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Correlation of arterial stiffness parameters with indicators of carotid atherosclerosis in patients with metabolic syndrome

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Abstract

Background: Many studies have shown that metabolic syndrome is accompanied by an increase in arterial stiffness. In connection therewith, early detection of an increase in arterial stiffness in patients with metabolic syndrome can help to prevent cardiovascular complications.

Aim: To determine the relationship between arterial stiffness parameters such as cfPWV and CAVI with carotid atherosclerosis indicators (intima-media thickness, carotid plaque presence) in patients with metabolic syndrome.

Material and methods: The study included 100 patients at the age of 40-70 years: 45 men and 55 women (56.54±8.98 years). Subjects were divided into 2 groups: 1st - 42 patients with metabolic syndrome; 2nd - 58 patients without metabolic syndrome. The arterial stiffness parameters such as CAVI and cfPWV were calculated. In the analysis we used threshold values recommended by manufacturers and European expert consensus document on arterial stiffness: for CAVI – <8, for cfPWV – ≤10 m/c). Duplex scanning carotid arteries was performed to evaluate the "intima-media thickness" and carotid plaque presence.

Results: In the group with metabolic syndrome the CAVI is significantly associated with the indicators of carotid atherosclerosis: intima-media thickness (OR=4.94 95%; CI: 1.49-3.80; p=0.047), carotid plaque presence (OR=3.06; 95% CI: 1.42-2.28; p=0.065). But statistically significant associations of cfPWV with indicators of carotid atherosclerosis were not obtained (p>0.05). In the group without metabolic syndrome none of the arterial stiffness parameters (CAVI, cfPWV) statistically significantly correlated with any of the carotid atherosclerosis indicators (p>0.05).

Conclusion: The CAVI parameter, in contrast to the cfPWV, statistically significantly correlated with indicators of carotid atherosclerosis in patients with metabolic syndrome. In this connection, this parameter can be used to identify signs of not only increased arterial stiffness but also to determine subclinical signs of carotid atherosclerosis in patients with metabolic syndrome.

Key words: metabolic syndrome, arterial stiffness, CAVI, carotid atherosclerosis

АРТЕРИЯ ҚАБЫРҒАСЫНЫҢ ҚАТАЮ ПАРАМЕТРЛЕРІНІҢ КАРОТИДТІ АТЕРОСКЛЕРОЗДЫҢ КӨРСЕТКІШТЕРІМЕН ӨЗАРА БАЙЛАНЫСЫ

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ТҰЖЫРЫМДАМА

Кіріспе: Көптеген зерттеушілер метаболикалық синдром кезінде артериялық қабырғаның қатаюы жоғарылайтындығын дәлелдеді. Осыған байланысты мұндай пациенттерде артериялық қабырға қатаюының жоғарылауын ерте анықтау жағымсыз жүрек-қантамыр асқынуларының алдын алуға мүмкіндік береді.

Мақсаты: Метоболикалық синдромы бар пациенттерде каротидті атеросклероздың (интим-медиа қалыңдығын, атеросклероздық түйіншектер болуы) көрсеткіштері бар кфПТЖ (пульс толқынының жылдамдығы) және CAVI секілді артериялық қабырғаның қатаю параметрлері арасындағы өзара байланысты анықтау.

Материалдар мен әдістер: Зерттеуге 40-70 жас аралығындағы 45 ер адам, 55 әйел (56,54±8.98 жас) 100 адам қатысты. Пациенттер екі топқа: 1-ші - метаболикалық синдромы бар 42; 2-ші - метаболикалық синдромы жоқ 58 адам болып бөлінді. КфПТЖ және CAVI секілді артериялық қабырғаның қатаю параметрлері есептелді. Шекті мүндері үшін өндірушілер мен артериялық қатаю бойынша сарапшылардың Еуропалық консенсусы ұсынған мөлшерлер (кфПТЖ≤10м/с; CAVI – <8) қабылданды. Ұйқы артериясындағы «интим-медиа қалыңдығын» және атеросклероздық түйіншектерді бағалау үшін ұйқы артерияларының дуплекстік сканирлеуі қолданылды.

