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Arterial stiffness as a factor of structural and functional cardiac remodeling in obesity

Druzhilov M. A., Kuznetsova T. Yu.

Aim. To analyze the association of parameters characterizing the degree of arterial stiffness and echocardiographic criteria for cardiac remodeling in patients with abdominal obesity. **Material and methods.** The study included 194 patients (men aged 46 to 55 years (49,0±2,3 years)), without hypertension (24-hour average blood pressure (BP) 117,5±5,5/73,0±4,1 mmHg), diabetes and cardiovascular diseases, with abdominal obesity (waist circumference >94 cm, body mass index 31,3±3,5 kg/m^2). Lipids and glucose concentrations were evaluated, and glomerular filtration rate was estimated using the CKD-EPI equation. We conducted 24-hour monitoring of blood pressure and arterial stiffness parameters (aortic pulse wave velocity (PWV), augmentation index (AIx) and systolic BP in the aorta), and echocardiography. **Results.** Left ventricular (LV) hypertrophy was detected in 14 (7,2%) patients, LV diastolic dysfunction — in 36 (18,6%) patients. The correlation of the average aortic PWV and the AIx with the LV mass index and the left atrial volume was shown. Patients with a high aortic PWV exceeding the 75th percentile of distribution (8,2 m/s) were characterized by a higher incidence of hypertrophy (18,8% vs 4,9%, p<0,01) and LV diastolic dysfunction (50,0% vs 12,3%, p<0,001). Patients with/without LV hypertrophy and diastolic dysfunction were characterized by higher values of average 24-hour aortic PWV, AIx and systolic BP in the aorta. According to the regression analysis, the predictors of LV diastolic dysfunction were age, waist circumference, aortic PWV, and AIx.

Conclusion. The relationship of parameters characterizing the degree of arterial stiffness, primarily, aortic PWV and echocardiographic parameters of the structural and functional cardiac remodeling in obese patients was revealed. Patients with a high aortic PWV (>8,2 m/s for men aged 46-55 years) are characterized by a higher prevalence of LV hypertrophy and diastolic dysfunction, as well as left atrial dilatation. This association is probably a reflection of one of the many pathogenesis links of HF and supraventricular cardiac arrhythmias in obese patients.

Key words: arterial stiffness, left ventricular hypertrophy, left ventricle diastolic dysfunction, obesity.

Relationships and Activities: none.

Petrozavodsk State University, Petrozavodsk, Russia.

Druzhilov M. A.* ORCID: 0000-0002-3147-9056, Kuznetsova T. Yu. ORCID: 0000-0002-6654-1382.

*Corresponding author:
drmark1982@mail.ru

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A large number of metabolic, neurohumoral and hemodynamic disorders in obesity, even in patients without associated diseases and medical conditions, lead to remodeling of cardiac structure and function, manifested in various patterns, including left ventricular (LV) concentric hypertrophy, left atrial (LA) dilatation, LV diastolic and systolic dysfunction [1].

Various pathophysiological pathways of this association are actively studied. The results of papers have demonstrated the dominate importance of abdominal visceral and ectopic (epicardial) obesity [2, 3], hyperactivation of sympathoadrenal and renin-angiotensin-aldosterone systems, selective leptin and insulin resistance [3, 4], chronic inflammation due to excessive secretion of pro-inflammatory adipocytokines, neprilysin hypersecretion, leading to more intense removal of circulating natriuretic peptides [5], decreasing adiponectin levels and the development of adiponectin resistance [6].

In addition, remodeling of cardiac structure and function is associated with increased arterial stiffness [7]. Currently, the related pathophysiological pathways are being specified, among which the dysfunction of smooth muscle cells and changes in its proportions with extracellular matrix are of major importance [8].

At present, the gold standard for assessing arterial stiffness is the definition of carotid-femoral pulse wave velocity (PWV) [9]. An alternative easy-to-use indicator, characterized by a high correlation with carotid-femoral PWV, is the aortic PWV [10]. In addition, an increase in the augmentation index, as well as the level of central blood pressure (BP), may indirectly indicate an increased vascular stiffness [11].

