

ORIGINAL ARTICLES

Arterial stiffness and cardiovascular risk

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Background: Vascular dysfunction, including the arterial stiffness, indicates systemic vulnerability for major cardiovascular events. Identifying these changes in the vascular structure and function during preclinical stages, as well as establishing their appropriate use for risk stratification in clinically manifested disease, will bring benefits for both individuals and populations. **Our study aims –** To analyze the arterial function using the arteriography method in asymptomatic subjects with cardiovascular risk profile assessed using the Framingham and SCORE prediction equations. **Materials and method –** 35 subjects from the Cardiovascular Rehabilitation Clinic - Institute of Cardiovascular Diseases Timisoara were included in the study. They were evaluated from several perspectives: global cardiovascular risk- SCORE risk charts, Framingham risk charts; cardio-metabolic risk: traditional cardiovascular risk factors, metabolic syndrome-the IDF criteria; hemodynamic profile- systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), pulse pressure (PP); arterial wall stiffness: carotid femoral pulse wave velocity (PWV_{FAO}) and the systolic augmentation expressed by the Arteriography (Aix). **Results –** We found positive correlations between: systolic augmentative index (Aix) and pulse wave velocity (PWV_{FAO}) ($p < 0.001$, $r = 0.28$), Aix and MBP (mean blood pressure) ($p < 0.005$, $r = 0.46$), and PWV_{FAO} and DBP (diastolic blood pressure) ($p < 0.001$, $r = 0.62$). The risk for fatal cardiovascular events in the next 10 years was significantly positively correlated with the arterial stiffness: Aix and risk Score ($p = 0.021$). **Conclusions –** We appreciated the arterial function using non invasive methods and we found statistical correlations between arterial function and hemodynamic variables of the cardiovascular risk. Metabolic syndrome variables were not statistically significant associated with arterial stiffness degree appreciated by Aix. We also found a statistically significant positive correlation between arterial stiffness and risk of fatal cardiovascular event over the next 10 years.

Keywords: atherosclerosis, arterial function, pulse wave velocity, pulse pressure, cardiovascular risk, arterial stiffness.

Rezumat: Disfuncția vasculară, incluzând rigiditatea arterială, sunt indicatori ai vulnerabilității sistemice pentru evenimente cardiovasculare majore. Identificarea acestor modificări ale structurii și funcției vasculare încă din stadii preclinice, precum și utilizarea acestora în stratificarea riscului cardiovascular în cazul patologiei clinice manifeste vor aduce beneficii atât la nivel individual, cât și la nivel populațional. **Scop –** Analiza funcției arteriale folosind metoda arteriograf în cazul subiecților cu risc cardiovascular calculat prin utilizarea diagramelor Framingham și SCORE. **Material și metodă –** Am inclus în studiu 35 de pacienți internați în Clinica de Recuperare Cardiovasculară – Institutul de Boli Cardiovasculare Timișoara. Acești pacienți au fost evaluați din mai multe perspective: riscul cardiovascular – risc SCORE, risc Framingham; risc cardio-metabolic: analiza factorilor de risc tradiționali, sindromul metabolic definit conform criteriilor IDF; profil hemodinamic: tensiune arterială sistolică (TAS), tensiune arterială diastolică (TAD), tensiune arterială medie (TAM), rigiditate vasculară, viteza undei pulsatile (PWV_{FAO}), și indexul sistolic de augmentație, obținut prin utilizarea metodei arteriograf (Aix). **Rezultate –** Am obținut corelații pozitive semnificative statistic între: Aix și viteza undei pulsatile (PWV_{FAO}) ($p = 0.001$, $r = 0.28$), Aix și TAM ($p < 0.005$, $r = 0.46$), PWV_{FAO} și TAD ($p < 0.001$, $r = 0.62$). Riscul pentru eveniment cardiovascular fatal în următorii 10 ani s-a corelat pozitiv semnificativ statistic cu rigiditatea arterială: Aix și riscul Score ($p = 0.021$). **Concluzii –** Am apreciat funcția arterială folosind metode non-invazive și am obținut corelații semnificative statistic între funcția arterială și componentele hemodinamice ale riscului cardiovascular. Variabilele sindromului metabolic nu s-au corelat semnificativ statistic cu gradul rigidității arteriale, apreciată prin Aix. De asemenea am obținut corelație pozitivă, semnificativă statistic între rigiditatea arterială și riscul pentru eveniment cardiovascular fatal în următorii 10 ani.

