0.191	5.330	<0.001
Glucose tolerance index ($R^2 = 0.155$, $P < 0.001$)					
HOMA-IR	34.913	4.110	0.311	8.496	<0.001
Age	19.514	4.874	0.145	4.004	<0.001
Gender[b]	57.691	8.146	0.259	7.082	<0.001

Abbreviations: AI, atherogenic index; HOMA-IR, homoeostasis model assessment of insulin resistance; MAP, mean arterial pressure; PWV, pulse wave velocity; SBP, systolic blood pressure; TG, triglycerides; WHR, waist-to-height ratio.
Body mass index, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, fasting plasma glucose and fasting serum insulin were not selected as a significant determinant in the relevant model.
[a]Age and gender were forced into all regression models as a covariate.
[b]Male subjects: 1, female subjects: 0.

Table 4 Associations of brachial-ankle PWV with the selected parameters in each component of metabolic syndrome by stepwise multivariate regression analysis

Variables[a]	*Regression coefficient*	*s.e.*	*β*	t	P-*value*
MAP	5.097	1.041	0.347	4.895	<0.001
AI	33.952	6.434	0.168	5.277	<0.001
HOMA-IR	15.138	3.622	0.135	4.179	<0.001
SBP	2.120	0.782	0.204	2.711	0.007
Age	13.482	4.039	0.100	3.338	0.001
Gender[b]	−1.322	8.010	−0.006	−0.165	0.869

Abbreviations: AI, atherogenic index; HOMA-IR, homoeostasis model assessment of insulin resistance; MAP, mean arterial pressure; PWV, pulse wave velocity; SBP, systolic blood pressure.
[a]Values entered in the model were body fat mass, waist-to-height ratio, mean arterial pressure, systolic blood pressure, atherogenic index, triglycerides and homoeostasis model assessment of insulin resistance. Age and gender were forced into the model as a covariate.
[b]Male subjects: 1, female subjects: 0.
Adjusted $R^2 = 0.425$, $P < 0.001$.

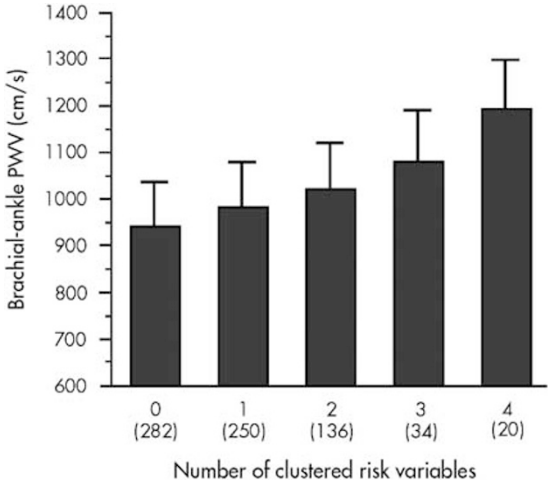

Figure 1 Comparisons of baPWV among subjects grouped according to the number of clustered metabolic risk variables. Vertical bars indicate mean ± s.d. Values in parentheses are numbers of subjects. Data were analysed using univariate one-way analysis of covariance, with age as a covariate. The *P* for trend was <0.001.

and HOMA-IR as the representatives in each component of metabolic syndrome. Subjects were defined as having components of metabolic syndrome if they had high values (>gender-specific top quartiles) for the four metabolic syndrome variables. For male subjects, the cutoff points for WHR, MAP (mm Hg), atherogenic index and HOMA-IR were 0.45, 85, 2.0 and 2.0, respectively; for female subjects, the cutoff points were 0.47, 80, 2.0 and 2.5, respectively. As shown in Figure 1, mean values of baPWV increased proportionally with an increasing number of clustered risk variables (941 ± 96, 983 ± 97, 1020 ± 101, 1079 ± 110 and 1192 ± 104 cm s^{-1}; $P < 0.001$ for trend).

When a metabolic syndrome was identified by the presence of a high value of WHR together with two high values of MAP, atherogenic index or HOMA-IR,

a total of 54 subjects (7.2%) satisfied the criteria for metabolic syndrome. The mean value of baPWV was significantly higher in the subjects with metabolic syndrome than in those without metabolic syndrome (1129 ± 122 vs $976 \pm 103\,cm\,s^{-1}$, one-way analysis of covariance $P<0.001$).

Discussion

The present cross-sectional study of healthy adolescents showed that baPWV was closely correlated with age and differed between genders, but BP, lipid profiles, insulin resistance and all adiposity measures were significantly related to baPWV after being statistically adjusted for the impact of age and gender. Clustering such metabolic risk variables contributed to the acceleration of an increase in baPWV. Therefore, obesity and its associated metabolic abnormalities are considered as important determinants of the baPWV of adolescents. The data lend support to the idea that the baPWV measurement is applicable to the assessment of the early progression of arterial stiffness and can provide useful information on the atherosclerotic cardiovascular risk of individuals during adolescence.

