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Determinants of arterial stiffness in physically active middle aged adults

Determinanţi ai rigidităţii arteriale la adulţii de vârstă medie activi fizic

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Abstract

Background. Increased arterial stiffness is considered an important predictor of cardiovascular events. It correlates with different classical cardiovascular risk factors and it may represent a cumulative measure of the impact of cardiovascular risk factors on the arterial wall. The influence of cardiovascular risk factors on arterial stiffness is not clearly established.

Aims. The aim was to evaluate the association of aortic pulse wave velocity (aPWV) and augmentation index (AIx) as parameters of arterial stiffness and cardiovascular risk factors in a group of physically active middle aged subjects.

Methods. This cross-sectional study included 59 subjects (25 males and 34 females) with normal arterial pressure and without manifest cardiovascular disease, aged 44.55 (±11.64) years. Parameters of arterial stiffness aPWV and AIx were measured using an oscillometric device.

Results. Aortic PWV positively correlated with age (r=0.65, p<0.001), fasting plasma glucose (r=0.31, p=0.02), systolic blood pressure (r=0.05, p=0.02), diastolic blood pressure (r=0.34, p=0.002), mean blood pressure (r=0.39, p=0.002) and heart rate (r=0.32, p=0.01). Brachial AIx directly correlated with age (r=0.42, p=0.01). After adjusting for age, in multiple regression analysis, the independent predictors for aPWV were fasting plasma glucose (r^2=0.32, p=0.03) and heart rate (r^2=0.33, p=0.04) and for AIx, abdominal circumference (r^2=0.22, p=0.03) and heart rate (r^2=0.22, p=0.02).

Conclusion. This study showed that fasting plasma glucose, abdominal circumference and heart rate are independent predictors of arterial stiffness. An early therapeutic intervention to optimize these parameters may reduce arterial stiffness and cardiovascular risk.

Keywords: cardiovascular risk factors, aortic pulse wave velocity, brachial augmentation index.

Rezumat

Premize. Creşterea rigidităţii arteriale este un important predictor al evenimentelor cardiovasculare. A fost corelată cu diferiţi factori de risc cardiovascular şi poate fi o consecinţă a acţiunii cumulative a acestora la nivelul peretelui vascular. Influenţa factorilor de risc asupra rigidităţii vasculare nu este clar cunoscută.

Obiective. Scopul studiului a fost de a evalua asocierea vitezei undei de puls aortice (aPWV) şi a indexului de augmentare brahial cu factorii clasici de risc cardiovascular la un grup de subiecţi de vârstă medie, fizic activi.

Metode. Acest studiu transversal a inclus 59 de subiecţi (25 de bărbaţi şi 34 de femei), cu vârsta medie de 44,55 (±11,64) ani. Parametrii rigidităţii arteriale (aPWV şi Aix) au fost determinaţi folosind un aparat oscilometric.

Rezultate. Viteza undei de puls aortice s-a corelat pozitiv cu vârsta (r=0,65, p<0,001), glicemia (r=0,31, p=0,02), presiunea arterială sistolică (r=0,05, p=0,02), presiunea arterială diastolică (r=0,34, p=0,002), presiunea arterială medie (r=0,39, p=0,002) şi frecvenţa cardiacă (r=0,32, p=0,01). Indexul de augmentare brahial s-a corelat direct cu vârsta (r=0,42, p=0,01). După controlarea vârstei, în regresie multiplă, glicemia (r^2=0,32, p=0,03) şi frecvenţa cardiacă (r^2=0,33, p=0,04) au fost predictori independenţi ai aPWV, iar pentru AIx, circumferinţa abdominală (r^2=0,22, p=0,03) şi frecvenţa cardiacă (r^2=0,22, p=0,02).

Concluzii. Acest studiu a arătat că glicemia, circumferinţa abdominală şi frecvenţa cardiacă sunt predictori independenţi ai rigidităţii arteriale. Intervenţia terapeutică precoce pentru optimizarea acestor parametri ar putea reduce rigiditatea arterială şi riscul cardiovascular.

