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Impact of the Defining Criteria and Components of Metabolic Syndrome on Arterial Stiffness Parameters

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Abstract

Background: Metabolic syndrome is associated with an increase in cardiovascular morbidity and mortality. Since the first description of MS, several definitions have been elaborated (IDF, AHA, Who, NCEP). Arterial stiffness is a strong independent predictor of cardiovascular events and cardiovascular mortality in various groups of patients. *Aim:* The purpose of present study was to investigate the impact of the different definitions of MS on arterial stiffness. *Material and Methods:* we investigated 214 patients, mean age 60.04±9.98 years. Arterial stiffness was evaluated using TensioMed TM Arteriograph. *Results:* Using the three definitions of the metabolic syndrome – IDF 2005, AHA, NCEP -, a proportion of 71.5% (153 patients), 72.9% (156 patients) and 62.1% (133 patients), respectively, had metabolic syndrome. Pulse wave velocity in the group of patients with metabolic syndrome was increased compared to those without metabolic syndrome, but the difference was not statistically significant (IDF - 10.37±2.13m/sec vs 10.04±2.21m/sec, AHA 10.40±2.14m/sec vs 9.93±2.19m/sec, NCEP 10.47±1.86m/sec vs 9.95±2.55m/sec). A statistically significant difference between pulse wave velocity in men with metabolic syndrome compared to those without metabolic syndrome was found, the relationship being not true in women. *Conclusion*: Patients with MS (especially men) have increased arterial stiffness parameters than those without metabolic syndrome. All the three definitions used have the same ability to identify patients with arterial stiffness. Arterial stiffness parameters are more altered as the number of criteria for the definition of metabolic syndrome increases, regardless of the definition used.

Keywords: Metabolic syndrome definitions; Arterial stiffness; Gender.

Introduction

Metabolic syndrome is associated with an increase in cardiovascular morbidity [1] and mortality [2] and with an increased incidence of type 2 diabetes mellitus [3]. In addition, hypertensive patients with metabolic syndrome have a cardiovascular risk at least two times higher than those without metabolic syndrome [4]. Since the first description of MS, several definitions have been elaborated, of which the best known and more widely used are: World Health Organization (WHO) [5] National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) [6], American Heart Association

(AHA) [7], and International Diabetes Federation (IDF) [8]. More recently, in 2009, the harmonization of MS definitions was attempted by IDF and AHA and a new common definition of the two organizations was proposed [9]. The evaluation of the impact of various cardiovascular risk factors in the general population by non-invasive methods remains one of the major objectives of the management of cardiovascular risk [10]. Recent advancements in pulse wave analysis allow the non-invasive investigation of arterial properties and represent a new marker of CV risk [10].

Arterial stiffness is a strong independent predictor of cardiovascular events and cardiovascular mortality in various groups of patients [11-14]. This can be evaluated by the measurement of carotid-femoral pulse wave velocity. The individual components of metabolic syndrome have been associated with an increase in arterial stiffness, consequently with an increase in pulse wave velocity [15, 16], mainly arterial hypertension [17]. Metabolic syndrome causes an increase in arterial stiffness independently of other cardiovascular risk factors [18]. The augmentation index, an indicator of reflected wave pressure, is influenced by the amplitude and the transit time of the anterograde and retrograde pulse wave. In addition to arterial properties, the heart rate, weight and sex are the important modulators of the augmentation index [19, 20].The relationship between arterial stiffness and metabolic syndrome has been investigated in several studies, most of which have used the ATPIII criteria for the MS definition [21-27]. The association of the reflected wave with metabolic syndrome has not been thoroughly explored so far.

Considering the important prognostic role of arterial stiffness and the reflected wave and taking into account the controversies regarding the definition of metabolic syndrome, the aim of this study was to investigate the impact of the different definitions of MS on arterial stiffness and the reflected wave. We monitored the relationship between the carotid-femoral pulse wave velocity, a direct measure of arterial stiffness, and the augmentation index, an index of arterial stiffness and of the reflected wave, and metabolic syndrome. We investigated if these arterial stiffness markers depend on the metabolic syndrome definition used.

Material and Method

The study included 214 consecutive patients (142 women, 66.4% of patients), investigated in the Department of Cardiology of the Rehabilitation Hospital Cluj-Napoca (October-December 2009). The mean age of the patients included in the study was 60.04 ±9.98 years (range values between 36 and 87 years).