In population studies, there are several noninvasive ways to assess atherosclerotic vascular damage.[15,16,20,21] PWV is one of the functional markers of vascular wall changes and mainly related to arterial elastic properties.[22] PWV is generally measured between the carotid and femoral arteries (carotid–femoral PWV). There are some reports showing that the carotid–femoral PWV is a maker of the severity of vascular damage and the prognosis of cardiovascular diseases.[2,23] BaPWV has been utilized as a simple, convenient and automatic method of PWV measurement. Because the baPWV is determined by brachial-ankle arterial pressure wave measurements using a fully automated device, it does not agree with the carotid–femoral PWV. However, the baPWV has been shown to have high correlation with invasively derived carotid–femoral PWV.[15] Likewise, although the carotid–femoral PWV is an established method of measuring PWV, this parameter cannot be obtained simply enough for screening of a general population. The measurement of baPWV has an advantage in primary care settings and in large population studies because its administration does not require special skills and is easy, quick and relatively free from operator bias compared with the other vascular assessments.[24,25]

The baPWV of adolescents in this study increased gradually with increasing age in both male and female subjects. Moreover, in multivariate regression analyses, age was a significant determinant of baPWV. In adults, the increase in PWV with age is mainly due to a decrease in elasticity caused by the degeneration of the arterial wall.[22] It is speculated, however, that the baPWV in adolescence is more strongly associated with the increase in cardiac output than with the decrease in elastin and increase in collagen. Adolescents are growing physically; therefore, increased cardiac output due to the development of cardiovascular system increases the arterial BP and also affects the baPWV. It is well known that BP directly affects pulse waves, and variations of BP are associated with PWV. In addition, some studies have reported that baPWV is strongly influenced by gender in adults and that the difference is due to the beneficial effect of female hormones on arterial stiffness.[26,27] In this study, the baPWV of adolescents was higher in male than in female subjects, and the difference was more evident with increasing age. This finding suggests that the influence of sex hormones contributes to arterial stiffness in postpubertal female adolescents. However, the relatively low cardiac output and arterial BP in female subjects appeared to account for an appreciable part of the gender difference in the PWV of adolescents.

In concordance with the results of earlier studies,[17,18] the baPWV of adolescents in this study was influenced by age and gender. However, a multivariate regression analysis revealed that MAP, atherogenic index, HOMA-IR and SBP were independently associated with baPWV after statistically adjusted for the impact of age and gender. The findings are important for understanding the determinants of baPWV in adolescence. It is suggested that in addition to the development of cardiovascular system that is accompanied by arterial pressure increase, obesity and its associated metabolic consequences contribute to the acceleration of baPWV of adolescents. Although mechanisms by which obesity is linked to arterial disease remain unclear, excess body fat, accumulation of abdominal visceral fat and large waist circumference have been identified as risk factors for accelerated arterial stiffening.[28,29] Obesity in adults is often associated with complications, such as hypertension, glucose intolerance and dyslipidaemia.[3] We found that obesity was related to similar changes in the metabolic profiles in adolescence and that all adiposity measures were significantly correlated with baPWV. Accordingly, the vascular effects of obesity may occur even in adolescents, who are at a very early stage of vascular aging. However, in a stepwise multivariate regression model, none of the adiposity measures was selected as an independent determinant of baPWV. The result suggests that relation of obesity to baPWV is largely mediated by the presence of raised BP, dyslipidaemia, insulin resistance and impaired glucose tolerance.

We also revealed a cumulative relationship between an increasing number of components of the metabolic syndrome and baPWV. The graded nature of the relationships occurred at levels that were low as compared with the levels associated with high atherosclerotic disease risk in adult population. In accordance with the findings, some researchers have shown inverse associations between arterial distensibility measured with an ultrasound scanning

technique and several risk factors, such as cholesterol levels[11] and atherosclerotic risk factors, in children and adolescents.[30,31] The observations in the present and earlier studies indicate that arterial wall structure and function can be influenced by atherosclerotic risk factors as early as the second decade of life, and the vascular changes in adolescents may not be confined to individuals suffering from severe obesity, hypertension, hyperlipidaemia or diabetes mellitus. This fact emphasizes not only the importance of strategies to control obesity and its metabolic consequences but also the need to evaluate arterial wall properties early in life.