Cuvinte cheie: ateroscleroză, funcție arterială, viteza undei pulsatile, risc cardiovascular, rigiditate arterială.

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INTRODUCTION

Vascular dysfunction, including arterial stiffness and preclinical morphologic changes in the arterial vascular bed, are abnormalities indicating systemic vulnerability for cardiovascular major events. Discovering these structural changes and vascular function during preclinical stages, and appropriate use for risk stratification during the disease stage, brings benefits for both the individuals and population^{1,2}. The early functional disorder primarily involves the resistance vessels (small arteries, arterioles) leading over the years to the loss of elasticity of medium and large arteries (high stiffness), then to macro-vascular atherosclerotic changes and finally, to the formation of the atherosclerotic plaques²⁻⁴.

In this stage of atherosclerosis, the first sign of macro-vascular atherosclerosis is represented by the decreasing of the aortic arterial wall elasticity, leading to the development of a high aortic stiffness (characteristic to the increase of PWVAo).

MATERIALS AND METHODS

Patients: In the study were included 35 patients with an accumulation of cardiovascular risk factors. They were hospitalized in the Cardiovascular Rehabilitation Clinic Institute of Cardiovascular Diseases Timisoara in order to study their arterial function and for the assessment of the cardiovascular risk. Inclusion criteria: asymptomatic with low and high cardiovascular risk, EF >35%. Exclusion criteria: arrhythmias, valvulopathies, congenital cardiac diseases, asymptomatic with medium cardiovascular risk, EF ≤35%.

Clinical Evaluation: for each patient were followed: anamnesis, family history of cardiovascular disease, quantified cardiovascular risk factors from SCORE risk prediction equations (age, sex, systolic blood pressure, smoking, total cholesterol) or the Framingham risk charts (age, sex, total cholesterol, HDL-C, smoking, systolic blood pressure).

Assessment of the absolute risk for cardiovascular events

We started the evaluation of the 10-year fatal cardiovascular risk using SCORE nomogram, in accordance with European Guidelines for Cardiovascular Disease Prevention www.heartscore.org. According to SCORE risk, patients were divided into two categories: asymptomatic with low cardiovascular risk and asymptomatic with high cardiovascular risk. We used the SCORE electronic version as well in order to take into account the HDL-c, noted as Score-HDL. We rated the group of patients by calculating the 10-year risk of coronary

heart disease according to the Framingham model, using the interactive electronic diagram calculation: <http://www.framinghamheartstudy.org/risk/> coronary.html.

Cardio-metabolic risk assessment

The lipid profile analysis was performed as recommended by guidelines of the *European Society of Cardiology*. The framing of the subjects in each risk category was made according to the recommendation of the *European Society of Cardiology Guidelines*. The metabolic syndrome was defined according to IDF criteria if they were associated with at least 3 of the 5 criteria.

Hemodynamic risk assessment

Based on the results of the 24h automatic recording (performed by the BTL-08 ABPM), the analysis of the arterial blood pressure was done. Measurements were performed every 15 minutes during the day (7 am-23 am) and every 30 minutes during the night (23-7 am). The monitoring was repeated when there were more than 30% artifacts. From the ambulatory blood pressure monitoring protocol, we used the following parameters: 24-hour SBP, 24-hour DBP, PP 24 hours, 24 hours MAP (3). We have defined the following categories: normal BP <130/85, hypertension: SBP ≥140 mmHg and / or DBP ≥90 mmHg or antihypertensive treatment, which corresponds to an average 24-hour BP >120/80 mmHg³. Mean 24-hour pulse pressure >60 mmHg was considered pathological.

Assessment of arterial function

We followed the exact recommendations of the evaluation protocol using the arteriography method as described by the bibliographic references². We analyzed the following parameters: arterial augmentation index (Aix) and aortic pulse wave velocity (PWVAo).

Statistical analysis of data: data normality was assessed using Shapiro-Wilk test. Data were analyzed using parametric tests-One Sample *t* test for comparing the mean values of two groups, and One Way ANOVA for comparing the mean values obtained in more than three groups. The testing of the association between qualitative variables was performed using Chi square test, and for testing correlations between numerical variables, we used Pearson correlation coefficient. For statistical analysis, P.A.S.W. statistics 18.0 was used.