In obesity, large elastic artery remodeling due to dysfunctional adipose tissue and dysadipokinemia develops faster than the "normal" aging process [12]. We also demonstrated the relationship of visceral obesity, verified by echocardiography with determination of epicardial fat thickness, and parameters characterizing arterial stiffness [13].

The aim of this study was to analyze the association of parameters characterizing the arterial stiffness and echocardiographic criteria for cardiac remodeling in patients with abdominal obesity. This study was performed in accordance with the Helsinki declaration. The medical ethics committees of the Ministry of Health of the Republic of Karelia approved this study. All patients signed informed consent.

Material and methods

The study included 194 patients (men aged 46 to 55 years (49,0±2,3)) without hypertension (mean BP — 117,5±5,5/73,0±4,1 mm Hg), diabetes and cardiovascular diseases, with abdominal obesity (waist circumference >94 cm, body mass index 31,3±3,5 kg/m^2). Patients did not receive any antihypertensive, lipid-lowering and antidiabetic drugs.

The study included 194 patients (men aged 46 to 55 years (49,0±2,3 years)), without hypertension (24-hour average blood pressure (BP) 117,5±5,5/73,0±4,1 mm Hg), diabetes and cardiovascular diseases, with abdominal obesity (waist circumference >94 cm, body mass index 31,3±3,5 kg/m^2). Patients did not receive any antihypertensive, lipid-lowering and antidiabetic drugs. Lipids and glucose concentrations were evaluated, and glomerular filtration rate was estimated using the CKD-EPI equation. We conducted 24-hour monitoring of blood pressure and arterial stiffness parameters (aortic pulse wave velocity (PWV), augmentation index (AIx) and systolic BP) (BPlab MnSDP-3 monitor, Vasotens 24 software, OOO Petr Telegin, Russia), and echocardiography (Logiq 5P Premium, General Electric, USA).

LV mass was calculated by the formula of American Society of Echocardiography (ASE). LV mass was indexed to height^{2,7} (LV mass/height^{2,7}). LV hypertrophy was considered LVMI ⩾50 g/m^{2,7} [14]. The relative wall thickness index (RWT) was calculated as RWT=(IVSd+PWTd)/LVIDd (with IVS: inter-ventricular septum; PWT: posterior wall thickness; LVID: LV internal diameter; d, in diastole). LA volume was calculated using an ellipsoid model, and then indexed to the body surface area and to height^{2,7}. LV diastolic function was investigated using pulsed-wave and tissue Doppler imaging. We calculated the average early diastolic mitral annular velocity, the early diastolic transmitral flow velocity and their ratio, the tricuspid regurgitation peak velocity, the transmitral flow deceleration time and the ratio of early to late filling velocity of LV. LV diastolic dysfunction was verified in accordance with guidelines of American Society of Echocardiography and the European Association of Cardiovascular Imaging [15].

Statistical processing was carried out using software packages Statistica 10, SPSS 22. The data are presented as the mean and standard deviation, as well as the frequencies. A correlation analysis was performed with the calculation of the Pearson's linear correlation coefficient (r) and related significance by the t-test. Group comparability was analyzed using the two-tailed Student's t-test and the Pearson's chi-squared test. Binary stepwise logistic regression was used. The differences were considered significant at $p<0,05$.

Results

Table 1 presents the main characteristics of subjects. Impaired fasting glycemia and impaired glucose

Table 1

The main characteristics of the patients

Parameter	Value
Age, years	49,0±2,3
Body mass index, kg/m^2	31,3±3,5
Body mass index ⩾30 kg/m^2, %	63,9
Body mass index 25-29, kg/m^2, %	36,1
Waist circumference, cm	104,8±7,3
Prediabetes, %	14,4
Impaired lipid metabolism, %	93,8
Average 24-hour SBP, mm Hg	117,5±5,5
Average 24-hour DBP, mm Hg	73,0±4,1
LV mass index, g/m^{2,7}	40,8±7,0
LV hypertrophy, %	7,2
LA volume, ml	44,6±7,3
Indexed LA volume, ml/m^2	21,5±3,2
Indexed LA volume, ml/m^{2,7}	10,2±1,9
LV diastolic dysfunction, %	18,6
Aortic pulse wave velocity, m/s	7,4±0,8
Average 24-hour aortic SBP, mm Hg	107,7±5,3
Average 24-hour augmentation index, %	-33,6±16,8

Abbreviations: DBP — diastolic blood pressure, LV — left ventricle, LA — left atrium, SBP — systolic blood pressure.

