Pulse Wave Velocity, Blood Pressure and Adipocytokines in Young Adults. The Rio de Janeiro Study

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Abstract

Background: Data on noninvasive vascular assessment and their association with cardiovascular risk variables are scarce in young individuals.

Objective: To evaluate the association between pulse wave velocity and blood pressure, anthropometric and metabolic variables, including adipocytokines, in young adults.

Methods: A total of 96 individuals aged 26 to 35 years (mean 30.09 ± 1.92; 51 males) were assessed in the Rio de Janeiro study. Pulse wave velocity (Complior method), blood pressure, body mass index, glucose, lipid profile, leptin, insulin, adiponectin and insulin resistance index (HOMA-IR) were analyzed. Subjects were stratified into three groups according to the PWV tertile for each gender.

Results: The group with the highest pulse wave velocity (PWV) tertile showed higher mean systolic and diastolic blood pressure, mean blood pressure, body mass index, insulin, and HOMA-IR, as well as lower mean adiponectin; higher prevalence of diabetes mellitus/glucose intolerance and hyperinsulinemia. There was a significant positive correlation of PWV with systolic blood pressure, diastolic blood pressure, pulse pressure and mean blood pressure, body mass index, and LDL-cholesterol, and a negative correlation with HDL-cholesterol and adiponectin. In the multiple regression model, after adjustment of HDL-cholesterol, LDL-cholesterol and adiponectin for gender, age, body mass index and mean blood pressure, only the male gender and mean blood pressure remained significantly correlated with PWV.

Conclusion: PWV in young adults showed a significant association with cardiovascular risk variables, especially in the male gender, and mean blood pressure as important determinant variables. The findings suggest that PWV measurement can be useful for the identification of vascular impairment in this age group. (Arq Bras Cardiol. 2013;100(1):60-66)

Keywords: Blood Pressure; Risk Factors; Pulse; Vascular Diseases / prevention & control; Adiponectin.

Introduction

It is currently accepted that atherosclerosis has its origin in childhood[1-3]. The search for markers of preclinical atherosclerosis/arteriosclerosis is directed to the noninvasive evaluation of the vascular involvement and some studies have demonstrated the association of risk factors (RF) in young individuals with impaired arterial elasticity in adulthood[4].

Among the markers of arterial disease, arterial stiffness has shown to be an important parameter for the assessment of cardiovascular risk. Of the several methods for the assessment of arterial stiffness, measurement of the carotid-femoral pulse wave velocity (PWV) is considered the gold standard method because it is relatively easy to perform and there is a large body of evidence demonstrating its association with cardiovascular disease, regardless of traditional risk factors in different populations[5,6].

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Previous studies on the association between PWV and conventional RF in young individuals are limited and the results are partially controversial[4]. In the Bogalusa study[7], systolic blood pressure (SBP), body mass index (BMI) and HDL-cholesterol (HDL-c) in childhood correlated inversely with PWV in adulthood. In another study[8], mean blood pressure (MBP), BMI, gender and homocysteine levels were independently associated with PWV. In the Arya study[9], no association was observed between blood pressure (BP) in adolescence and PWV in adulthood.

Therefore, some authors have suggested that in normotensive young adults, PWV is most likely determined by other factors, rather than those found in older individuals with hypertension[10]. They may be associated with primary abnormalities in the structure or function of the vascular wall[4,11].

Studies on this subject have been carried out in young populations, seeking to evaluate RF and early vascular abnormalities. Such information could be useful for better identification and risk stratification in young adults[12].

The present study is part of the Rio de Janeiro study (ERJ)[13-15], a longitudinal line of research on blood pressure (BP) and other cardiovascular RF in children and adolescents and their families,

which has been developed since 1983 and aims to evaluate the association between PWV and BP, anthropometric and metabolic variables, including adipocytokines, in young adults.