Cuvinte cheie: factori de risc cardiovascular, viteza undei de puls aortic, indexul brachial de augmentare.

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Introduction

Cardiovascular disease is the leading cause of morbidity and mortality in industrialized countries. The risk for developing atherosclerosis is only partly explained by the contribution of well known classical cardiovascular risk factors. Over the past decade accumulating data have supported the independent value of arterial stiffness as a predictor of future cardiovascular events, in different populations (Laurent et al., 2007). Aortic pulse wave velocity (aPWV) is considered the "gold standard" method for the measurement of arterial stiffness. The determination of aPWV is a simple and non-invasive method that has shown its relevance in predicting cardiovascular events, in many epidemiological studies (Laurent et al., 2007). Arterial stiffness has also an important clinical relevance. Stiffening causes the incident and reflected waves to travel faster, leading to the early return of the reflected wave to the heart. This increases left ventricle afterload that predisposes to left ventricular hypertrophy and left ventricular dysfunction. Arterial stiffness reduces diastolic blood pressure with an alteration in coronary perfusion that causes myocardial ischemia (O'Rourke, 2008; Adji & O'Rourke, 2011). Increased pulsatile pressure may produce damage in the microcirculation of the brain and kidneys and predispose to cerebral lacunar infarction and albuminuria (Franklin et al., 1997; Lee & Oh, 2012).

Age and blood pressure are very important determinants of arterial stiffening. The relation of other traditional risk factors with arterial stiffness seems to be less clear (Ceceljia & Chowienczyk, 2009; Wilkinson et al., 2011). The aim of this study was to evaluate the relationship of arterial stiffness with classical cardiovascular risk factors in middle aged adults without known cardiovascular diseases.

Hypothesis

We considered that in active middle aged subjects, without arterial hypertension, arterial stiffness may be influenced by other classical risk factors than age and blood pressure.

Material and methods

We included in this prospective cross-sectional study 59 patients (25 males and 34 females) who were evaluated in the 2nd Internal Medicine Department from Cluj-Napoca for functional digestive diseases, between September 2011 and April 2012. The exclusion criteria were: arterial hypertension or treatment with antihypertensive drugs, known cardiovascular disease, arrhythmia, diabetes mellitus, pulmonary or renal diseases, infection, and cancer. All patients signed the informed consent and the study was approved by the ethical committee of our institution.

A complete clinical examination was performed in all patients and the presence of a family history of cardiovascular diseases was noted. The body mass index (BMI) was calculated as the ratio between weight in kilograms and the square of height (Kg/m²). Abdominal circumference was measured at the midpoint between the lowest rib and the top of the iliac crest. The parameters of glucose, fasting plasma glucose (FGP) and lipid metabolism, total cholesterol and triglycerides, were measured in all patients. Hypercholesterolemia was defined as a plasma total cholesterol level > 200 mg/dl. Subjects were defined depending on their smoking habits as being current smokers or non-smokers.

Vascular examination

Vascular parameters were measured using an oscillometric device, Arteriograph (TensioMed, Budapest, Hungary). All measurements were done under standardized conditions (Laurent et al., 2007). The Arteriograph initially measures systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP) and brachial pulse pressure (PP) in the upper arm. Then the device produces a cuff pressure that exceeds by 35 mmHg the SBP measured. Pulse pressure waves detected at this susprasystolic pressure are detected by the cuff and then sent to a computer. The software of Arteriograph analyzes the pressure waves resulting from the superposition of the descending forward wave and the reflected wave. The forward wave caused by the left ventricular systolic contraction travels forward and reflects at the aortic bifurcation, returning to the heart as a reflected wave. The distance traveled by the wave is equal to the length of the descending aorta. The length of the aorta is represented approximately by the distance between the jugular fossa and the symphysis. The travel time is the reflection time at 35 mmHg suprasystolic pressure (RT 35). PWV is calculated automatically as the ratio between the jugular fossa and the symphysis and RT 35. The augmentation index was calculated as follows: AIx=(P2-P1)/PP(%), where P2-P1 is the peak pressure difference between the early systolic pressure wave and the late systolic pressure wave and PP is the pulse pressure (Magometschnigg, 2005, Baulmann et al., 2008).

