Changes in Arterial Wall Stiffness in Patients with Obesity and Paroxysmal Form of Atrial Fibrillation

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Aim. To study changes in vascular wall stiffness in patients with obesity and paroxysmal atrial fibrillation (AF) during sinus rhythm retention.

Material and methods. The study included 86 obese patients aged 38 to 72 years. Patients were divided into 2 groups: 42 patients with paroxysmal AF and obesity (Group I) and 44 patients with obesity and without rhythm disturbance (Group II). All patients were evaluated for the main parameters of arterial wall stiffness: the heart-ankle vascular index (CAVI) and the ankle-brachial index (ABI) in the right and left main arteries.

Results. Body mass index (BMI) did not differ significantly between groups. The prevalence of visceral obesity in patients with paroxysmal AF was significantly higher than in patients without heart rhythm disorders. The study of vascular wall rigidity revealed a significant increase in the CAVI index in patients with paroxysmal AF compared with this in patients without cardiac arrhythmia. The average value of the CAVI index was 9.61±1.51 and 7.92±0.18, respectively (p=0.0003). In patients with obesity and paroxysmal AF, correlations were found between waist circumference to hip circumference (WC/HC) ratio and CAVI index (r=0.455, p=0.004); WC/height ratio and CAVI index (r=0.443, p=0.003); between WC and CAVI index (r=0.493, p=0.002). A positive direct relationship was found between CAVI index and the frequency of AF attacks during the year: r=0.782 (p=0.001).

Conclusion. A significant increase in the CAVI index, indicating a change in vascular wall stiffness, was found in patients with obesity and paroxysmal AF when compared with overweight patients without heart rhythm disorders. The increase in the CAVI index was correlated with the increase in WC, the WC/HC ratio, and WC/height ratio. There was a significant direct relationship between the CAVI index and the frequency of arrhythmia attacks in patients with obesity and paroxysmal AF.

Keywords: atrial fibrillation, obesity, vascular wall stiffness.

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Obesity is a growing epidemic while its prevalence rate has doubled over the past 30 years. Overweight is considered as an independent risk factor for hypertension, diabetes mellitus, coronary artery disease and chronic heart failure. The role of obesity as one of the predisposing factors for the onset and progression of atrial fibrillation (AF) is being discussed. It has been proven that an increase in body mass index (BMI) by 5 kg/m^2 contributes to higher risk of cardiac arrhythmias (up to 30%) [1].

Contemporary literature describes several mechanisms how excess body weight contributes to the risk of cardiac arrhythmias: activation of the sympathoadrenal nervous system, increased activity of the renin-angiotensin-aldosterone system, progression of hypertension, insulin resistance, lipid metabolism disorders and systemic inflammation [2-7]. One of the most poorly understood mechanisms associated with AF development in obesity is the cardiovascular remodeling. It has been shown that an increase in the stiffness of the arterial wall is accompanied by the diastolic dysfunction of the left ventricular myocardium and volume overload of the left atrium, that is fundamental for AF pathogenesis [8,9].

The effect of obesity on the elasticity characteristics of the vascular wall was first demonstrated in the work of J.J. Toto-Moukouo et al. [10]. When comparing groups of patients with long-term hypertension who had normal and overweight, it turned out that regardless of age, gender and blood pressure level, the pulse wave velocity in the vessels of the upper extremities was significantly higher in obese patients.

The independent role of obesity in the formation of vascular changes was demonstrated by J. Orr et al. [11]. The study included young healthy men who were measured for the vascular wall stiffness in the setting of a high-calorie diet, leading to an average increase in body weight of 5 kg over 6-8 weeks. With weight gain, the authors noted a statistically significant increase in the stiffness of the carotid arteries and a decrease in their elasticity. More expressed vascular changes were associated with the visceral type of obesity, determined by computed tomography and increased waist circumference. Researchers have shown that moderate, high-calorie-induced weight gain, even in healthy individuals, can lead to increased arterial stiffness [11].