Methods

We evaluated 96 individuals (51 men), from the ERJ cohort, aged 26 to 35 years (mean 30.09 ± 1.92 years). All of them underwent the evaluation protocol which included measurement of BP, waist circumference (WC), weight, height, and BMI calculation, as well as measurement of blood glucose, total cholesterol, HDL cholesterol and triglycerides (TG) levels after a 12-hour fasting. Leptin, insulin, adiponectin levels were also determined; the insulin resistance index HOMA-IR was calculated and PWV was obtained.

The individuals were stratified by gender according to PWV tertiles in three groups: 1st tertile (Group 1) comprising men with PWV < 8.69 m/s and women with PWV < 7.66 m/s; 2nd tertile (Group 2) consisting of men with PWV ≥ 8.69 m/s and women with PWV ≥ 7.66 m/s; 3rd tertile (Group 3) consisting of men with PWV ≥ 9.65 m/s and women with PWV ≥ 8.31 m/s (Table 1).

WC was obtained according to the procedure described by Callaway et al[16] and defined as increased when > 102 cm in men and > 88 cm in women, according to the VI Brazilian Guidelines on Hypertension[17].

Blood pressure was measured on the brachial artery using a mercury sphygmomanometer, with a cuff of appropriate size and width, according to the recommendations of the Brazilian Society and Cardiology (SBC)[17]. Two BP measurements were obtained at a five-minute interval and the final measurement was used for the analysis. Subjects were considered hypertensive when the blood pressure values were ≥ 140 x 90 mmHg, according to the recommendations of the VI Brazilian Guidelines on Hypertension[17].

Plasma glucose, total cholesterol, HDL-cholesterol and triglyceride levels were determined using the Konelab kit (BI WINER 3000). Cholesterol levels were determined based on the values established by the IV Brazilian Guidelines on Dyslipidemia and Atherosclerosis Prevention Guidelines of the Department of Atherosclerosis of the Brazilian Society of Cardiology[18]. Glucose values were interpreted according to the recommendations of the American Diabetes Association[19].

Quantitative analysis of serum insulin, leptin and adiponectin levels were performed by fluoroimmunoassay (Luminex xMAP, Luminex Corporation, 12212 Technology Blvd. Austin, TX 78727 U.S.) with the kits CAT#HGT-68K-02 for insulin and leptin and CAT#HCVD1-67AK-03 for adiponectin. For the determination of hyperinsulinemia a cutoff of 20 (μU/mL) was used, as recommended by the manufacturer of the method used.

Table 1 – Values corresponding to PWV (m/s) tertiles for gender

	Tertile 1	Tertile 2	Tertile 3
Men (n = 51)	< 8.69	≥ 8.69 and < 9.65	≥ 9.65
Women (n = 45)	< 7.66	≥ 7.66 and < 8.31	≥ 8.31

The insulin resistance index HOMA-IR was calculated according to the equation proposed by Mathews in 1995: HOMA-IR = fasting insulin (μU/mL) x fasting glucose (mmol/L) / 22.5[20].

Pulse wave velocity (PWV) was measured using the automated computerized system Complior (Complior, Colson, Garger les Genosse, France - Createch Industrie) according to the methodology described by Asmar et al[21]. The mean of 10 measurements was considered for each individual. All measurements were obtained by the same examiner.

ANOVA was used to compare the means of continuous variables complemented by paired analysis. The Chi-square test was used to compare the frequency distributions of categorical variables for independent samples. Linear regression, complemented by analysis of variance, was used for correlation of continuous variables. The level of significance was set at 5% for all analyses, assuming a probability "p" equal to or less than 0.05 to reject the null hypothesis.

The study protocol was approved by the Institutional Ethics and Research Committee and all subjects gave written consent to participate in the study.

Results

Tables 2 and 3 show the characteristics of the study population stratified by PWV tertiles, regarding pressure, anthropometric and metabolic variables.