Table 2

Echocardiographic parameters of the structural and functional cardiac remodeling with/without high aortic pulse wave velocity

Parameter	Aortic PWV >8,2 m/s (n=32)	Aortic PWV <8,2 m/s (n=162)
LV mass index, g/m^{2,7}	45,1±7,0**	39,9±6,7**
LV relative wall thickness index	0,42±0,03*	0,40±0,04*
LV hypertrophy, %	18,8*	4,9*
Indexed LA volume, ml/m^2	23,1±3,0*	21,2±3,1*
Indexed LA volume, ml/m^{2,7}	11,0±1,9*	10,0±1,9*
LV diastolic dysfunction, %	50,0**	12,3**

Note: * — p<0,01, ** — p<0,001.
Abbreviations: LV — left ventricle, LA — left atrium, PWV — pulse wave velocity.

tolerance were detected in 28 patients (49,4%), various dyslipidemia types — in 182 (93,8%) patients.

The average 24-hour aortic PWV, systolic BP, and augmentation index were 7,4±0,8 m/s, 107,7±5,3 mm Hg and -33,6±16,8%, respectively. The 75th percentile for aortic PWV was 8,2 m/s. LVMI, LV volume and indexed volume were 40,8±7,0 g/m^{2,7}, 44,6±7,3 ml and 21,5±3,2 ml/m^2 (10,2±1,9 ml/m^{2,7}), respectively. LV hypertrophy was revealed in 14 (7,2%) patients. The LV ejection fraction by Simpson's rule exceeded 60% in all patients; LV diastolic dysfunction was detected in 36 (18,6%) cases.

To assess the relationships of arterial stiffness and echocardiographic parameters of cardiac remodeling, a correlation analysis was performed. The Pearson's linear correlation coefficient for aortic PWV with LVMI and indexed LA volume (ml/m^{2,7}) was 0,32 (p<0,001) and 0,31 (p<0,001), for aortic systolic

Table 3

Arterial stiffness parameters in subgroups of patients with/without left ventricular hypertrophy and diastolic dysfunction

Parameter	LVH+ (n=14)	LVH- (n=180)	LVDD+ (n=36)	LVDD- (n=158)
Aortic pulse wave velocity, m/s	8,1±0,2***	7,3±0,8***	8,0±0,5***	7,2±0,7***
Average 24-hour aortic SBP, mm Hg	110,9±3,4**	107,4±5,3**	110,3±4,1***	107,1±5,3***
Average 24-hour augmentation index, %	-22,4±22,0*	-34,5±16,5*	-21,7±16,7**	-36,3±15,7**

Note: * — p<0,05, ** — p<0,01, *** — p<0,001.
Abbreviations: LVH — left ventricular hypertrophy, LVDD — left ventricular diastolic dysfunction, SBP — systolic blood pressure.

Table 4

Results of the regression analysis of LV diastolic dysfunction predictors

Predictor	Unstandardized coefficient	Standardized coefficient	p
Age	0,263	0,101	<0,01
Waist circumference	0,068	0,034	<0,05
Aortic PWV	1,427	0,384	<0,001
Augmentation Index	0,03	0,015	<0,05
Constant	-31,74	7,469	<0,001

Abbreviations: PWV — pulse wave velocity.

BP — 0,20 (p<0,01) and 0,15 (p<0,05), for the augmentation index — 0,31 (p<0,001) and 0,49 (p<0,001), respectively.

