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Arterial stiffness in routine clinical practice: what is important to know for a clinical practitioner

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Change of elastic properties of arterial wall has an important meaning for pathogenesis of lesions of all organs in arterial hypertension (AH). This article reviews all parameters characterizing vascular elasticity, approaches to their measurement and prognostic value. These parameters include ankle-brachial index, pulse pressure, augmentation index, pulse wave velocity in aorta, and cardio-ankle vascular index. Moreover, this article considers information about the use of mentioned parameters for evaluation of cardiovascular risk and control of therapy in different categories of patients.

Keywords: *Arterial stiffness, ankle-brachial index, pulse pressure, augmentation index, pulse wave velocity in aorta, cardio-ankle vascular index*

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Relevance

A wide range of measures aimed at combating cardiovascular mortality has brought to its gradual decrease in recent years [1]. However, cardiovascular disease (CVD) continues to be the leading cause of death in the Russian Federation. Thus, according to the Federal State Statistics Service 940.5 thousand people died from CVD in 2015, representing more than half from total number of deaths [2].

Nowadays the fight against CVD is based on the "risk factor concept", which aims to identify people with high

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probability of developing cardiovascular system disease and to subsequently perform preventive measures [3]. With a certain degree of conditionality, all preventive measures can be divided into two groups: primary preventive measures and secondary preventive measures. To a large extent the latter ones represent the direct subject of activity of a practicing physician. One of the factors influencing secondary prevention efficiency is the timing of its starting. Accordingly, the early identification of subclinical lesions of target organs becomes crucially important meaning detection of such health condition of an individual when the risk factors have already influenced it in negative and often irreversible way. Subclinical markers of CVD include left ventricular myocardial hypertrophy (LVH), chronic cerebrovascular disease, chronic kidney disease stage 3, albuminuria, and retinopathy. The lesions of vascular wall being a target organ by itself have an important meaning in pathogenesis of various organ lesions. Subclinical markers of vascular wall lesions include the calcification of coronary arteries, the presence of atherosclerotic plaques in coronary arteries, increased arterial stiffness, augmentation of central blood pressure (BP), decreased ankle-brachial index, etc. Recently, most attention has been given to the evaluation of arterial stiffness due to its role in CVD development.

The damaging effects of high vascular stiffness on organs are closely associated with impaired damping function of the arterial system, which smooths out pressure fluctuations caused by cyclical ejection of blood from the left ventricle and transforms pulsating arterial blood flow into continuous blood flow required for peripheral tissues. Impaired damping function of the arterial system leads to several pathophysiological events increasing CVD risk. These events include elevated systolic blood pressure (SBP) that occurs due to lack of transformation of the kinetic energy of left ventricular blood flow into the potential energy of stretching aortic wall. It increases left ventricular afterload that leads to LVH, elevates oxygen consumption, impairs diastolic function, decreases cardiac output and in the end results in development of chronic heart failure. More than that, increased velocity of shock and reflected waves propagation through rigid vessels shifts the time of reflected wave return from diastole to late systole being the cause of decreased diastolic BP (DBP) and resulting in decreased coronary perfusion. Lowered DBP and elevated SBP together lead to the increase of pulse pressure (PP) which accelerates arterial lesions and is associated with target organ lesions [4].

Methods of vascular stiffness evaluation

In clinical practice arterial stiffness can be evaluated using various techniques. Nowadays the most studied ones include PP, ankle-brachial index (ABI), augmentation index (AI), aortic pulse wave velocity (APWV), cardio-ankle vascular index (CAVI).

PP is one of the first parameters that estimates arterial stiffness. The mechanism of PP elevation as the consequence of increased arterial stiffness is described above. In 1994 S. Madhaven demonstrated for the first time that PP>63 mm Hg has negative influence on the coronary heart disease (CHD)-related mortality of patients with arterial hypertension (AH) [5]. The Framingham heart study provided convincing evidences of the negative influence of high PP on prognosis of patients with cardiovascular pathology [6]. It was demonstrated that the coronary risk was significantly elevated and correlated with target organ lesions in case of SBP levels between 130- and 170-mm Hg and increased PP. The PIUMA study [7] demonstrated a high prognostic value of the average PP, in particular, its increase above 53 mm Hg led to five-fold elevation of the risk of all cardiovascular complications. Another study showed a stronger correlation between left ventricular myocardium mass index with PP rather than peripheral BP [8]. Low cost and high availability of the use of PP for arterial stiffness evaluation is another advantage of this technique. At the same time, PP levels depend on stroke volume, heart rate and initial BP levels that restricts the applicability of this parameter especially in young patients with hyperkinetic circulation type.

Estimation of ABI is another simple and available method of vascular stiffness evaluation. ABI reflects the ratio of SBP measured at the ankle to SBP measured in the upper arm. ABI decrease below 0,9 is a predictor of CHD, stroke, transitory ischemic attacks, renal failure, and total mortality [3]. It is necessary to highlight that neither ABI nor PP may be considered highly specific markers of arterial rigidity since they are influenced by atherosclerotic lesions of the lower limbs [9].

AI is a less studied criterion of arterial rigidity comparing with ABI and PP. Nevertheless, the existing data demonstrate that it may be used as an independent predictor of coronary events and significantly correlates with the degree of LVH [10]. However, AI has an independent predictive value for prognosing the risk of total mortality in patients with established CHD diagnosis [11].