Subanalysis of the LIFE study demonstrated that an increase in vascular wall stiffness in hypertensive patients contributed to the risk of AF. In a large population of patients, it has been proven that an increase in pulse pressure, being indirect marker of the stiffness of the vascular wall, was considered an independent predictor for new cases of arrhythmia [9].

L.F. Drager et al. found a relationship between the indicators of vascular wall stiffness and the size of the left atrium in patients with obstructive sleep apnea syndrome. The authors concluded that high rigidity of the vascular wall was an independent risk factor for the onset of AF [12].

Clinical publications regarding the rigidity of the vascular wall in patients with obesity and paroxysmal AF are currently lacking.

Aim of the study: to evaluate changes in vascular wall stiffness in patients with obesity and paroxysmal AF during the period of sinus rhythm.

Material and methods

The study included 86 obese patients (BMI from 30 to 44 kg/m^2) aged 38 to 72 years (mean age 61.2±4.7 years). The patients were divided into two groups depending on the presence of AF. Inclusion criterion for group I (n=42) was the presence of documented paroxysm of AF in obese patients, confirmed by electrocardiographic study (ECG) or Holter ECG monitoring. The comparison group (group II; n=44) consisted of obese patients without cardiac arrhythmias.

Exclusion criteria: exertional angina of I-IV functional class, history of myocardial infarction or cerebral stroke, acute coronary syndrome, chronic heart failure of III-IV functional class, inflammatory heart disease, heart defects, decompensated chronic kidney disease, severe pathology of liver, lungs, anemia, oncological diseases, pregnancy, mental illness. All patients signed written informed consent. The study was approved by the Local Ethics Committee (Protocol No. 10-19 dated July 17, 2019).

When included in the study, all patients underwent a general clinical examination with an assessment of anthropometric parameters: BMI, waist circumference (WC), hip circumference (HC), ratio of WC/HC and WC to height, sagittal abdominal diameter. Visceral obesity was diagnosed in patients with WC/HC ratio >1.0 and WC/height ratio >0.6.

To assess the stiffness of the wall of the great arteries, a VaSera device (VS-1000) (FucudaDenshi, Japan) was used, which made it possible to automatically determine and calculate the main indicators of the stiffness of the vascular wall – the cardio-ankle vascular index (CAVI), biological age of the arteries and ankle-brachial index (ABI) in the right and left main arteries. The CAVI index was calculated automatically based on the registration of plethysmograms of 4 limbs, electrocardiogram and phonocardiogram, using a special algorithm (Bramwell-Hil formula) [13].

The myocardial structure and functional parameters were assessed by echocardiography using Siemens software (Germany) and a sensor with a frequency of 3.74 MHz. Standard echo positions were used.

Standard technology of information processing and SPSS 23.0 software were used for statistical analysis. Numerical data were described using the arithmetic mean value (M) and its standard deviation (σ). Statistical analysis was carried out using the parametric Student's test. Pearson's correlation test was used for correlation analysis. The result was considered statistically significant in case of low error probability (p value <0.05).

Results

The clinical and demographic characteristics of patients are presented in Table 1.

The studied groups were comparable by sex, prevalence of hypertension, diabetes mellitus and smoking. Patients with obesity and paroxysmal AF were statistically significantly older than the comparison group. The prevalence of cardiovascular risk factors was similar in patients of groups I and II. Most of the patients included in the study had more than two risk factors, which determined high total cardiovascular risk. When comparing the overall number of risk factors, there was no statistically significant difference between groups.

The level of total blood plasma cholesterol in group I was 6.1±1.9 mmol/L, in group II – 5.9±2.6 mmol/L, low density lipoproteins – 3.4±0.3 and 3.1±0.2 mmol/L, high density lipoproteins – 1.2±0.1 and 1.4±0.1 mmol/L, triglycerides 1.9±0.2 and 1.7±0.1 mmol/L, glucose 5.9±1.1 and 6.2±1.2 mmol/l, respectively, without statistically significant differences.