Нәтижелер: Метоболикалық синдромы тобында CAVI параметрі каротидті атеросклероздың көрсеткіштерімен: интим-медиа қалың-

дығын (OR=4.94 95%; CI: 1.49-3.80; p=0.047) және ұйқы бездерінде атеросклероздық түйіншектер болуымен (OR=3.06; 95% CI: 1.42-2.28; p=0.065) статистикалық маңызды сәйкес келді. Алайда кфПТЖ параметрлерінің каротидті атеросклероздың көрсеткіштерімен статистикалық маңызды өзара байланысы анықталмады (p>0.05). Метоболикалық синдромы жоқ топта артериялық қабырға қатаюының ешқандай параметрі каротидті атеросклероздың көрсеткішіне (p>0.05) сәйкес келмеді.

Қорытынды: CAVI параметрі кфПТЖ параметріне қарағанда метаболикалық синдромы бар пациенттердің тобындағы каротидті атеросклероздың көрсеткіштерімен статистикалық мейлінше сәйкес келді. Осыған байланысты, беріліп отырған параметр артериялық қабырғаның қатаюын бағалау үшін ғана қолданылмай, сондай-ақ пациенттердің осы топтарындағы каротидті атеросклероздың субклиникалық белгілерін анықтау үшін де қолданыла алады.

Негізгі сөздер: метаболикалық синдром, артерия қабырғасының қатаңдығы, каротидті атеросклероз

ВЗАИМОСВЯЗЬ ПАРАМЕТРОВ ЖЕСТКОСТИ АРТЕРИАЛЬНОЙ СТЕНКИ С ПОКАЗАТЕЛЯМИ КАРОТИДНОГО АТЕРОСКЛЕРОЗА

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РЕЗЮМЕ

Введение: Многими исследованиями доказано, что при метаболическом синдроме отмечается повышение жесткости артериальной стенки. В связи с этим раннее обнаружение повышенной жесткости артериальной стенки у таких пациентов может предотвратить возникновение неблагоприятных сердечнососудистых осложнений.

Цель: Определить взаимосвязь между такими параметрами жесткости артериальной стенки, как кфСПВ и CAVI с показателями каротидного атеросклероза (толщина интима-медиа, наличие атеросклеротических бляшек) у пациентов с метаболическим синдромом.

Материал и методы: В исследование включено 100 человек в возрасте 40-70 лет: 45 мужчин, 55 женщин (56.54±8.98 лет). Пациенты разделены на 2 группы: 1ая - 42 с метаболическим синдромом; 2ая – 58 без метаболического синдрома. Вычислялись такие параметры жесткости артериальной стенки, как кфСПВ и CAVI. За пороговые значения приняты величины, рекомендованные производителями и Европейским консенсусом экспертов по артериальной жесткости (кфСПВ≤10м/с; CAVI – <8). Для оценки «толщины интима-медиа» и атеросклеротических бляшек в сонных артериях применялось дуплексное сканирование сонных артерий.

Результаты: В группе с метаболическим синдромом параметр CAVI статистически значимо коррелировал с показателями каротидного атеросклероза: толщина интима-медиа (OR=4.94 95%; CI: 1.49-3.80; p=0.047) и наличием атеросклеротических бляшек в сонных артериях (OR=3.06; 95% CI: 1.42-2.28; p=0.065). Однако статистически значимых взаимосвязей параметра кфСПВ с показателями каротидного атеросклероза не выявлено (p>0.05). В группе без метаболического синдрома ни один из параметров жесткости артериальной стенки не коррелировал ни с одним из показателей каротидного атеросклероза (p>0.05).

Выводы: Параметр CAVI в отличие от параметра кфСПВ статистически значимо коррелировал с показателями каротидного атеросклероза в группе пациентов с метаболическим синдромом. В связи с этим, данный параметр может быть использован не только для оценки жесткости артериальной стенки, но и для определения субклинических признаков каротидного атеросклероза у данной группы пациентов.