The results of this study have indicated that baPWV has potential as a useful indicator of atherosclerotic cardiovascular risk over other conventional indicators in adolescents. However, as mentioned above, the baPWV of adolescents is influenced by age and gender, and the impact of obesity and metabolic risk variables on baPWV might be masked by the effect of these factors. For instance, an earlier study using children of wide age range could not show the correlation of baPWV with obesity index.[17] We selected the adolescents, aged 15–17 years, as study population to clarify the relationship of obesity and metabolic risk variables with baPWV by eliminating the impact of age- and development-related changes as much as possible. The baPWV is obtained simply and non-invasively; therefore, it can be applied for the screening of early arterial wall changes in adolescent population. However, some adjustments for age as well as gender are required in the interpretation of baPWV values compared with the normal standard. It is desirable that a future study with the use of a large sample size will be carried out to establish baPWV reference values for adolescents based on age and gender.

Several potential limitations of this study should be considered. First, the subjects we analysed were school-based, healthy adolescents. Persons with severe obesity, hypertension, hyperlipidaemia and hyperglycaemia were not included. Thus, it may be inappropriate to generalize all of the results obtained in this study. Our data show the associations between baPWV and the variables that may contribute to the acceleration of vascular stiffening. Therefore, baPWV is considered useful for identifying early arterial wall changes in adolescents. However, we did not compare the validity of baPWV with the other available vascular assessment techniques. In addition, because arterial stiffness is an important cause of atherosclerotic cardiovascular disease in adulthood, baPWV has the potential to provide useful information on the risk of developing such diseases. However, the prognostic significance of baPWV in adolescents must be defined in controlled long-term prospective studies.

In conclusion, increased baPWV in healthy adolescents has a significant association with the clustering of metabolic risk variables, including high values of waist circumference, BP, lipid profiles and insulin resistance. The findings suggest the importance of obesity and its associated metabolic abnormalities in the evolution of arterial stiffness in adolescents and emphasize the need for preventive strategies early in life. The baPWV may be a useful method to estimate atherosclerotic cardiovascular risk and, thereby, identify individuals who should be subject to further observation and consideration of other risk factors.

What is known about topic

- Pulse wave velocity (PWV) reflects arterial stiffness, and it is a marker of both the severity of vascular damage and the prognosis of cardiovascular diseases. Recently, the measurement of brachial-ankle PWV (baPWV) has been commonly reported as a simple and practical method for screening arterial stiffness in general population.
- Less is known whether baPWV of adolescents is affected by obesity and its associated metabolic abnormalities and whether it is applicable to the investigation of early arterial wall changes in this population.

What this study adds

- In adolescents, baPWV was positively correlated with age and differed between genders. After being statistically adjusted for age and gender, blood pressure, lipid profiles, insulin resistance and all adiposity measures were significantly related to baPWV. Clustering such metabolic risk variables at high values contributed to the acceleration of an increase in baPWV.
- The results suggest that baPWV is a useful method to estimate early arterial wall changes in adolescents and, thereby, identify individuals who should be subject to further observation and consideration of other risk factors.

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References

1 London GM, Marchais SJ, Guerin AP, Pannier B. Arterial stiffness: pathophysiology and clinical impact. *Clin Exp Hypertens* 2004; **26**: 689–699.
2 Laurent S, Katsahian S, Fassot C, Tropeano AI, Gautier I, Laloux B *et al.* Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. *Stroke* 2003; **34**: 1203–1206.
3 World Health Organization. *Report of a WHO Consultation: Definition, diagnosis and classification of diabetes mellitus and its complications: Part 1: Diagnosis and classification of diabetes mellitus*. World Health Organization, Department of Noncommunicable Disease Surveillance: Geneva, Switzerland, 1999.
4 Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J *et al.* The metabolic syndrome and total and cardiovascular disease