As shown in Table 2, patients with a "high" aortic PWV exceeding the 75th percentile of distribution (n=32) were characterized by a higher LVMI (45,1±7,0 g/m^{2,7} vs 39,9±6,7 g/m^{2,7}, p<0,001), LV relative wall thickness index (0,42±0,03 vs 0,40±0,04, p<0,01), indexed LA volume (23,1±3,0 ml/m^2 vs 21,2±3,1 ml/m^2, p<0,01; 11,0±1,9 ml/m^{2,7} vs 10,0±1,9 ml/m^{2,7}, p<0,01). This subgroup was characterized by a higher incidence of LV hypertrophy (18,8% vs 4,9%, p<0,01) and LV diastolic dysfunction according to echocardiography (50,0% vs 12,3%, p<0,001).

We carried out a comparative analysis of arterial stiffness parameters in subgroups with/without LV hypertrophy and LV diastolic dysfunction (Table 3). Patients with LV hypertrophy had a higher average 24-hour aortic PWV (8,1±0,2 m/s vs 7,3±0,8 m/s, p<0,001), average augmentation index (-22,4±22,0% vs -34,5±16,5%, p<0,05) and average 24-hour aortic systolic BP (110,9±3,4 mm Hg vs 107,4±5,3 mm Hg, p<0,01). A similar data was observed in patients with/without LV diastolic dysfunction: 8,0±0,5 m/s vs 7,2±0,7 m/s (p<0,001), -21,7±16,7% vs — 36,3±15,7% (p<0,01) and 110,3±4,1 mm Hg vs 107,1±5,3 mm Hg (p<0,001), respectively.

The risk of LV diastolic dysfunction in patients with abdominal obesity was evaluated by binary logistic regression analysis. Clinical and laboratory data, 24-hour BP monitoring indicators, aortic PWV, augmentation index and systolic BP were studied as predictors (Table 4). The components of the mathematical model were age, waist circumference, aortic PWV and augmentation index: -31,74+0,263*age+0,068*waist circumference+1,427*aortic PWV+0,03*augmentation index. Moreover, aortic PWV was characterized by the highest standardized regression coefficient (0,384, p<0,001). The significance level of the Hosmer-Lemeshow test was 0,76, which indicates adequate goodness of fit.

Discussion

Various epidemiological studies and their meta-analyzes confirmed the independent role of obesity in the pathogenesis of cardiac remodeling and heart failure, and based on the results of experimental and clinical studies, numerous underlying etiopathogenetic pathways have been identified [1, 3]. There is more and more evidence for the presence of neurohormonal imbalance in patients with visceral obesity,

which becomes the subsequent basis for cardiac pathology [5].

To assess the association of arterial stiffness and echocardiographic parameters, we specifically included obese patients without hypertension, diabetes and any cardiovascular diseases in order to exclude the contribution of comorbidities. Moreover, in 7,2% and 18,6% of cases, LV hypertrophy and diastolic dysfunction were detected, which emphasizes the independent role of obesity in their development.

Probably, pathophysiological pathways that specify the processes of cardiac and vascular remodeling in obese patients are common. Reflection of the latter is excessive arterial stiffness. At the same time, the developing vascular wall changes are already becoming an independent component in the pathogenesis of further cardiac remodeling.

In our studies, we repeatedly analyzed the relationship of obesity, verified by various criteria, including ectopic (epicardial) visceral obesity, with arterial stiffness [12, thirteen].

In this study, we demonstrated the association of vascular and cardiac remodeling parameters in obese patients. The performed correlation analysis revealed correlation of aortic PWV and augmentation index with indexed LV mass and LA volume. It was shown that patients with a high aortic PWV are more likely to have LV hypertrophy and diastolic dysfunction, and both remodeling and LV hypertrophy are concentric in nature. The results of binary logistic regression analysis showed the leading role of arterial stiffness parameters in assessing the likelihood of echocardiographic signs of LV diastolic dysfunction in a patient with abdominal obesity.