Statistical analysis

Data were expressed as means and standard deviation (mean±SD) for continuous variables and as percentage for categorical data. The mean values between two groups were compared using Mann Whitney U test and numerical correlations were established using linear correlation analysis. The independent association between the variables was examined using multiple regression analysis. $P<0.05$ was considered statistically significant. All statistical evaluations were performed using the SPSS 13.0 statistics software.

Results

The clinical characteristics of the study group are noted in Table I. There were 33.9% active smokers and no ex-smokers in this study, and 12 patients (20.3%) with hypercholesterolemia. All patients declared to be physically active.

Data are means ± standard deviations.

In linear correlation analysis, aPWV positively correlated with increasing age, fasting plasma glucose blood pressure (systolic, diastolic and mean values) and heart rate (Table II). Brachial AXi correlated with age (Table III).

Table I
Characteristics of the study population.

Parameter	Study group N=59
Age (years)	44.55±11.64
Male gender	25 (42%)
Family history of cardiovascular diseases	33(55.9%)
Smokers, n (%)	20(33.9%)
Body mass index (Kg/m²)	26±9.81
Abdominal circumference (cm)	91.2±57
Fasting plasma glucose (mg%)	101.77±45.90
Total cholesterol (mg%)	176.87±55.51
Triglycerides (mg%)	112.27±70
Systolic blood pressure (mmHg)	124.48 ± 12.37
Diastolic blood pressure (mmHg)	76.27±9.78
Pulse pressure (mmHg)	48.75±9.81
Mean blood pressure (mmHg)	92.19±12.2
Aortic pulse wave velocity (m/s)	8.51 ±2.02
Brachial augmentation index (%)	-20.98±29.75
Heart rate (beats/min)	68.7±4.2
Hypercholesterolemia n, (%)	12 (20.3%)

Table II
Relationship between aPWV and classical cardiovascular risk factors.

Aortic pulse wave velocity (m/s)	r	p
Age (years)	r= 0.65	<0.001
Male gender	-	p=0.83
Family history of cardiovascular diseases, n (%)	-	p=0.85
Smokers, n (%)	-	p=0.54
Body mass index (Kg/m²)	r=0.19	p=0.15
Abdominal circumference (cm)	r=0.13	p=0.33
Fasting plasma glucose (mg%)	r=0.31	p=0.02
Total cholesterol (mg%)	r=0.17	p=0.21
Triglycerides (mg%)	r=0.09	p=0.50
Systolic blood pressure (mmHg)	r=0.29	p=0.02
Diastolic blood pressure (mmHg)	r=0.34	p=0.002
Mean blood pressure (mmHg)	r=0.39	p=0.002
Pulse pressure (mmHg)	r=-0.009	p=0.94
Heart rate (beats/min)	r=0.32	p=0.01
Hypercholesterolemia	-	0.31

Table III
Relationship between brachial AXi and classical cardiovascular risk factors.

Brachial augmentation index (%)	r	p
Age (years)	0.42	0.001
Male gender	-	0.09
Family history of cardiovascular diseases, n (%)	-	0.27
Smokers, n (%)	-	0.49
Body mass index (Kg/m²)	-0.04	0.79
Abdominal circumference (cm)	-0.13	0.34
Fasting plasma glucose (mg%)	0.17	0.19
Total cholesterol (mg%)	0.008	0.95
Triglycerides (mg%)	-0.07	0.61
Systolic blood pressure (mmHg)	0.002	0.98
Diastolic blood pressure (mmHg)	0.15	0.24
Mean blood pressure (mmHg)	0.09	0.50
Pulse pressure (mmHg)	-0.11	0.41
Heart rate (beats/min)	-0.17	0.19
Hypercholesterolemia (%)	-	0.41

We performed multiple linear regression adjusted for age to determine the independent predictors of aPWV and brachial Aix, taking into account only the modifiable risk factors. Independent variables that entered the models were modifiable cardiovascular risk factors: smoking status, male gender, abdominal circumference, BMI, FPG, total cholesterol, triglycerides, diabetes, systolic blood pressure, diastolic blood pressure, pulse pressure, mean blood pressure and heart rate. The variables that are independently associated with parameters of arterial stiffness are listed in table IV.