All patients underwent a complete clinical examination, including the measurement of blood pressure, abdominal circumference, and ankle-arm index. According to the guide of the European Society of Hypertension, blood pressure ≥140 mm Hg and/or ≥90 mm Hg was considered as arterial hypertension. Pulse pressure was calculated by the difference between systolic BP and diastolic BP. Height and weight were measured and the body mass index was calculated. Each patient filled a form regarding their eating habits, current and past smoking status, alcohol use, sedentary life. All patients signed an informed consent of participation in the study, which was approved by the Ethics Committee.

Diagnosis of Metabolic Syndrome

The best known definitions of metabolic syndrome were used: 1. IDF criteria that require the presence of abdominal obesity (abdominal circumference ≥94 cm in men and ≥80 cm in women) and two of the following abnormalities: BP >130/85 mmHg, serum triglycerides ≥150 mg/dl, HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women, and serum glucose ≥100 mg/dl; 2. NCEP/ATP III criteria: three or more of the following: abdominal circumference ≥102 cm in men and ≥88 cm in women, serum triglycerides ≥150 mg/dl, HDL-cholesterol <40 mg/dl in men and <50 mg/dl in women, glycemia ≥ 110 mg/dl; blood pressure >130/85 mmHg; 3. The latest definition of 2009 (AHA, IDF), which attempts to unify the different definitions elaborated so far and requires the presence of three abnormalities of the following five (IDF abandoning a fix criterion of the presence of abdominal obesity): increase in abdominal circumference above the limit specific for the population concerned, increase in triglyceride values ≥150 mg/dl, decrease in HDL-cholesterol below 40 mg/dl in men and below 50 mg/dl in women, BP ≥130/85 mm Hg, and glycemia ≥100 mg/dl.

Arterial Stiffness and the Evaluation of the Reflected Wave

The measurement of carotid-femoral pulse wave velocity, a faithful index of arterial stiffness, was performed using the TensioMed TM Arteriograph device. The augmentation index is a reflected wave index. It measures the magnitude of the reflected wave and at the same time, arterial stiffness influenced by the reflected wave transit time. The augmentation index is calculated by the P2/P1 ratio (%), as shown in Figure 1.

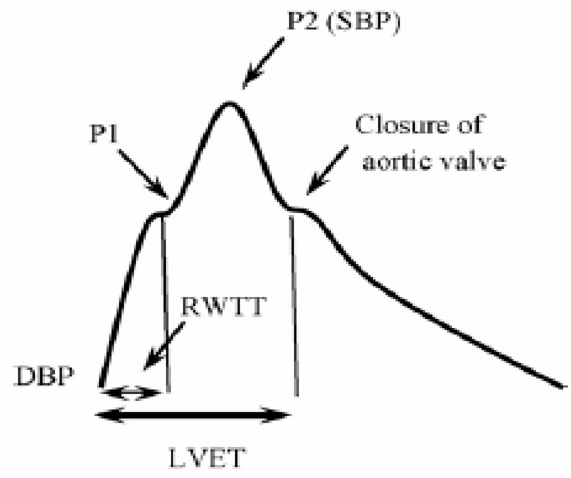

Figure 1. Analysis of the central pressure wave. Augmentation index (AI): P2/P1. P1, the inflection point of the reflected wave; RWTT, the reflected wave transit time; P2, the maximum point of systolic pressure determined by the return of the reflected wave; SBP systolic blood pressure, DBP diastolic blood pressure; LVET, left ventricular ejection fraction.

The local institutional Ethics Committee approved the study and all participants gave their written informed consent.

Statistical Analysis

Statistical analysis was performed using the programs SPSS 16.0 for Windows. Qualitative data was described by absolute and relative frequencies, quantitative data was described by means, standard deviations, minimum and maximum values. Quantitative data normality was assessed with QQ plots. For the analysis of the differences between qualitative variables, the $\chi 2$ test was used. The differences between the means of continuous quantitative variables were evaluated using the Student test for independent samples using equal or unequal variances (assessed by Levene test) and ANOVA test. A p value <0.05 was considered as statistically significant. For all tests the two tail p value was used.