The data obtained allow to consider arterial stiffness parameters, as a possible additional predictor that broadens indications for echocardiography. At the same time, understanding the etiopathogenesis of structural and functional cardiac impairment in obesity will allow to develop both pharmacological and non-pharmacological methods for preventing the development and progression of cardiac disease.

Conclusion

The relationship of parameters characterizing the degree of arterial stiffness, primarily, aortic PWV and echocardiographic parameters of the structural and functional cardiac remodeling in obese patients was revealed. Patients with a high aortic PWV (>8,2 m/s for men aged 46-55 years) are characterized by a higher prevalence of LV hypertrophy and diastolic dysfunction, as well as LA dilatation. This association is probably a reflection of one of the many pathogenesis links of HF and supraventricular cardiac arrhythmias in obese patients.

Relationships and Activities: none.

References

1. Chumakova GA, Veselovskaya NG, Kozarenko AA, et al. Heart morphology, structure, and function in obesity. Russian Journal of Cardiology. 2012;4:93-9. (In Russ.) doi:10.15829/1560-4071-2012-4-93-99.
2. Neeland I, Gupta S, Ayers C, et al. Relation of regional fat distribution to left ventricular structure and function. Circ Cardiovasc Imaging. 2013;6(5):800-7. doi:10.1161/CIRCIMAGING.113.000532.
3. Gritsenko OV, Chumakova GA, Shevlyakov IV, et al. The mechanisms of heart failure development in obesity. Russian Journal of Cardiology. 2018;(5):81-6. (In Russ.) doi:10.15829/1560-4071-2018-5-81-86.
4. Faulkner J, Bruder-Nascimento T, Belin de Chantemèle E. The regulation of aldosterone secretion by leptin: implications in obesity-related cardiovascular disease. Curr Opin Nephrol Hypertens. 2018;27(2):63-9. doi:10.1097/MNH.0000000000000384.
5. Packer M. Leptin-Aldosterone-Neprilysin Axis Identification of Its Distinctive Role in the Pathogenesis of the Three Phenotypes of Heart Failure in People With Obesity. Circulation. 2018;137(15):1614-31. doi:10.1161/CIRCULATIONAHA.117.032474.
6. Engin A. Adiponectin-resistance in obesity. Adv Exp Med Biol. 2017;960:415-41. doi:10.1007/978-3-319-48382-5_18.
7. Nilsson P. Hemodynamic Aging as the Consequence of Structural Changes Associated with Early Vascular Aging. Aging Dis. 2014:5(2):109-13. doi:10.14336/AD.2014.0500109.
8. Lacolley P, Regnault V, Avolio A. Smooth muscle cell and arterial aging: basic and clinical aspects. Cardiovascular Research. 2018;114(4):513-28. doi:10.1093/cvr/cvy009.
9. Van Bortel L, Laurent S, Boutouyrie P, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. Hypertension. 2012;30(3):445-8. doi:10.1097/HJH.0b013e32834fa8b0.
10. Posokhov I. Pulse wave velocity 24-hour monitoring with one-site measurements by oscillometry. Medical Devices: Evidence and Research. 2013;6:11-5. doi:10.2147/MDER.S42082.
11. Vasyuk YuA, Ivanova SV, Shkolnik EL, et al. Consensus of Russian experts on the evaluation of arterial stiffness in clinical practice. Cardiovascular Therapy and Prevention. 2016;15(2):4-19. (In Russ.) doi:10.15829/1728-8800-2016-2-4-19.
12. Pérez L, Pareja-Galeano H, Sanchis-Gomar F et al. “Adipaging”: ageing and obesity share biological hallmarks related to a dysfunctional adipose tissue. J Physiol. 2016;594(12):3187-207. doi:10.1113/JP271691.
13. Druzhilov MA, Kuznetsova TYu. Visceral obesity as risk factor of early vascular aging. Cardiologiia. 2016;2(56):52-6. (In Russ.) doi:10.18565/cardio.2016.2.52-56.
14. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021-104. doi:10.1093/eurheartj/ehy339.
15. Nagueh SF, Smiseth OA, Appleton CP et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016;29(4):277-314. doi:10.1016/j.echo.2016.01.011.