The group with the highest PWV tertile had higher SBP, DBP, pulse pressure (PP) and MBP than the group with the lowest PWV tertile (Table 2), although the prevalence of hypertension was similar in the three groups (Table 3).

The group with the highest PWV tertile had higher mean BMI. There was no statistically significant difference between groups for the other anthropometric parameters (weight, height and waist circumference - Table 2). There was also no difference between groups regarding the prevalence of elevated waist circumference and the prevalence of overweight/obesity (Table 3).

The analysis of metabolic variables showed that the group with the highest PWV tertile had higher mean insulin and HOMA-IR, and lower mean adiponectin levels (Table 2) when compared to the other groups. The third tertile group also showed a higher prevalence of diabetes mellitus/glucose intolerance (DM/GI) and hyperinsulinemia (Table 3).

Table 4 describes the univariate correlations of PWV with the study variables. A significant positive correlation with SBP, DBP, MBP, BMI, waist circumference, LDL-cholesterol, and a negative correlation with HDL-cholesterol and adiponectin can be observed. In the multivariate regression analysis, the inclusion of age, gender, BMI and blood pressure in the model with HDL-cholesterol, LDL-cholesterol and adiponectin, showed that PWV had a significant association only with the male gender and MBP (Table 5).

Discussion

The present study demonstrated the association of PWV with a worse cardiovascular profile, especially regarding metabolic features, such as higher BP, BMI and insulin and

Table 2 – Blood pressure, anthropometric and metabolic variables means, according to the PWV tertile

Variable (unit)	Tertile 1 n = 32	Tertile 2 n = 32	Tertile 3 n = 32	F	p	2 x 2
Age (years)	30.72 ± 1.78	29.47 ± 1.56	30.09 ± 2.22	3.553	0.033	1 > 2.3 = 1. 3 = 2
SBP (mmHg)	114.94 ± 14.48	121.00 ± 16.20	128.56 ± 17.63	5.709	0.005	1 = 2. 2 = 3. 3 >1
DBP (mmHg)	75.75 ± 11.31	80.44 ± 12.50	86.19 ± 14.46	5.318	0.007	1 = 2. 2 = 3. 3 >1
MBP (mmHg)	88.81 ± 11.58	93.95 ± 13.21	100.31 ± 14.97	5.977	0.004	1 = 2. 2 = 3. 3 >1
PP (mmHg)	39.19 ± 9.73	40.56 ± 8.81	42.38 ± 9.20	0.954	0.389	
HR (bpm)	69.19 ± 7.80	72.84 ± 11.59	72.94 ± 10.78	1.409	0.250	
Weight (Kg)	72.88 ± 18.71	74.50 ± 18.71	80.58 ± 18.40	1.522	0.224	
Height (cm)	169.91 ± 11.12	170.30 ± 9.42	169.61 ± 8.93	0.039	0.962	
BMI (Kg/m^2)	25.03 ± 4.89	25.38 ± 4.31	28.17 ± 6.84	3.179	0.046	1=2. 2<3. 1.3
WC (cm)	87.73 ± 11.68	89.06 ± 14.19	94.35 ± 15.01	2.090	0.129	
Glucose (mg/dl)	80.00 ± 10.18	82.63 ± 12.75	87.06 ± 14.52	2.442	0.093	
TC (mg/dl)	180.23 ± 36.26	181.03 ± 36.66	189.65 ± 34.02	0.666	0.516	
HDL-c (mg/dl)	50.34 ± 16.03	50.50 ± 14.37	46.32 ± 14.65	0.708	0.496	
LDL-c (mg/dl)	112.27 ± 31.53	112.27 ± 31.95	120.75 ± 32.75	0.628	0.536	
TG (mg/dl)	100.27 ± 61.34	107.69 ± 61.56	111.28 ± 52.88	0.270	0.764	
Insulin (µU/ml)	12.26 ± 7.46	9.19 ± 8.00	16.73 ± 14.67	4.119	0.019	1 = 2. 1 = 3. 3 >2
HOMA-IR	2.49 ± 1.54	1.93±1.89	3.82±4.01	4.013	0.021	1 = 2. 1 = 3. 3 >2
Leptin (ng/ml)	13.269±12.796	17.989 ± 18.519	19.839 ± 183	1.316	0.273	
Adiponectin (ug/mL)	0.010 ± 0.004	0.008 ± 0.004	0.007 ± 0.002	4.342	0.016	1 = 2. 2 = 3. 3 <1