Ключевые слова: метаболический синдром, артериальная жесткость, каротидный атеросклероз, CAVI

Introduction

It is commonly known, that arterial wall refers to the surrogates of the cardio-vascular diseases (CVD) [1-4]. Increased arterial stiffness is one of the clinically significant indicators for stratification of the CVD hazard, which is reflected in the European Recommendations on Diagnosis and Management of Arterial Hypertension (AH), in which the arterial wall is characterized as a target organ [5]. At the same time, changes in the parameters of arterial stiffness with metabolic disorders are widely studied. According to contemporary views, metabolic syndrome (MetS) refers to a symptom group that is characterized by abdominal obesity (AO), AH, hyperglycemia, dyslipidemia (a decrease in the level of High density: HDL-C and an increase in the concentration of triglycerides - TG) [6]. According to figures provided by various authors, the prevalence of MetS in the world ranges from 4 to 28.7%, which is primarily due to the high prevalence of obesity. Beyond that, a number of studies have shown that MetS is accompanied by an increase in arterial stiffness, which is also a predictor of cardiovascular complications [7-11]. In connection therewith, early detection of an increase in arterial stiffness in patients with MetS can help to prevent cardiovascular complications in patients of this category.

The most common parameters characterizing arterial stiffness due to their measurement simplicity and accessibility include indirect methods for determining regional stiffness of the arterial wall, such as the Cardio-Ankle Vascular Index (CAVI), as well as carotid-femoral Pulse Wave Velocity (cfPWV). It is worth noting that the determination of the PWV in the aorta (determined by the carotid-femoral Pulse wave velocity cfPWV) is currently the clinical "gold standard" for measuring the stiffness (rigidity) of the arterial wall. By the Recommendations of the American Heart Association (2015), arterial wall should be determined non-invasively by measuring cfPWV (class I, evidence level A) [12]. At the same time, several studies have shown a higher information content of another arterial wall's parameter (CAVI) in the diagnosis of preclinical damage to the arterial wall in diseases associated with atherosclerosis [13-22]. CAVI makes it possible to evaluate vascular stiffness regardless of the level of blood pressure (BP) having an effect on the artery wall at the time of a pulse wave registration.

Among the "earliest" markers of atherosclerosis with subclinical progress, an increase in "intima-media thickness" (IMT) of the carotid arteries is considered. Its increase for every 0.1mm is associated with an increase in the risk of myocardial infarction by 11% [23-25]. The detection of carotid plaque is also a highly specific method for identifying individuals with a high cardiovascular risk among asymptomatic individuals suffering from atherosclerosis [26-29]. The diagnosis of plaque is an unconditional confirmation of the presence of atherosclerosis and, therefore, high cardiovascular risk.

In a number of large, multicenter epidemiological studies, such as the Rotterdam study [2] and ARIC [30], the connections between the cfPWV and signs of carotid atherosclerosis (IMT and "plaque presence") were revealed.

However, we have not found works in the available literature that are devoted to the study of the interrelation between the arterial stiffness parameters with indicators of carotid atherosclerosis in individuals with a metabolic syndrome.

The aim of this study was to determine the relationship between arterial stiffness parameters such as cfPWV and CAVI with indicators of carotid atherosclerosis (IMT, "carotid plaque presence") in patients with metabolic syndrome.

Material and methods

The study included 100 patients at the age of 40-70 years: 45 men and 55 women, the average age was 56.54±8.98 years. All were followed in outpatient clinics for prevention check-up and/or monitoring of cardiovascular risk factors. All of them satisfied the inclusion criteria and giving written informed consent. Patients were divided into 2 groups: 1st group comprises 42 patients with MetS; 2nd group comprises 58 patients without MetS. At the same time, the separation of groups by gender according to age was not performed, since the main goal of the study was to determine the relationship between the parameters of arterial stiffness with indicators of carotid atherosclerosis in individuals with and without MetS, regardless of age and gender.

MetS was diagnosed with 3 out of 5 of the following criteria [6,31]:

- abdominal obesity with a waist circumference (WC)>102cm for men and >88cm for women;
- TG>150 mg/dl (>1.7mmol/l) or lipid-lowering therapy;
- cholesterol-HDL<40mg/dL (<1.0mmol/l) in men and <50mg/dl (<1.2mmol /l) in women or lipid-lowering therapy;
- systolic arterial pressure (SBP) ≥130mmHg or diastolic arterial pressure (DBP) ≥85mmHg, or antihypertensive therapy;
- the plasma glucose level in the fasted state ≥110mg/dl (≥6.0mmol/l).

Inclusion criteria: Patients (men and women) at the age from 40 to 70 years, the presence and absence of MetS (comparison group).