RESULTS

We studied 35 patients, asymptomatic in terms of cardiovascular, but presenting the accumulation of



Figure 1. The lot gender.

cardiovascular risk factors, hospitalized in Clinic of Cardiovascular Rehabilitation-Institute of Cardiovascular Diseases Timisoara, of which a higher percentage (68.6%) was represented by women, the average age of the sampled patients was 49.51 (± 17.19) years, 11.4% of patients had diabetes mellitus, 20% of patients had a SCORE risk $\geq 5\%$, 5.71% had a Framingham risk ≥ 20 and 48.57% were smokers (Figure 1, Table 1).

Arterial stiffness behavior according to hemodynamic profile of the sampled patients

We have obtained a positive correlation between the aortic augmenting index and the two variables that characterize the hemodynamic profile of SBP ($p < 0.003$, $r = 0.48$) and MAP ($p < 0.005$, $r = 0.46$) (Table 2).

Table 1. Clinical, hemodynamic and laboratory data of the group		
Characteristics	Mean	Standard Deviation
Age	49.51	17.19
Height	166.743	8.79
Weight	72.43	14.12
Abdominal circumference	86.2	12.26
Systolic blood pressure	134.63	19.22
Diastolic blood pressure	84	11.25
Mean blood pressure	100.857	13.27
Aix	27.78	27.61
PWVAo	9.02	2.17
Heart rate	69.257	10.50
Cholesterol total	171.54	25.22
HDL-C	47.463	11.31
LDL-C	103.5	25.23
Triglycerides	116.77	50.57
Fasting plasma glucose	88.775	10.55

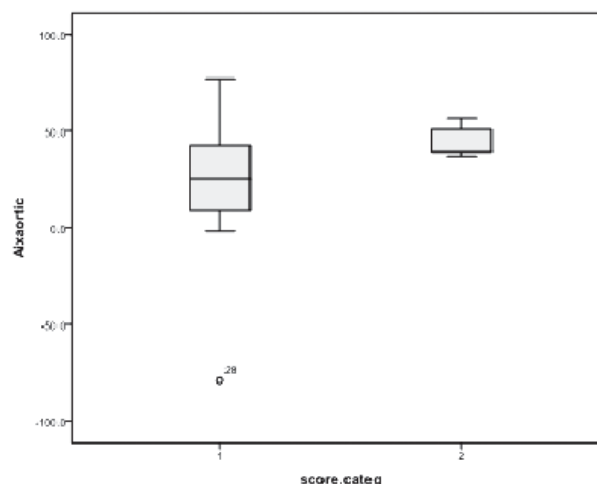


Figure 2. The Aixaortic in the risk Score categories (1-asymptomatic with low cardiovascular risk and 2-asymptomatic with high cardiovascular risk).

The correlation between arterial stiffness and risk of fatal cardiovascular event over the next 10 years

For the estimation of the risk of fatal cardiovascular event in the next 10 years, we used three methods of calculation as detailed in Material and Methods section. We obtained significant differences of mean aortic Aix in the SCORE risk categories ($p = 0.021$). We found increasing augmentation index (Aix) proportionally with the increasing of the risk Score, as shown in Figure 2, Table 3 and Table 4.

We obtained a statistically significant association relationship between Aix aortic and risk Framingham ($p = 0.034$, test Chi2 95% CI), but we didn't found significant differences of average Aix aortic in Framingham risk categories ($p = 0.255$ Test Man-Whitney 95% CI) as shown in Figure 3.

DISCUSSION

Our study demonstrates the relationship between arterial stiffness (PWVAo) and hemodynamic parameters (SBP, DBP, MAP, PP), age and risk of cardiovascular events in 10 years (SCORE risk, SCORE- HDL risk, Framingham risk).