Anthropometric measurements revealed that BMI did not differ significantly between studied groups. The number of anthropometric markers of visceral obesity was statistically higher in group I than in group II (Table 2). In addition to that, group I patients were characterised by high prevalence of visceral obesity compared to those in group II (42 [100%] patients vs 32 [72%] patients; p=0.0002).

Evaluation of the vascular wall rigidity revealed a statistically significant increase in the CAVI index in patients with paroxysmal AF than in patients without cardiac arrhythmias (Fig. 1).

Office systolic blood pressure (BP) in patients of group I was 147±5.2 mm Hg, among group II –

Table 1. Clinical characteristics of patients

Parameters	Group I (n=42)	Group II (n=44)	P value
Age, years	63.5±4,8	56.7±4.5	0.002
Females, n (%)	25 (60)	28(64)	>0.05
Males, n (%)	17 (40)	16(36)	>0.05
Hypertension, n (%)	36 (85.7)	36 (81.8)	>0.05
I degree	3 (7.1)	3 (6.8)	>0.05
II degree	20 (47.6)	18 (41)	>0.05
III degree	13 (31)	15 (34)	>0.05
History of hypertension, years	8.8±1.4	7.9±1.9	>0.05
Diabetes mellitus, n (%)	17 (40)	18 (41)	>0.05
Smoking, n (%)	3 (9)	3 (10)	>0.05

Data are presented as M±σ or n (%)

Table 2. Anthropometric indicators in patients of groups I and II

Parameters	Group I (n=42)	Group II (n=44)	P value
BMI, kg/m^2	32.9±0.9	32.1±0.9	>0.05
WC, cm	119.3±4.0	106.27±2.7	0.03
HC, cm	105.5±3.57	109±2.7	>0.05
WC/HC	1.37±0.09	0.84±0.06	0.002
WC/height	0.72	0.64	0.001
Sagittal abdominal diameter, cm	38.0±1.3	31.9±0.9	0.002

Data are presented as M±σ

BMI – body mass index, WC – waist circumference, HC – hip circumference

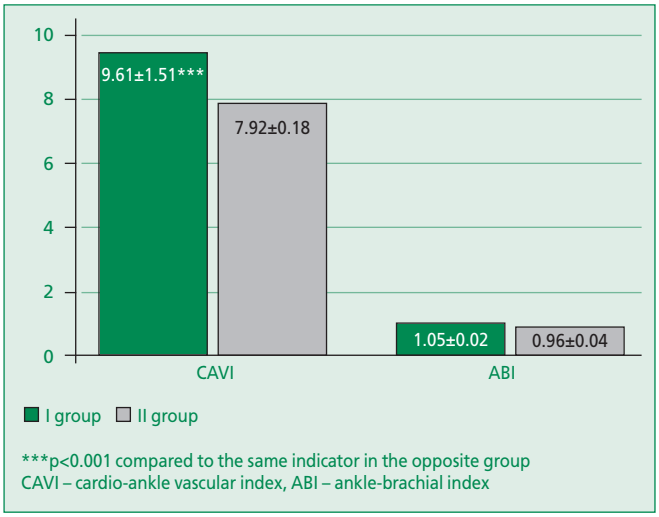

Figure 1. Vascular wall stiffness indicators in patients of the studied groups

Table 3. Echocardiography parameters in patients of groups I and II

Parameters	Group I (n=42)	Group II (n=44)	P value
LVEF, %	58.1±6.1	56.0±7.6	>0.05
LV EDV, ml	114.8±12.2	114.0±10.9	>0.05
LV ESV, ml	47.8±9.3	49.0±9.8	>0.05
LV myocardial mass index, g/m^2	183.3±21.5	160.7±24.6	0.03
LA volume, ml	70.2±3.3	58.3±4.8	0.004
E/A	0.80±0.15	1.01±0.14	0.002
Epicardial adipose tissue thickness, mm	9.60±1.12	7.09±1.08	0.001