Exclusion criteria: Peripheral vascular disease with proximal artery stenosis; ankle-brachial index <0.9 or amputation of a limb; surgical interventions at the level of the carotid artery, femoral artery or aorta; body mass index (BMI)>40kg/m²; atrial fibrillation or clinically significant arrhythmia; diseases associated with atherosclerosis (coronary heart disease, myocardial infarction, stroke, aortic aneurysm, etc.).

The study was a randomized controlled, open-label study in a single center. The examination of patients was carried out on the basis of JSC "Scientific-Research Institute of Cardiology and Internal Diseases" (Almaty, Kazakhstan). The study was approved by the Ethics Committee of this institute.

After a general clinical examination (anthropometric measurements, general and biochemical blood tests, ECG, etc.), the following were measured in patients:

I. CAVI is an index of arterial stiffness was calculated automatically using the VaSera-1500, Vascular Screening System (Fukuda Denshi, Japan) as previously described [13-22]. CAVI was determined using the following equation: CAVI=1/a [1/k2(lnPs/Pd)PWV'2 + b], where Ps is a systolic arterial pressure, Pd is diastolic arterial pressure, PWV' is the pulse wave velocity from the aortic root to the ankle pneumatic cuffs; k, a, b are constant values. We used the standard values of CAVI which the VaSera system incorporated for each age and gender. The average of right and left CAVI was used for analysis. According to the manufacturer's instructions, a CAVI less than 8.0 is supposed to be normal.

II. The SphygmoCor CPV System (Complior, ALAM Medical, Vincennes, France) with the determination of another arterial wall parameter – cfPWV. Carotid-femoral PWV was measured in the section from the carotid artery to the femoral. The cfPWV was determined by the classical method, i.e. simultaneously two qualitative sphygmograms were recorded at the points indicated above and the delay between the moments of the appearance of pulsations at the studied points of the vascular bed. PWV was calculated as the ratio between the distance traveled by the pulse wave and the foot-to-foot time delay and expressed in meters per second. The average of the 10 successive measurements (to cover a complete respiratory cycle) was used in the analyses. The distance between the carotid and femoral arteries was determined according to the Recommendations of European experts using a tape measurer from the middle of one sensor to the middle of another; this distance was multiplied by 0.8 to obtain the real distance between the arteries [1,12].

Measurements (BP, cfPWV and CAVI) were carried out after 5–10 min of rest in order to obtain a stable hemodynamic state, which avoided randomness in the order of measurement of PWV and CAVI. As mentioned above the indicated threshold values for cfPWV (>10m/s) and CAVI (>8) were taken according to the manufacturer's instruction and the expert consensus document on arterial stiffness [1,12, 32].

III. Duplex scanning carotid arteries (DSCA) was performed on a Vivid 9 (JA, USA) with linear-array 12-MHz transducer to evaluate the intima-media thickness (IMT), the presence of plaques in the carotid arteries (carotid plaque presence) in accordance with the recommendations of the American Society of Echocardiography and Society for vascular medicine and biology (2008) [33]. The following study protocol was used:

- scanning in the B-mode of the common carotid artery (CCA) from the mouth to the area of bifurcation, internal (ICA) and external (ECA) carotid arteries in the cross and longitudinal sections; the study of these arteries was carried out in a pulse-wave Doppler mode and in the color Doppler mapping mode to detect plaques. Plaques were diagnosed in the case of detecting a local thickening of the arterial wall by at least 50% compared with its adjacent sections or when identifying a local section of the intima-media complex with a thickness of more than 1.5 mm, which has distinct boundaries. IMT assessment was carried out using the "Technology of automatic contouring of the intima - media thickness" in B-mode by scanning the distal CCA (1-2 cm) on both sides in two mutually perpendicular planes (anteroposterior and lateral) while synchronizing the image with an ECG;
- measuring the average IMT parameter of the wall farthest from the sensor in three cardiac cycles (from the obtained three measurements, the maximum was selected on each side). Based on the expert consensus the carotid atherosclerosis was defined when carotid ultrasound findings met the following criteria: IMT>0.9 mm and the presence of carotid plaque [5,24,33].