The study conducted by Hansen TW and colleagues (1) has demonstrated the necessity of measuring arterial stiffness's (PWVAo) for asymptomatic people wi-

Table 2. Aix and the hemodynamic profil			
Dependent variable	Independent variables	Pearson correlation coefficient	Statistically significance
Aix	TAS	$r=0.48$	$p<0.003$
	TAM	$r=0.46$	$p<0.005$
	PWVAo	$r=0.28$	$p<0.001$

Table 3. Aix aortic and Risc Score categories (1-asymptomatic with low cardiovascular risk and 2-asymptomatic with high cardiovascular risk)

Aixaortic				
score.category		Mean	N	Std. Deviation
dimension I	1	23.586	28	29.2369
	2	44.571	7	8.0205
	Total	27.783	35	27.6170

Table 4. Aix aortic in risc Score categories 1 and 2

Ranks				
	score.category	N	Mean Rank	Sum of Ranks
Aixaortic	1	28	16.00	448.00
	2	7	26.00	182.00
	Total	35		

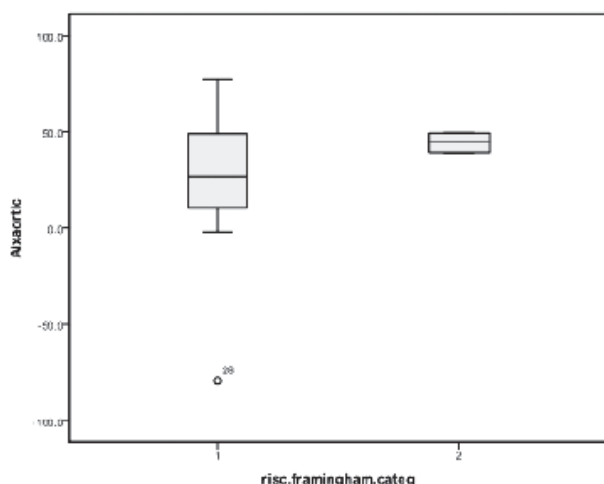


Figure 3. Aixortic and risc Framingham categories (1-asymptomatic with low cardiovascular risk and 2-asymptomatic with high cardiovascular risk).

thout cardiovascular disease, proving that the rate of aortic pulse wave propagation alone, without keeping track of the independent classical risk factors, is an effective predictor of cardiovascular mortality based on a follow-up period of 9 years⁶⁻⁸.

In our study, we have demonstrated the existence of correlations between arterial stiffness, hemodynamic parameters and SCORE risk. With or without being associated with the traditional risk factors, PWV represents a very important predictor of cardiovascular events⁹⁻¹¹.

The predictive value of Aix for cerebrovascular events should not be considered only in terms of hemodynamics, but also in terms of cardio-metabolic. G. Leoncini and co. have studied the association between Aix and the metabolic profile of 156 non-diabetic, hypertensive patients, and concluded that the prevalence of increased Aix was higher in patients with metabolic syndrome¹²⁻¹⁴.

Aortic PWV measurement supplies information, primarily on the properties of the aortic wall. The more rigid and impervious the aortic wall is, the faster the pulse wave travels along it.

We must take into account situations where there is an increase of the ejected blood volume in the aorta (e.g. hypertension, tachycardia, increased cardiac output), circumstance that determines an increase in aorta diameter, therefore increasing the parietal blood pressure, resulting in an increase in propagation velocity of wave pulse.

In conclusion, aortic PWV provides a prognostic value only if it was measured in isobaric conditions, that means in normotensive conditions^{9,15-17}.

The correlation between the arterial stiffness and the cardiovascular risk was conclusively demonstrated in the study conducted by Guerin and co. in 2001, performed on a group of patients in end-stage kidney disease. They effectively decreased the blood pressure and followed the changes of aortic PWV in parallel. In the group that besides lowering blood pressure, the aortic PWV was decreased as well, all patients survived the tracking period. Instead, the group in which the lowered blood pressure was not accompanied by a decrease in the aortic PWV, all patients died by the end of follow-up period of 51 months¹⁸⁻²¹.

This shows, that in this second group, contrary to the first group, the increased aortic PWV was not caused by parietal tension due to hypertension, but rather by morphological vessel lesions.

CONCLUSIONS

- We assessed arterial function using noninvasive methods and we found statistical correlation between arterial stiffness and hemodynamic variables of cardiovascular risk, but not with metabolic profile.
- We also found statistically significant positive correlation between arterial stiffness and risk of fatal cardiovascular event in the next 10 years.
- It is essential to detect real individual risk, even in early reversible stages of atherosclerosis, when most patients are still asymptomatic and without subjective complaints, therefore we have the chance to favorably influence the process thru.

Conflict of interest: none declared.

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