Discussion

This study assessed the relationship between arterial stiffness (as measured by aortic PWV and brachial AIx) and classical cardiovascular risk factors in patients without hypertension or manifest cardiovascular disease. Aortic PWV is the speed of wave travel and intrinsically reflects arterial stiffness. Brachial AIx is an indirect marker of arterial stiffness, being more influenced by endothelial function and peripheral vascular tone. In this study, both markers of arterial stiffness showed a strong correlation with age. For aPWV, a positive correlation was also found with FPG, heart rate, systolic, diastolic and mean blood pressure. Brachial AIx correlated with age. The other cardiovascular risk factors that were taken into consideration did not independently correlate with parameters of arterial stiffness.

The influence of age on arterial stiffness was shown in previous studies (Laurent et al., 2007). The main structural modification with age is medial degeneration which leads to progressive stiffening of large elastic arteries. The mechanical effect of arterial pulsation in large arteries causes structural changes in elastin fibers and increases collagen content in the arterial wall (Lee & Oh, 2010; Lakatta & Levy, 2003). Collagen cross-links due to non-enzymatic glycation increase with age and contribute to age related arterial stiffness (Lakatta & Levy, 2003; Kass et al., 2001). Arterial hypertension, another important factor associated with stiffened arteries, augments mechanical vascular stress that leads to alterations in the extracellular matrix of the media and adventitia (Safar & London, 2000).

A recent systematic review of cross-sectional published literature reporting independent associations of carotid-femoral (aortic) PWV in multivariate regression models found that age and blood pressure were consistently independently associated with increased aPWV. This review also pointed out the fact that the majority of the studies found no independent association between aPWV and sex, total cholesterol, low density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, smoking, or body mass index (Cecelja & Chowienczyk, 2009).

After adjusting for age in our study, FPG and heart rate were the only independent predictors of aPWV. The independent predictors for brachial AIx were abdominal

Table IV
Multiple linear regression analysis showing the determinants of aortic PWV and brachial AIx after adjustment for age.

Parameter	Coefficient	SE	T value	r²	p
Aortic pulse wave velocity (m/s)					
Fasting plasma glucose (mg%)	0.02	0.007	2.2	0.32	0.03
Heart rate (beats/min)	0.04	0.02	1.96	0.33	0.04
Brachial augmentation index (%)					
Abdominal circumference (cm)	-0.61	0.28	-2.18	0.22	0.03
Heart rate (beats/min)	-0.79	0.34	-2.3	0.22	0.02

Abbreviations: SE=standard error

circumference and heart rate.

Regarding the relationship between FPG and arterial stiffness, in a recent study FPG was positively and independently associated with brachial-ankle PWV in non-diabetic healthy adults, after correcting for confounding variables (Shin et al., 2011). Our results support the same linear, independent relationship between FPG and arterial stiffness in non-diabetic adults and that arterial stiffness may already be occurring in persons with FPG within normal ranges. Compared with this previous study, we measured aPWV and not ankle–brachial PWV. Aortic PWV is considered a more precise measure of central arterial stiffness and it is more closely related to cardiovascular outcomes than is ankle-brachial PWV (Laurent et al., 2007; Sugawara et al., 2005).

There are some other studies that link arterial stiffness with increasing levels of FPG. Lukish et al found a positive correlation between FPG, HbA1c and arterial stiffness in a study that included 284 Caucasian subjects (Lukich et al., 2010). Another study suggests the association of arterial stiffness with increasing levels of FGP in normoglycemic to diabetic subjects (Ohnish et al., 2003). At the same time, some studies have shown that increased FPG, even in normal ranges, is a risk factor for cardiovascular diseases (Bjornholt et al., 1999, Gerstein et al., 1999). We can speculate that increased arterial stiffness in these patients may be one of the factors underlying the increase in their cardiovascular risk.