Weka (Waikato Environment for Knowledge Analysis) is a cross-platform open source, written in Java. We used InfoGainAttributeEval single-attribute evaluator with Ranker search method in Weka 3.6.3. InfoGainAttributeEval evaluates selected attributes by measuring their information gain according to the class – using discretization method. Ranker ranks individual attributes (not subsets) according to their evaluation [28].

Results

The basic characteristics of the studied population are shown in Table 1. It can be seen that the mean age is 60.04±9.98 years, the mean body mass index, 29.22±4.98 kg/m², is within the overweight limits, and mean systolic and diastolic blood pressure is within normal limits. The mean values of the biochemical constants include increased mean glycemia values, hypercholesterolemia, hypo-HDL-cholesterolemia, and mild hyper-triglyceridemia. The arterial parameters evidence upper limit values for the augmentation index and the pulse wave velocity.

The percentage of patients with hypertension was 70.6%, of diabetic patients 24.3%, of smokers 16.8%, of obese patients 40.2%. 80 patients (37.4%) had cardiovascular diseases. Of all patients, 89.3% had a large abdominal circumference, according to the IDF criteria (>80 in women and >94 in men).

Table 1. Baseline characteristics of the study population

	Minimum	Maximum	Mean	SD
Age (years)	36.00	87.00	60.04	9.98
Weight (kg)	47.00	166.00	81.55	16.46
BMI - body mass index (kg/m^2)	17.51	60.97	29.22	4.98
SBP - systolic blood pressure (mm Hg)	100.00	205.00	138.49	18.30
DBP - diastolic blood pressure (mm Hg)	60.00	120.00	86.20	10.93
Glycemia (mg/dl)	63.00	208.00	102.90	25.28
Total cholesterol (mg/dl)	100.00	325.00	213.05	44.29
LDL - low-density lipoprotein cholesterol (mg/dl)	43.00	247.00	135.95	37.44
HDL - high-density lipoprotein cholesterol (mg/dl)	21.00	86.00	45.03	9.84
TG - triglycerides (mg/dl)	51.00	665.00	160.67	81.28
Arterial stiffness parameters				
AixAo - aortic augmentation index (%)	1.50	72.10	38.62	14.68
PWVAo - pulse wave velocity (m/s)	1.10	19.20	10.28	2.16
PP - pulse pressure (mmHg)	34.00	102.00	54.18	14.34

Continuous variables are presented as mean value±1 standard deviation.

Using the three definitions of the metabolic syndrome – IDF 2005, AHA, NCEP -, a proportion of 71.5% (153 patients), 72.9% (156 patients) and 62.1% (133 patients), respectively, had metabolic syndrome.

The percentage of patients with hypertension was 70.6%, of diabetic patients 24.3%, of smokers 16.8%, of obese patients 40.2%. 80 patients (37.4%) had cardiovascular diseases. Of all patients, 89.3% had a large abdominal circumference, according to the IDF criteria (>80 in women and >94 in men).

Pulse wave velocity in the group of patients with metabolic syndrome was increased compared to those without metabolic syndrome, but the difference was not statistically significant (Table 2), regardless of the definition used. The augmentation index and pulse preasure were also different between the two groups, but with a statistically insignificant difference.

Table 2. Arterial parameters in patients with metabolic syndrome and without metabolic syndrome, depending on the definition used

	Metabolic syndrome +	Metabolic syndrome -	p
IDF - International Diabetes Federation			
AixAo - aortic augmentation index (%)	37.94 ± 14.49	40.30 ± 15.13	NS
PWVAo - pulse wave velocity (m/s)	10.37 ± 2.13	10.04 ± 2.21	NS
PP - pulse pressure (mmHg)	55.15 ± 14.71	51.72 ± 13.14	NS
AHA - American Heart Association			
AixAo - aortic augmentation index (%)	38.01 ± 14.40	40.24 ± 15.40	NS
PWVAo - pulse wave velocity (m/s)	10.40 ± 2.14	9.93 ± 2.19	NS
PP - pulse pressure (mmHg)	55.11 ± 14.68	51.64 ± 13.13	NS
NCEP - National Cholesterol Education Program			
AixAo - aortic augmentation index (%)	37.93 ± 14.67	39.75 ± 14.71	NS
PWVAo - pulse wave velocity (m/s)	10.47 ± 1.86	9.95 ± 2.55	NS
PP - pulse pressure (mmHg)	55.22 ± 14.60	52.44 ± 13.81	NS

The analysis of arterial stiffness parameters in the groups of patients shows a statistically significant difference between pulse wave velocity in men with metabolic syndrome compared to those without metabolic syndrome (Figure 2). All the three definitions used in this study have the same ability to identify patients with arterial stiffness. Thus, depending on the definition used, the difference between men with MS and those without MS is statistically significant, with p-0.003 for NCEP, p-0.015 for IDF, and p-0.004 for the AHA definition. In women, there are no statistically significant differences between those with MS and those without MS, regardless of the definition used (Figure 1).