Data are presented as M±σ

EF – ejection fraction, LV – left ventricle, EDV – end diastolic volume, ESV – end systolic volume, LA – left atrium, E/A – peak early diastolic LV filling velocity/peak atrial filling velocity ratio

152±6.8 mm Hg, diastolic BP – 88.7±2.8 and 86±2.1 mm Hg, heart rate (HR) – 77.0±3.8 and 75.5±2.9 beats per minute, respectively. There were no statistically significant differences in BP and HR between the study groups.

We also evaluated the correlation between the anthropometric indicators of visceral obesity and the vascular wall stiffness index in the studied groups. In obese patients with paroxysmal AF, correlations between CAVI and WC, WC/HC and HC/height ratios were found (Fig. 2).

Echocardiography demonstrated normal values of the left ventricular ejection fraction (LVEF) as well as end-diastolic and end-systolic volumes of the left ventricle in all included patients (Table 3).

Patients of group I had statistically significantly larger left atrial (LA) volume, LV myocardial mass index and epicardial adipose tissue thickness when compared with similar indicators in group II (Table 3). At the same time, the values of the E/A ratio in obese patients with paroxysmal AF were less than 1.0, that represented the signs of LV diastolic dysfunction.

Correlation analysis was held to assess the relationship between the indicators of vascular wall stiffness and the rate of AF recurrences in patients of group I. A positive direct correlation was found between the CAVI index and the frequency of AF episodes within a year (r=0.782, p=0.001; Fig. 3). This fact demonstrates a direct relationship between

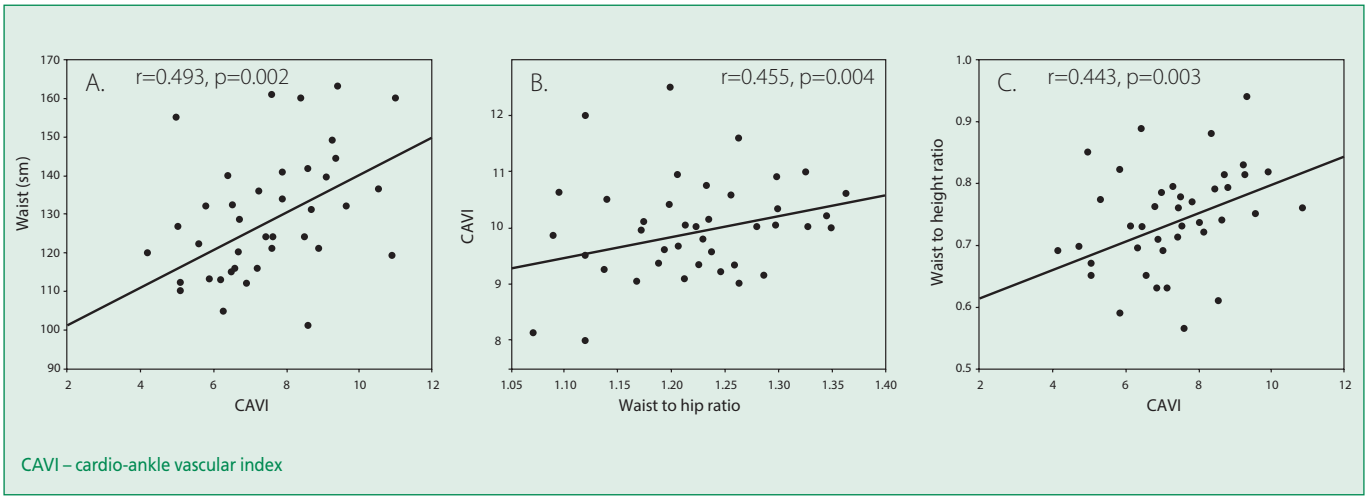

Figure 2. Correlation between the CAVI index and waist (A), waist to hip ratio (B), waist to height ratio (C) in patients of group I