mortality in middle-aged men. *JAMA* 2002; **288**: 2709–2716.
5 Matsushita Y, Yoshiike N, Kaneda F, Yoshita K, Takimoto H. Trends in childhood obesity in Japan over the last 25 years from the national nutrition survey. *Obes Res* 2004; **12**: 205–214.
6 Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA* 2006; **295**: 1549–1555.
7 Srinivasan SR, Myers L, Berenson GS. Predictability of childhood adiposity and insulin for developing insulin resistance syndrome (syndrome X) in young adulthood: the Bogalusa Heart Study. *Diabetes* 2002; **51**: 204–209.
8 Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW *et al.* Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; **350**: 2362–2374.
9 Celermajer DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OI, Sullivan ID *et al.* Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. *Lancet* 1992; **340**: 1111–1115.
10 McGill Jr HC, McMahan CA, Zieske AW, Tracy RE, Malcom GT, Herderick EE *et al.* Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. *Arterioscler Thromb Vasc Biol* 2000; **20**: 1998–2004.
11 Leeson CP, Whincup PH, Cook DG, Mullen MJ, Donald AE, Seymour CA *et al.* Cholesterol and arterial distensibility in the first decade of life: a population-based study. *Circulation* 2000; **101**: 1533–1538.
12 McGill Jr HC, McMahan CA, Malcom GT, Oalmann MC, Strong JP. Effects of serum lipoproteins and smoking on atherosclerosis in young men and women. The PDAY Research Group. Pathobiological Determinants of Atherosclerosis in Youth. *Arterioscler Thromb Vasc Biol* 1997; **17**: 95–106.
13 Lehmann ED. Clinical value of aortic pulse-wave velocity measurement. *Lancet* 1999; **354**: 528–529.
14 van Popele NM, Grobbee DE, Bots ML, Asmar R, Topouchian J, Reneman RS *et al.* Association between arterial stiffness and atherosclerosis: the Rotterdam Study. *Stroke* 2001; **32**: 454–460.
15 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**: 359–364.
16 Yamashina A, Tomiyama H, Arai T, Hirose K, Koji Y, Hirayama Y *et al.* Brachial-ankle pulse wave velocity as a marker of atherosclerotic vascular damage and cardiovascular risk. *Hypertens Res* 2003; **26**: 615–622.
17 Niboshi A, Hamaoka K, Sakata K, Inoue F. Characteristics of brachial-ankle pulse wave velocity in Japanese children. *Eur J Pediatr* 2006; **165**: 625–629.
18 Im JA, Lee JW, Shim JY, Lee HR, Lee DC. Association between brachial-ankle pulse wave velocity and cardiovascular risk factors in healthy adolescents. *J Pediatr* 2007; **150**: 247–251.
19 Lee JW, Lee DC, Im JA, Shim JY, Kim SM, Lee HR. Insulin resistance is associated with arterial stiffness independent of obesity in male adolescents. *Hypertens Res* 2007; **30**: 5–11.
20 Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW *et al.* Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study. *Stroke* 1995; **26**: 386–391.
21 Mullen MJ, Kharbanda RK, Cross J, Donald AE, Taylor M, Vallance P *et al.* Heterogenous nature of flow-mediated dilatation in human conduit arteries *in vivo*: relevance to endothelial dysfunction in hypercholesterolemia. *Circ Res* 2001; **88**: 145–151.
22 Sawabe M, Takahashi R, Matsushita S, Ozawa T, Arai T, Hamamatsu A *et al.* Aortic pulse wave velocity and the degree of atherosclerosis in the elderly: a pathological study based on 304 autopsy cases. *Atherosclerosis* 2005; **179**: 345–351.
23 Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA *et al.* Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. *Circulation* 2006; **113**: 657–663.
24 Sankatsing RR, Fouchier SW, de Haan S, Hutten BA, de Groot E, Kastelein JJ *et al.* Hepatic and cardiovascular consequences of familial hypobetalipoproteinemia. *Arterioscler Thromb Vasc Biol* 2005; **25**: 1979–1984.
25 Berry KL, Skyrme-Jones RA, Meredith IT. Occlusion cuff position is an important determinant of the time course and magnitude of human brachial artery flow-mediated dilation. *Clin Sci (Lond)* 2000; **99**: 261–267.
26 London GM, Guerin AP, Pannier B, Marchais SJ, Stimpel M. Influence of sex on arterial hemodynamics and blood pressure. Role of body height. *Hypertension* 1995; **26**: 514–519.
27 Tomiyama H, Yamashina A, Arai T, Hirose K, Koji Y, Chikamori T *et al.* Influences of age and gender on results of noninvasive brachial-ankle pulse wave velocity measurement—a survey of 12517 subjects. *Atherosclerosis* 2003; **166**: 303–309.
28 Amar J, Ruidavets JB, Chamontin B, Drouet L, Ferrières J. Arterial stiffness and cardiovascular risk factors in a population-based study. *J Hypertens* 2001; **19**: 381–387.
29 Resnick LM, Militianu D, Cunnings AJ, Pipe JG, Evelhoch JL, Soulen RL. Direct magnetic resonance determination of aortic distensibility in essential hypertension: relation to age, abdominal visceral fat, and *in situ* intracellular free magnesium. *Hypertension* 1997; **30**: 654–659.
30 Whincup PH, Gilg JA, Donald AE, Katterhorn M, Oliver C, Cook DG *et al.* Arterial distensibility in adolescents: the influence of adiposity, the metabolic syndrome, and classic risk factors. *Circulation* 2005; **112**: 1789–1797.
31 Urbina EM, Brinton TJ, Elkasabany A, Berenson GS. Brachial artery distensibility and relation to cardiovascular risk factors in healthy young adults (The Bogalusa Heart Study). *Am J Cardiol* 2002; **89**: 946–951.