The analysis of arterial stiffness in patients with metabolic syndrome depending on the number of criteria for the definition of metabolic syndrome shows that the greater the number of criteria, the more increased arterial stiffness is (Table 3). This finding is present regardless of the definition used.

Table 3. Arterial parameters depending on the number of MS criteria, in relation to the definition used

No. OF MS COMPONENTS	0	1	2	3	4	5
IDF /AHA						
AIXAo (%)*	35.54 ± 8.83	41.24 ± 17.94	40.22 ± 14.99	36.47 ± 15.29	37.63 ± 13.90	40.97 ± 13.64
PWVAo (m/s)*	10.73 ± 3.09	9.95 ± 2.17	9.86 ± 2.19	10.03 ± 2.05	10.49 ± 2.40	10.85 ± 1.76
NCEP						
AIXAo (%)*	37.74 ± 12	40.91 ± 16.36	39.11 ± 13.91	35.41 ± 15.81	39.82 ± 12.78	40 ± 15.31
PWVAo (m/s)*	9.73 ± 2.7	9.77 ± 1.94	10.11 ± 2.95	10.18 ± 1.66	10.4 ± 2.03	11.38 ± 1.75

AixAo=aortic augmentation index, PWVAo=pulse wave velocity, PP=pulse pressure (the mean values±SD),MS=Metabolic syndrome.* p=NS

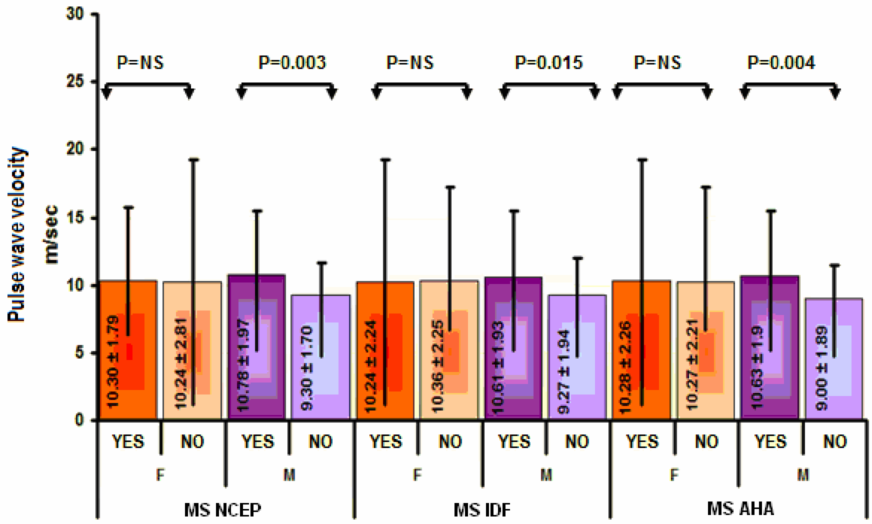

Figure 2. Influence of the definitions of metabolic syndrome on arterial stiffness parameters (mean, minimum and maximum values) in women and men. Abbreviations: MS – metabolic syndrome, F – female, M – male, IDF, International Diabetes Federation; AHA, American Heart Association; NCEP, National Cholesterol Education Program.

Using InfoGainAttributeEval, Ranker method, we evaluated the criterions' importance in arterial stiffness determination (a value of PWVAo more than 9.7 m/sec being considered increased) - the results are presented in Table 4. As it is shown, using AHA or IDF definition, hypertension seems to be the most important factor in arterial stiffness determination. For NCEP definition, glycoregulation malfunction seems to be in the first place.