IV. Blood lipid parameters were determined [31]: total cholesterol (norm≤5.0 mmol/l; deviation from the norm>5.0 mmol/L), low-density lipoprotein-cholesterol, (LDL-C norm≤3 mmol/l; deviation from the norm>3,0 mmol/l), high-density lipoproteins-cholesterol (HDL-C, norm: w-1.2 mmol/l; m-1.0 mmol/l; deviation: w<1.0; m<1.2 mmol/l), triglycerides (TG, norm≤1.7 mmol/l; deviation from the norm>1.7 mmol/l). ARCHitect with SysteMetS 8000 and a homogeneous method was used.

Statistical data processing was carried out using the software package Statistics 10.0. Data are presented in form of a median value, lower and upper quartiles and deviation rates (in %). A comparison between groups was carried out using ANOVA tests. For comparing proportions, Fisher's two-tailed exact test was used. To evaluate the relationship between the studied parameters multiple logistic analyses were performed. The logistic regression results were expressed as the odds ratio with a 95% confidence interval (CI) and p value. The p values <0.05 were considered statistically significant.

Results

General characteristics of patients are presented in the Table 1. As can be seen from Table 1, the median age of patients of the two groups did not significantly differ (58.5 and 57.5 years), while the number of people over 60 in each group was 19%. The group with MetS included mainly patients with increased body weight: the number of people with increased BMI in the group with MetS was significantly higher than in the group without MetS (95% versus 29.2%; p=0.001). This is to be expected since one of the criteria for MetS is the presence of abdominal obesity. From indicators of blood lipid profile, statistically significant differences were observed in the number of patients with a decreased level of HDL-C (in the group with MetS more: p=0.05) and with increased TG (in the group with MetS more: p=0.001), while significant differences in the number of patients with high levels of total cholesterol and LDL-C were not detected (p>0.05). It should be noted that before the inclusion of the study, patients of the two groups did not take lipid-lowering therapy. In the group with MetS, there were statistically significantly more patients with increased glucose levels than in the group without MetS (p=0.001). This is understandable since increased glucose is also one of the criteria for MetS. Moreover, in the group with MetS there were 19% of patients with diabetes mellitus (DM) while in the group without MetS there were no people with diabetes mellitus.

It should be emphasized that in our study, the number of individuals with increased cfPWV did not significantly differ between the groups (52.5% and 41.3%; p=0.31). There were significantly more patients with diagnosed carotid plaques in the group with MetS than in the group without MetS (71.4% versus 44.8%; p=00.1). In this case, the parameter "carotid plaque presence" was used for analysis, since the largest percentage of patients was with the presence of 1-2 plaques. At the same time, only 2.3% (1 patient) with 3 or more plaques in the group with MetS were revealed; in the group without MetS - 0%. In the group with MetS, statistically significantly more patients with IMT higher than the threshold value in comparison with the group without MetS (IMT>0.9: 76.1% versus 41.3%; p=0.001) were revealed.

In the group with MetS, the number of patients with arterial hypertension (AH) was significantly higher than in the group without MetS (81% versus 53.4%; p=0.001). However, at the time of the start of the study, only 8.8% of patients in the group with MetS had a diagnosis of AH and were taking antihypertensive therapy. The rest were diagnosed with 1st degree AH during the period of inclusion in the study and, accordingly, antihypertensive therapy was prescribed. In the group without MetS, the diagnosis of AH before inclusion in the study had 6.4% of patients; in 93.6%, the diagnosis of AH was established after inclusion in the study. Thus, the number of patients diagnosed with AH and accordingly taking antihypertensive therapy before inclusion in the study did not differ significantly between the groups (8.8% versus 6.4%; p>0.05). For another thing, in our study there were statistically significantly more smokers in the group with MetS than in the group without MetS (28.5 and 10.3%, respectively; p=0.03).

We have applied the method of multiple logistic analyses to determine the relationship between the studied parameters. The results of the analysis for a group of patients with MetS are given in Tables 2 and 3.

From the data presented in Tables 2 and 3 followed that in the group with MetS, more correlations of the CAVI with the studied parameters were revealed, namely: statistically significant correlations of the parameter were determined with such lipid profile indicators as TC (OR=5.26; 95 % CI: 1.08-29.18; p=0.039) and LDL-C (OR=6.88; 95% CI: 1.35-40.99; p=0.034), as well as BMI (OR=8.42; 95% CI: 1.04-22.11; p=0.044) and WC (OR=14.02; (95% CI: 1.34-74.7; p=0.021). In addition, the CAVI is significantly associated with the parameters of carotid atherosclerosis: IMT (OR=4.94 95%; CI: 1.49-3.80; p=0.047) and carotid plaque presence (OR=3.06; 95% CI: 1.42-2.28; p=0.065).