SBP : systolic blood pressure, DBP : diastolic blood pressure, PP : pulse pressure, MBP : mean blood pressure, HR : heart rate, BMI : body mass index, WC : waist circumference; TC : total cholesterol, HDL-c : high-density lipoprotein, LDL-c : low-density lipoprotein;[17] TG : triglycerides.

lower plasma adiponectin levels, higher HOMA-IR index and prevalence of diabetes mellitus/glucose impairment (DM / GI) and hyperinsulinemia in young adults with the highest PWV tertile.

Age and blood pressure are the major determinants of PWV. It is believed that age-related vascular stiffening is accelerated by the chronic elevation of blood pressure caused by structural and functional changes in central elastic arteries.

In turn, arterial stiffening partly promotes changes in systolic and diastolic blood pressure related to age, particularly in older individuals[5,21,22].

In individuals younger than 40 years, when the effects of aging on the arterial wall structure and consequent pattern of vascular stiffening is not yet fully developed, the conventional association between age and hypertension become less evident[23], suggesting that the increased stiffness assessed by arterial PWV in young adults is influenced by other factors such as increased sympathetic nervous system activity and increased peripheral vascular resistance[10].

In the present study, PWV showed a strong correlation with blood pressure, reflected by higher SBP, DBP, and MBP means in the group with the highest PWV tertile, as well as significant correlations of MBP with PWV, even after adjustments for age, gender and BMI.

Regarding age, the age range of the study population was too narrow and did not represent an important factor in the determination of PWV in the study population, showing no influence on the other study findings.

In relation to the anthropometric indices, this study showed a strong association of PWV with BMI and waist circumference. These findings are also in agreement with previous studies. Zebekakis et al[24] demonstrated a strong correlation between PWV and high BMI and waist-hip ratio, regardless of age, gender, ethnicity and systolic blood pressure. Two other studies controlling the interference caused by age demonstrated positive associations between PWV and several obesity indices, both in a population with a wide age range (20-77 years)[25] and in a younger population (36 years)[26].

In the present study there was no difference between groups regarding associations either with the means or with the prevalence of possible abnormalities in lipid parameters; however, PWV significantly correlated with LDL-cholesterol and HDL-cholesterol.

The evidence on the correlation between arterial stiffness and lipid levels is controversial. Wang et al[27] showed a positive association between PWV and total cholesterol and LDL-cholesterol and an inverse correlation with HDL-cholesterol, with no correlation between PWV and triglycerides (TG)[27]. On the other hand, Ferreira et al[28] could not demonstrate an association between dyslipidemia (elevated TG and low

Table 3 – Distribution of gender and presence of hypertension, overweight/obesity, diabetes/glucose intolerance and hyperinsulinemia, according to the PWV tertile