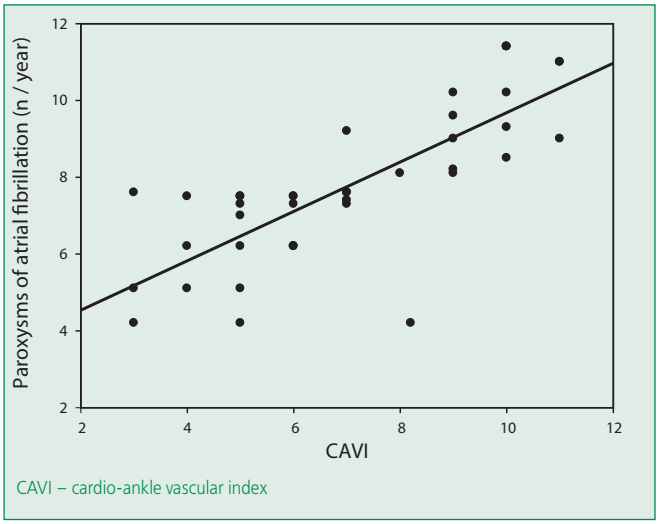

Figure 3. Correlation of CAVI with the frequency of paroxysms of atrial fibrillation in patients of group I

vascular lesions and the onset of AF paroxysms in patients with visceral obesity. While at the same time there were no statistically significant correlations between the CAVI index and age.

Discussion

Nowadays, possible mechanism how obesity contributes to the AF pathogenesis remains a subject of discussion. Our study demonstrated that in patients with paroxysmal AF the prevalence of visceral obesity was statistically significantly higher than in those without cardiac arrhythmias. In addition to escalation of some parameters – WC, sagittal abdominal diameter, WC/HC, WC/height ratio, patients with AF demonstrated statistically significant increase in the thickness of epicardial adipose tissue. In the Framingham study cardiac magnetic resonance imaging in obese patients showed enlarged volume of epicardial adipose tissue that was accompanied by LA dilation and this fact contributed to the appearance of supraventricular arrhythmias [14]. It can be assumed that fatty infiltration of the myocardium leads to disruption of intercellular interaction and contributes to progression of fibrosis with subsequent changes in atrial electrophysiology.

Remodeling of the vascular wall can be considered as another potentially significant mechanism of AF in obesity. The statistically significant increase in the CAVI index was demonstrated in group I patients. At the same time, only among overweight patients with paroxysmal AF there was found a correlation between the CAVI index and anthropometric markers of visceral obesity. The results of our study suggest that visceral obesity definitely contributes to the pathological cardiovascular remodeling. Recent studies demonstrated that high level of adipocytokines in visceral obesity had been associated with impaired endothelial function, activation of monocytes and macrophages along with lipoprotein metabolism disorders and led to overproduction of inflammatory factors [15-17].

Our study revealed association between frequency of AF episodes and increase in the CAVI index. Such correlation demonstrates direct interrelationship between the vascular wall lesion and cardiac arrhythmias in visceral obesity: from an increase in the stiffness of the vascular wall toward the LV diastolic dysfunction with LA enlargement and subsequent onset of AF.

Conclusion

Significant increase in the CAVI index, indicating a change in vascular wall stiffness, was found in patients with obesity and paroxysmal AF when compared with overweight patients without heart rhythm disorders. The increase in the CAVI index correlated with high value of WC, the ratio of WC/HC and WC/height.

There was a significant direct association between the CAVI index and the frequency of arrhythmia episodes in patients with obesity and paroxysmal AF.

Disclosures. All authors have not disclosed potential conflicts of interest regarding the content of this paper.

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