Table 1 Characteristics of the study population

	MetS (n=42)				Non-MetS (n=58)				p
	median	low quartil.	high quartil.	%*	median	low quartil.	high quartil.	%*	
Age, y.	58.50	51.00	67.00	—	57.50	53.00	64.00	—	
BMI, kg/m2 (>0.25)	31.50	27.96	34.55	95	27.15	25.15	29.20	29.2	0.001
WC, sm (m>102; w >88)	104.4	94.2	108.0	100	93.5	85.5	98.2	56.8	0.001
TC, mmol/l (>5.0)	5.55	4.85	6.85	62.5	5.25	4.25	5.90	45	0.10
LDL-C, mmol/l (>3.0)	3.90	3.05	4.50	62.5	3.29	2.70	3.86	44	0.07
HDL-C, mmol/l (m<1.2; w<1.0)	1.20	0.95	1.45	32.5	1.48	1.20	1.85	15.6	0.05
TG, mmol/l (>1.7)	1.92	1.50	2.80	67.5	1.20	0.90	1.46	12	0.001
Glucose, mmol/l (>6.0)	6.15	5.45	6.90	52.3	5.25	4.95	5.55	3.4	0.001
cfPWV, m/s (>10)	10.22	9.55	11.25	52.5	9.40	8.15	10.6	41.3	0.31
CAVI (>8)	8.45	7.50	9.30	66.6	8.12	7.10	8.90	49.8	0.01
IMT, mm (>0.9)	0.80	0.74	0.89	76.1 (32)	0.60	0.54	0.69	41.3 (24)	0.001
Carotid plaque presence	---	---	---	71.4 (30)	---	---	---	44.8 (26)	0.001
PP, mm Hg (>40)	46.5	42.5	51.5	52.3	56.0	49.0	59.0	36.2	0.15
AH	---	---	---	81.0	---	---	---	53.4	0.001
Smoking	---	---	---	28.5	---	---	---	10.3	0.03

* — number pts with deviation from the threshold value; p — differences of deviation rate between groups by Fisher's two-sided exact test (в %).
MetS —metabolic syndrome; BMI — body mass index; WC — waist circumference; TC – total cholesterol; LDL-C — low-density lipoprotein-cholesterol; HDL-C — high-density lipoprotein-cholesterol; TG — triglyceride; cfPWV — carotid-femoral pulse wave velocity; CAVI — Cardio-Ankle Vascular Index; IMT – intima-media thickness; AH- arterial hypertension; PP – pulse pressure.

Table 2 Correlation between CAVI and study parameters in group with metabolic syndrome (n=42)

Parameters	OR (95% CI)	p
BMI >0.25кг/м2	8.42 (1.04 - 22.11)	0.044
WC:m >102 см;w>88см	14.02 (1.34 - 74.70)	0.021
PP>40 mmHg	1.3 (0.24 - 7.36)	0.728
TC >5.0mmol/l	5.26 (1.08 - 29.18)	0.039
LDL-C >3.0 mmol/l	6.88 (1.35 - 40.99)	0.034
HDL-C m<1.0; w<1.2 mmol/l	1.35 (0.84 - 2.16)	0.613
TG >1.7 mmol/l	2.40 (0.24 - 63.60)	0.856
IMT >0.9мм	4.94 (1.49 - 3.80)	0.047
Carotid plaque presence	3.06 (1.42 - 2.28)	0.065
Multiple logistic analyses were used to evaluate the correlation between study parameters. Abbreviations as in table 1.		

Table 3 Correlation between cfPWV and study parameters in group with metabolic syndrome (n=42)

Parameters	OR (95% CI)	p
BMI >0.25кг/м2	5.04 (0.34 - 31.45)	0.201
WC:m >102 см;w>88см	4.33 (0.79 - 34.9)	0.141
PP>40 mmHg	6.73 (1.17 - 52.7)	0.029
TC >5.0mmol/l	2.89 (0.68 - 16.79)	0.307
LDL-C >3.0 mmol/l	4.79 (0.77 - 55.2)	0.131
HDL-C m<1.0; w<1.2 mmol/l	0.45 (0.07 - 2.73)	0.615
TG >1.7 mmol/l	7.47 (0.80 - 4.15)	0.147
IMT>0.9мм	1.17 (0.63 - 2.18)	0.60
Carotid plaque presence	0.72 (0.03 - 18.7)	0.84
Multiple logistic analyses were used to evaluate the correlation between study parameters. Abbreviations as in table 1.		