	Variable	Tertile 1 n (%)	Tertile 2 n (%)	Tertile 3 n (%)	χ^2	p
Gender	Male	17 (53.1)	17 (53.1)	17 (53.1)	0.000	1.000
	Female	15 (46.9)	15 (46.9)	15 (46.9)		
SAH	No	25 (78.1)	21 (65.6)	19 (59.4)	2.668	0.263
	Yes	07 (21.9)	11 (34.4)	13 (40.6)		
Waist	Normal	23 (71.9)	21 (65.6)	17 (53.1)	2.518	0.284
	High	09 (28.1)	11 (34.4)	15 (46.9)		
O/OB	No	16 (50.0)	16 (50.0)	12 (37.5)	1.343	0.511
	Yes	16 (50.0)	16 (50.0)	20 (62.5)		
Dyslipidemia	No	17 (53.1)	13 (40.6)	14 (43.8)	1.091	0.580
	Yes	15 (46.9)	19 (59.4)	18 (56.3)		
TC	Normal	22 (71.0)	22 (68.8)	21 (67.7)	0.079	0.961
	High	09 (29.0)	10 (31.3)	10 (32.3)		
LDL-c	Normal	20 (69.0)	20 (69.0)	17 (65.4)	0.106	0.949
	High	09 (31.0)	09 (31.0)	09 (34.6)		
HDL-c	Normal	23 (74.2)	22 (71.0)	19 (67.9)	0.288	0.866
	Low	08 (25.8)	09 (29.0)	09 (32.1)		
TG	Normal	25 (80.6)	25 (80.6)	24 (80.0)	0.005	0.997
	High	06 (19.4)	06 (19.4)	06 (20.0)		
DM/GI	No	32 (100.0)	30 (93.8)	26 (81.3)	7.636	0.022
	Yes	0 (0)	02 (06.3)	06 (18.8)		
Insulin	Normal	26 (81.3)	30 (93.8)	22 (68.8)	6.564	0.038
	High	06 (18.8)	02 (06.3)	10 (31.3)		

SAH : systemic arterial hypertension; O/OB : Overweight / Obesity; TC : total cholesterol, HDL-c : high-density lipoprotein, LDL-c : low-density lipoprotein; TG : triglycerides; DM/GI : Diabetes Mellitus/Glucose Intolerance.

HDL-cholesterol) with PWV in a population of young adult women, and a major population study[6] did not identify any influence of dyslipidemia on PWV.

As this association appears to be complex, it is possible that several existing mechanisms for the association between plasma lipids and arterial stiffness involve situations and concomitant risk factors, such as the development of atherosclerotic plaques, oxidative stress, local and systemic inflammation, endothelial dysfunction, low bioavailability of nitric oxide and endothelin action[29].

The group with the highest PWV tertile showed a higher prevalence of individuals with DM/GI, although there was no significant difference in the comparison of mean glucose levels between the groups. It is noteworthy that the group with the highest PWV tertile also showed higher serum insulin levels, higher prevalence of hyperinsulinemia and increased HOMA-IR.

Table 4 – Univariate correlations of PWV

Variable	r	p
Age	-0.028	0.786
SBP	0.505	< 0.001
DBP	0.499	< 0.001
PP	0.202	0.048
MBP	0.522	< 0.001
HR	0.184	0.072
BMI	0.286	0.005
AC	0.320	0.001
Glucose	0.197	0.058
TC	0.088	0.399
HDL-c	-0.393	< 0.001
LDL-c	0.216	0.049
TG	0.106	0.326
log Insulin	0.124	0.229
HOMA-IR	0.183	0.079
Leptin	-0.094	0.361
Adiponectin	-0.351	< 0.001

SBP : systolic blood pressure; DBP : diastolic blood pressure; PP : pulse pressure; MBP : mean blood pressure; HR : heart rate; BMI : body mass index; AC : abdominal circumference; TC : total cholesterol; HDL-c : high-density lipoprotein; LDL-c : low-density lipoprotein; TG : triglycerides; HOMA-IR : homeostasis model assessment of insulin resistance.

Table 5 – Multivariate Analysis. PWV adjusted for age, gender, BMI and MBP

Variable	PC	p
Model 1 (R^2 = 0.420, p < 0.001)		
HDLc	-0.090	0.386
Age	-0.130	0.133
Gender	-0.380	0.001
BMI	0.084	0.456
MBP	0.346	0.003
Model 2 (R^2 = 0.427, p < 0.001)		
LDLc	-0.072	0.463
Age	-0.182	0.041
Gender	-0.447	< 0.001
BMI	0.145	0.228
MBP	0.348	0.003
Model 3 (R^2 = 0.434, p < 0.001)		
Adiponectin	-0.108	0.236
Age	-0.077	0.356
Gender	-0.350	< 0.001
BMI	0.014	0.896
MBP	0.436	< 0.001

HDL-c : high-density lipoprotein; LDL-c : low-density lipoprotein; BMI : body mass index; MBP : mean blood pressure; PC : partial coefficient of correlation.