Heart rate, an independent risk factor associated with both aPWV and AIx in our study, was previously independently associated with markers of arterial stiffness. Aortic PWV correlated with heart rate after adjustment for age and blood pressure in normal subjects in different studies (Lantelme et al. 2002; Johansen et al., 2012). Nevertheless, a recent large study reported that PWV was significantly dependent on heart rate, but after further adjustment for sex, quadratic age, and MBP, the influence of heart rate remained very small (***, 2010). Brachial AIx is much more sensitive to the effects of heart rate than aPWV (Lantelme et al. 2002; Albaladejo et al., 2001; Wilkinson et al., 2002). A plausible explanation for the relationship between arterial stiffness and heart rate may be the fact that the rate of elastin fracture depends on the number of stress cycles, that is, the number of heartbeats (Greenwald, 2007). Heart rate in large population groups was shown to be an independent marker of cardiovascular risk (Palatini & Julius, 1997) and we may suppose here a possible implication of increased arterial stiffness.

In our study, abdominal circumference was an independent predictor of AIx and not of aPWV. In a recent prospective study that evaluated risk factors for aortic stiffness in men, waist circumference was independently associated with both these markers of arterial stiffness (Carmel et al., 2010). Other previous studies reported the independent association of abdominal obesity particularly with aPWV (Recio-Rodriguez et al., 2012; Scuteri et al., 2012).

In our study, factors linked to aPWV were partly different from those linked to AIx, supporting the idea that they cannot be used interchangeably as indexes of arterial stiffness, providing different and complementary information (Laurent et al., 2007; Carmel et al., 2010).

One important limitation of our study is the small number of patients, which does not allow us to generalize our results. Another limitation is related to the cross-sectional design of the study, further longitudinal follow-up studies being necessary to confirm a cause-effect relationship between cardiovascular risk factors and the markers of arterial stiffness. Regarding the correlations of FPG with arterial stiffness, we did not evaluate different levels of FPG to assess the influence of high plasma levels on these parameters.

Conclusions

1. Our results suggest that after an adjustment for age, in middle aged physically active adults, without hypertension and overt cardiovascular diseases, FPG and heart rate are independent predictors for aPWV.

2. Heart rate and abdominal circumference are independently correlated with brachial AIx. As FPG, heart rate and abdominal circumference are modifiable risk factors, an early therapeutic intervention to optimize these parameters may reduce arterial stiffness and, as a consequence, the risk for cardiovascular disease.

Conflicts of interests

There are no conflicts of interests.

Authors' contributions: A. Elloumi had the greatest contribution in patient selection, examination and preparation of the manuscript, D. Leucuta performed statistical analyses, M. Mohamed participated in the selection of references and preparation of the manuscript and A. Albu suggested the design of the study and revised the manuscript for important scientific content.

References

Adji A, O'Rourke MF, Namasyvayam M. Arterial stiffness, its assessment, prognostic value and clinical implications for treatment. Am J Hypertens, 2011; 24(1):5-17.

Albaladejo P, Copie X, Boutouyrie P, et al. Heart rate, arterial stiffness, and wave reflections in paced patients. Hypertension, 2001; 38:949-952.

Baulmann J, Schillings U, Rickert S, et al. A new oscillometric method for assessment of arterial stiffness: comparison with tonometric and piezo-electric methods. J Hypertens, 2008; 26:523-528.

Bjornholt JV, Erikssen G, Aaser E, et al. Fasting blood glucose: an underestimated risk factor for cardiovascular death. Results from a 22-year follow-up of healthy nondiabetic men. Diabetes Care, 1999; 22:45-49.

Carmel M. McEniery, Michael Spratt, Margaret Munnery, et al. An Analysis of Prospective Risk Factors for Aortic Stiffness in Men 20-Year Follow-Up From the Caerphilly Prospective Study. Hypertension, 2010; 56:36-43.

Cecelja M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension. Hypertension, 2009; 54:1328-1336.

Ceceljia M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertensive: a systematic review. Hypertension, 2009; 54:1328-1336.