Table 4. Ranking by disease attribute evaluation process result

	AHA & IDF			NCEP		
	Info Gain	Rank	Attribute	Info Gain	Rank	Attribute
Increase of arterial stiffness	0.013195	1	**HTA**	0.0284039	1	**Glycemia increase /DM**
	0.012415	2	**Glycemia increase /DM**	0.0131951	2	**HTA**
	0.003151	3	**Sex**	0.0031510	3	**Sex**
	0.000570	4	**CA increase**	0.0000691	4	**CA increase**
	0	5	**HDL low**	0	5	**HDL low**
	0	6	**TG increase**	0	6	**TG increase**

HTA = hypertension, CA increase= increase of abdominal circumference,
Glycemia increase/DM= increase of glycemia over the established values or presence of diabetes mellitus, HDL low = low values of HDL-cholesterol, TG increase = increase values of triglycerides

Discussion

It is known that patients with metabolic syndrome have a much higher mortality risk compared to those without metabolic syndrome [29]. It has been demonstrated [29] that relative mortality risk associated with metabolic syndrome is higher in studies using the NCEP definition versus other definitions (p=0.0002), which suggests the role of the definitions in the identification of patients at increased cardiovascular risk. The cardiovascular risk of patients with metabolic syndrome is correlated with arterial stiffness.

The majority of the studies that have shown the association of metabolic syndrome with arterial stiffness have used the NCEP definition for metabolic syndrome [16, 22, 31, 32].

This study aimed to monitor the impact of the most widely used definitions of metabolic syndrome: NCEP/ATPIII, AHA and IDF on arterial stiffness parameters: pulse wave velocity and the augmentation index.

Pulse wave velocity, the gold standard of arterial stiffness, has been described as being significantly higher in patients with metabolic syndrome compared to those without metabolic syndrome, the majority of the studies using the NCEP definition [16, 22, 31]. There are few studies that have used the IDF definition [18], and very few that have compared the different definitions. The study performed by Sipilä et al. [18] shows that pulse wave velocity is significantly higher in men compared to women. The present study found a higher pulse wave velocity in patients with metabolic syndrome compared to those without metabolic syndrome, but the difference was not statistically significant. Regarding the impact of the three definitions on pulse wave velocity, there was no statistically significant difference in pulse wave velocity between patients with metabolic syndrome and those without metabolic syndrome for all the three definitions.

In contrast, a statistically significant difference in pulse wave velocity was seen between men with metabolic syndrome and those without metabolic syndrome and this difference was maintained regardless of the definition used. This statistically significant difference was not found in the group of women with and without metabolic syndrome.

An issue raised by this study was the existence of gender differences concerning arterial stiffness, pressure wave reflections and their relation to CV risk. In what way different CV risk factors such as elevated BP, insulinresistance, hyperglycemia, smoking and renal dysfunction may interact with sex hormones to modify the intrinsic elastic properties of the arterial wall and pressure wave reflections remains to be established.

Unlike these results obtained in the present study, Protogerou et al. [10] show that there is a statistically significant difference only in the pulse wave velocity of women with MS/without MS and that in the group of men, this difference is not seen. However, if we compare pulse wave velocity between women with MS and men with MS, there are no statistically significant differences, which is in accordance with other published studies [32].

Regarding the augmentation index, a "composite" measure of arterial stiffness and of the reflected wave, this was changed in patients with metabolic syndrome compared to those without metabolic syndrome, but this difference was not statistically significant. In contrast, when comparing the group of women with MS and the group of men with metabolic syndrome, a statistically significant difference in the augmentation index was found between the two groups. This finding was present regardless of the definition used. In conclusion, all the three definitions have the same ability to identify patients with arterial stiffness. This observation has also been made in other studies, but none of these have used the definition elaborated in 2009 by IDF/AHA.

The influence of the number of components of metabolic syndrome on arterial stiffness parameters is known [33]. In this study, pulse wave velocity and the augmentation index are found to be higher as the number of metabolic syndrome components increases. This finding is true for all the three definitions.

Conclusions

In conclusion, this study proves that patients with MS have increased arterial stiffness parameters than those without metabolic syndrome, being statistically significant for the subgroup of men with metabolic syndrome. All the three definitions used have the same ability to identify patients with arterial stiffness. Arterial stiffness parameters are more altered as the number of criteria for the definition of metabolic syndrome increases, regardless of the definition used.

Ethical Issues

The local institutional Ethics Committee approved the study and all participants gave their written informed consent.

Conflict of Interest

The authors declare that they have no conflict of interest.

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