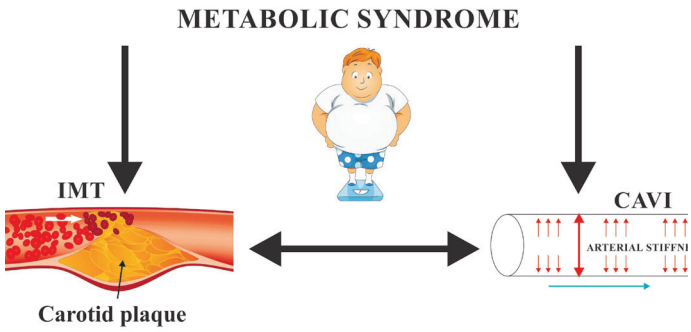
Table 4 Correlation between CAVI and study parameters in group without metabolic syndrome (n=58)

Parameters	OR (95% CI)	p
BMI >0.25кг/м2	1.10 (0.26 - 4.55)	0.885
WC:m >102 см;w>88см	0.70 (0.36 - 1.34)	0.761
PP>40 mmHg	2.40 (0.88 - 6.53)	0.068
TC >5.0mmol/l	1.15 (0.62 - 2.14)	0.891
LDL-C >3.0 mmol/l	2.11 (0.78 - 5.65)	0.142
HDL-C m<1.0; w<1.2 mmol/l	1.23 (0.69 - 2.17)	0.753
TG >1.7 mmol/l	1.70 (0.56 - 1.89)	0.911
IMT>0.9мм	4.33 (0.79 - 34.9)	0.141
Carotid plaque presence	2.33 (0.29 - 14.9)	0.161
Multiple logistic analyses were used to evaluate the correlation between study parameters. Abbreviations as in table 1.		

Table 5 Correlation between cfPWV and study parameters in group without metabolic syndrome (n=58)

Parameters	OR (95% CI)	p
BMI >0.25кг/м2	1.05 (0.25 - 4.32)	0.942
WC:m >102 см;w>88см	0.66 (0.35 - 1.28)	0.680
PP>40 mmHg	3.60 (1.01 - 12.97)	0.018
TC >5.0mmol/l	0.94 (0.49 - 1.80)	0.874
LDL-C >3.0 mmol/l	1.06 (0.49 - 2.28)	0.875
HDL-C m<1.0; w<1.2 mmol/l	1.32 (0.73 - 2.36)	0.610
TG >1.7 mmol/l	0.64 (0.36 - 1.12)	0.250
IMT >0.9мм	1.85 (0.84 - 4.86)	0.122
Carotid plaque presence	0.26 (0.10 - 0.64)	0.570
Multiple logistic analyses were used to evaluate the correlation between study parameters. Abbreviations as in table 1.		

Graphical abstract: The association between CAVI and carotid atherosclerosis indicators (IMT, carotid plaque presence) in patients with metabolic syndrome



At the same time, another parameter of arterial stiffness (cfPWV) reliably significantly correlated only with the "pulse pressure" (OR=6.73; 95% CI: 1.17-52.7; p=0.029). Statistically significant associations of cfPWV with indicators of both blood lipid profile and parameters of carotid atherosclerosis were not obtained (p>0.05).

By these means, in the group with MetS, slightly more statistically significant correlations of the CAVI with the studied parameters were revealed than in the cfPWV parameter.

We conducted a multiple logistic analysis of the studied parameters for a group of patients without MetS. The results are presented in Tables 4 and 5.

As shown in Tables 4 and 5 in the group without MetS, none of the arterial stiffness parameters (CAVI, cfPWV) statistically significantly correlated with any of the lipid profile indicators, nor with BMI, not with carotid atherosclerosis (p>0.05). Only the dependence of the cfPWV on the value of the "pulse pressure" was obtained (p=0.018).