Franklin SS, Gustin W 4th, Wong ND, et al. hemodynamic patterns of age-related changes in blood pressure:the Framingham Heart Study. Circulation, 1997; 96:308-315.

Gerstein HC, Pais P, Pogue J, Yusuf S. Relationship of glucose and insulin levels to the risk of myocardial infarction: a case-control study. J Am Coll Cardiol, 1999; 33:612-619.

Greenwald SE. Ageing of the conduit arteries. J Pathol, 2007; 211:157-172.

Johansen NB, Vistisen D, Brunner EJ, et al. Determinants of aortic stiffness: 16-year follow-up of the Whitehall II study. PLoS One 2012;7(5):e37165. Epub 2012 May 22.

Kass DA, Shapiro EP, Kawaguchi M, et al. Improved arterial compliance by a novel advanced glycation end-product crosslink broker. Circulation, 2001; 104:1464-1470.

Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises. Part I: Aging arteries: A "set up"for vascular disease. Circulation, 2003; 107:139-146.

Lantelme P, Mestre C, Lievre M, et al. Heart rate: an important confounder of pulse wave velocity assessment. Hypertension, 2002;39(6):1083-1087

Laurent S, Cockroft JR, Van Bortel LM, et al. Abridged version of the expert consensus document on arterial stiffness. Artery Res, 2007; 1:2-12.

Lee HY, Oh BH. Aging and arterial stiffness. Circ J, 2010; 74:2257-2262.

Lee H-Y, Oh B-H. Aging and arterial stiffness. Circ J, 2012; 74:2257-2262.

Lukich E, Matas Z, Boaz M, Shargorodsky M. Increasing derangement of glucose homeostasis is associated with increased arterial stiffness in patients with diabetes, impaired fasting glucose and normal controls. Diabetes Metab Res Rev, 2010; 26:365-370.

Magometschnigg D. Blood pressure and arterial stiffness. A comparison of two devices for measuring augmentation index and pulse wave velocity. Wien Med Wochenschr, 2005; 155:404-410.

O'Rourke MF. How stiffening of the aorta and elastic arteries leads to compromised coronary flow. Heart, 2008; 94:690-691.

Ohnish H, Isobe T, Saitoh S, et al. Pulse wave velocity as an indicator of atherosclerosis in impaired fasting glucose. Diabetes Care, 2003; 26:437-440.

Palatini P, Julius S. Heart rate and the cardiovascular risk. J Hypertens, 1997; 15:3-17.

Recio-Rodriguez JI, Gomez-Marcos MA, Patino-Alonso MC, et al. Abdominal obesity vs general obesity for identifying arterial stiffness, subclinical atherosclerosis and wave reflection in healthy, diabetics and hypertensive. BMC Cardiovasc Disord, 2012; 12:3

http://www.biomedcentral.com/1471-2261/12/3

Safar ME, London GM. Therapeutic studies and arterial stiffness in hypertension: recommendation of the European Society of Hypertension, 2000; 18:1527-1535.

Scuteri A, Orru' M, Morrell CH, Tarasov K, et al. Associations of large artery structure and function with adiposity: effects of age, gender, and hypertension. The SardiNIA Study. Atherosclerosis, 2012; 221(1):189-197.

Shin JY, Lee HR, Lee DC. Increased arterial stiffness in healthy subjects with high-normal glucose levels and in subjects with pre-diabetes. Cardiovasc Diabetol, 2011; 10:30.

http://www.cardiab.com/content/10/1/30

Sugawara J, Hayashi K, Yokoi T, et al. Brachial-ankle pulse wave velocity: an index of central arterial stiffness? J Hum Hypertension, 2005; 19:401-406.

Wilkinson IB, McEniery CM, Cockroft JR. Arteriosclerosis and atherosclerosis. Guilty by association. Hypertension, 2011; 54:1213-1215.

Wilkinson IB, Mohamad NH, Tyrrel S, et al. Heart rate dependency of pulse pressure amplification and arterial stiffness. Am J Hypertens, 2002; 15:24-30.

***. The Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. Eur Heart J, 2010; 31:2338-2350.