Different authors have reported that PWV is higher in diabetic[30] and glucose intolerant individuals[31], regardless of BP levels and the patient's age[32]; however, no association has been demonstrated between arterial stiffening and normal fasting glucose levels[33].

Reduced arterial elasticity can result from the direct action of hyperglycemia and/or hyperinsulinemia or may be a consequence of the action of advanced glycation end products on the vascular matrix proteins, with consequent increased production of collagen fibers[30].

The role of insulin resistance in the pathogenesis of premature vascular sclerosis may be an important early feature of subclinical disease[34]. The increase of arterial stiffness is proportional to the degree of insulin resistance, regardless of age, degree of obesity, serum lipids and blood pressure, and can be one of the mechanisms involved in this association[35], involving alterations such as endothelial dysfunction, inflammation and sympathetic activation[28].

Importantly, this study demonstrated an association between lower levels of adiponectin and arterial stiffness assessed by PWV, with a strong inverse correlation between adiponectin levels and PWV. These data are consistent with Mahmud's findings[36], which showed a significant inverse association between plasma adiponectin levels and PWV in hypertensive individuals and a negative association between adiponectin and plasma glucose, suggesting that insulin resistance, which admittedly increases PWV, may be one of the mechanisms[36].

The discovery and study of adipokines, such as leptin and adiponectin, have contributed to the understanding of the role of the adipose tissue in the metabolic homeostasis. These molecules may play an important role in the development of insulin resistance and its consequences. Serum leptin concentrations have been associated with cardiovascular risk factors, hypertension and dyslipidemia. Adiponectin is an important insulin resistance-modulating adipokine with anti-inflammatory and anti-atherogenic properties[37]. Low concentrations of adiponectin are associated with the presence of cardiovascular risk factors[38].

Windham et al[39] demonstrated that leptin was involved in the association between abdominal obesity and arterial stiffness, and that there was a correlation, independent of leptin, adiponectin and resistin, with PWV.

Gauthier et al[38] observed a positive association between PWV and leptin/adiponectin ratio adjusted for gender and age.

In this study, although BP greatly contributed to a higher PWV, metabolic variables such as HDL-cholesterol, LDL-cholesterol, insulin, HOMA-IR, glucose intolerance and hyperinsulinemia also correlated with PWV. These variables are pathophysiologically related, often coexist in young adults[10] and are associated with arterial structure and function impairment[40].

The cross-sectional nature of this study limits our ability to infer a causal relationship between the different variables analyzed and the measurement of arterial stiffness provided by PWV in young adults. Since this is an exploratory study that used several multivariate models to adjust the formulated hypotheses, it is estimated that some biases may have occurred. Thus, we believe that further studies are required to determine how the cardiovascular risk variables analyzed in this study contribute to determine arterial stiffness and, ultimately, to develop arteriosclerosis.

In conclusion, the results of this study demonstrated that the vascular involvement assessed by PWV in young individuals was significantly associated with BP, serum lipids, insulin and HOMA-IR, and adiponectin levels.

It is noteworthy that the male gender and mean blood pressure played an important role in the determination of higher PWV in young adults. These findings suggest that the noninvasive analysis of the vascular structure and function by measuring PWV can be useful for the identification of early vascular involvement in young individuals. Thus, the data shown here are added to previous studies which suggest that the structural integrity and stiffness of the arterial wall in young individuals are determined by several pathogenic mechanisms related to different cardiovascular risk factors, thereby creating a scenario of high potential for prevention in this age group.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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