Discussion

As mentioned above, in our study the number of individuals with increased cfPWV did not significantly differ between the groups (p=0.31). However, N. Nakanishi et al. as a result of a 9-year prospective observation of 2073 patients has revealed a significant increase of PWV in people with MetS compared with people without MetS [7]. In the group with MetS, which we have studied, there were significantly more patients with increased CAVI than in the group without MetS (p=0.01). These data are consistent with the results of a study conducted by N. Satoh et al., which showed that the value of CAVI in individuals with MetS was significantly higher than in individuals without MetS [10].

By these means, in the group with MetS, more statistically significant correlations of the CAVI with the studied parameters were revealed than in the cfPWV parameter. This difference is difficult to explain. It is probably due to the fact that CAVI reflects structurally determined changes in arterial wall as opposed to PWV, which reflects arterial wall at the moment and is a dynamic value that depends on arterial pressure, arterial wall elasticity and inflammation [4, 34].

As previously described the CAVI statistically significantly associated with such lipid profile indicators as TC and LDL-C (p<0.05) in the group with MetS. Our captured data partially coincide with the data of Laucevicius A. et al., which revealed, as a result of examination of 2106 individuals with metabolic syndrome, that an increase in CAVI level was reliably correlated with an increase in the level of triglycerides, cholesterol, and LDL-C. But, in contrast to our study, they also found the relations of CAVI with a reduced level of HDL-C [9]. Although in a study conducted by Gomez-Sanchez L. et al., it was shown that all components of the metabolic syndrome were associated with arterial stiffness indicators, with the exception of reduced levels of HDL-C. The level of HDL-C in this study, as in ours, was not reliably related with either the ankle-brachial PWV or CAVI (in this study, it was used unlike our abPWV) [11]. In addition, as in our study, they obtained correlations between the WC and the CAVI only.

It should be added that Liu H. et al. surveyed 222 people of Chinese origin aged 50-92 years, as a result of which it was found that the CAVI was significantly higher in individuals with abdominal obesity, as well as in individuals with low levels of HDL-C [8]. The revealed dependences allowed the authors to conclude that abdominal obesity and a decreased level of HDL-C were the main factors affecting the arterial stiffness in Chinese population.

We have found out that another parameter of arterial stiffness, cfPWV significantly reliably correlated only with the parameter "pulse pressure". This correlation can be explained by the fact that the value of the cfPWV parameter directly depends on the level of blood pressure. The value of the CAVI parameter does not depend on the level of blood pressure. Similar results were obtained by Russian researchers who did not find the dependence of the cfPWV parameter with any of the indicators of the metabolic syndrome [35]. Although Finnish researchers found that adults who had metabolic syndrome in childhood had higher values of PWV than people without metabolic syndrome [36].

As written above, the CAVI parameter significantly reliably correlated with the indicators of carotid atherosclerosis in patients with MetS. Although we have not found in the available literature studies devoted to the study of the relationship between the parameters of arterial stiffness and carotid atherosclerosis in individuals with MetS, our data are consistent with the results of studies on this issue in other diseases. So, Izuhara M. et al. with multiple logistic analyses have found that CAVI correlated to a greater degree than the PWV with signs of both carotid (IMT and "carotid plaque presence") and coronary atherosclerosis in individuals with various cardiovascular risk factors [37]. Okura T. et al. also discovered the relationship of the CAVI parameter with IMT and "carotid plaque presence" in patients with arterial hypertension [38]. Suzuki Jun et al. examined young people aged 20-44 years and determined that CAVI statistically significantly correlated with indicators of carotid atherosclerosis (IMT and "carotid plaque presence") [39].

In the group without MetS we have not found out statistically significant associations between any of the arterial stiffness parameters (CAVI, cfPWV) with any of the lipid profile indicators, nor with BMI, not with carotid atherosclerosis (p>0.05). The absence of reliable correlations in this group of patients between the studied parameters was probably since the median values of both cfPWV (9.40 cm/s) and CAVI (8.12) did not go beyond the threshold values.

Conclusion

The CAVI parameter, in contrast to the cfPWV, was statistically significantly correlated with indicators of carotid atherosclerosis (IMT and "carotid plaque presence") in patients with metabolic syndrome. In this connection, this parameter can be used to identify signs of not only increased arterial stiffness but also to determine subclinical signs of carotid atherosclerosis in people with metabolic syndrome.

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