According to some data [12], AI elevation may be diagnosed even before the identification of such indi-

cators as increased thickness of the carotid intima-media complex and decreased endothelium-dependent vasodilation. AI can be determined by recording and subsequent automatic analysis of the sphygmogram. This feature is realized in such devices as the VaSera VS-1500N volumetric sphygmograph and the BpLab 24h-blood pressure monitoring system with Vasotens extension.

The positive aspects of AI, as a method for assessing vascular stiffness, should include high sensitivity as well as variability in response to therapy. The results of our own observations confirm the high value of the method for the assessment of antihypertensive therapy effectiveness [13]. The negative side of the method is its dependence on heart rate and baseline BP. Another important disadvantage is the lack of reference values. It is only known that the AI measured on the brachial artery should be in the range of negative values.

APWV evaluation is rightly considered to be the "golden standard" for assessing vascular stiffness. Measuring the characteristics of wave propagation along the aortic pathway is the most appropriate from clinical point of view, since the aorta and its main branches are responsible for most of the pathophysiological effects of arterial stiffness. According to the guidelines of the American Heart Association, arterial stiffness should be measured noninvasively via carotid-femoral pulse wave velocity (PWV) evaluation [14, 15]. APWV in other segments like ankle-brachial one may be useful, but currently no long-term study of this method is available in the USA or in Europe. The determination of PWV in other arterial segments like carotid-radial one is not recommended since it has no prognostic value.

The prognostic value of APWV evaluation in terms of cardiovascular risk has a wide evidence base. 5-year observation on patients with AH demonstrated the increase of the risk of cardiovascular complications and death by 1,4 times for each increase of APWV by 3,5 m/s independently from any other known risk factor [16]. Some authors consider that APWV correlates with the risk of acute myocardial infarction, acute cerebrovascular accident, cardiovascular and total mortality more tightly than age, BP levels, smoking, LVH, and CHD [17].

Different approaches for wave registration can be used for APWV measurement. The corresponding sensors can reflect the pressure, the dilation of the arterial wall, and the blood flow velocity measured by the Doppler method. The path travelled by the wave is usually equated to the surface distance between the two registration areas.

A piezoelectric tonometer is used in the methods based on applanation tonometry (for example, the "traditional" SphygmoCor device). The SphygmoCor device has been used in studies of arterial wall stiffness in chronic kidney disease, as well as in some other studies. Since January 2016 the SphygmoCor technology has been approved for measuring CBP, AI, APWV in routine clinical practice in the USA, and the costs are reimbursed by insurance companies.

The Complior system is an example of devices using mechanical sensors for registering pulse waves. This technique has been used in most epidemiological studies that have demonstrated the prognostic value of APWV for cardiovascular events.

One type of the devices registering arterial wall oscillations is volumetric sphygmometers equipped with 4 oscillometric cuffs located on both hands and ankles (Omron VP1000, VaSera VS-1500N, ABI-system 100). In addition, the system for 24h BP monitoring BpLab with Vasotens extension is also able to calculate APWV by registering a sphygmogram at one point using a specific mathematical algorithm.

Despite the large evidence base, it is necessary to emphasize some limitations of the use of APWV for evaluation of arterial rigidity. In particular, some difficulties preventing high-quality registration of pressure pulse waves with mechanical sensors and applanation tonometry on femoral artery may occur in patients with metabolic syndrome, obesity, diabetes mellitus and peripheral artery disease [18]. The presence of aortic, ileal or proximal femoral stenosis can distort the results of any measurement method. Abdominal obesity especially in men and large breast in women lead to errors in measuring the distance between two registration points [19]. It requires precise measurement of the distance because even small errors may influence the absolute values of APWV [20]. Different researchers recommend either using the total distance between registration points on the carotid and femoral arteries or subtracting the distance from the carotid artery to the jugular notch from the total distance or subtracting the distance from the carotid artery to the jugular notch from the distance between the jugular notch and the measurement site on the femoral artery [19]. All three options allow only approximate estimation of the distance which is irrelevant for the studies aiming at identifying difference between the original and repeated measurements. However, the differences in distance measurement

methods become critically significant in comparison of the results of different studies, and it imposes certain restrictions on the use of this method. In addition, APVW values depend on initial BP levels.

In recent years, CAVI, a new marker of high vascular stiffness, which does not depend on the initial BP levels, has attracted increasing attention. It is proved that the level of CAVI reflects the severity of coronary atherosclerosis in patients with established CHD [21]. Angiographic studies demonstrated that CAVI increases proportionally with the number of coronary arteries affected with atherosclerotic lesions [22], as well as the extent and the degree of stenosis [21]. More than that, CAVI is an independent parameter positively associated with the coronary calcium score and the degree of coronary stenosis [23]. There is a significant correlation between CAVI and severity of atherosclerosis in the carotid arteries in patients with cerebrovascular disease [24].

CAVI measurement is performed using a VaSera VS-1500N volumetric sphygmograph. Apart from CAVI, this device can measure ABI, AI, and APWV. Simultaneous analysis of the main markers of high vascular stiffness allows using this device for screening of subclinical vascular lesions. It should also be noted that according to the order of the Ministry of Health of the Russian Federation dated December 26, 2016. No. 997n "On Approval of the Rules for Functional Diagnostics", volumetric sphygmometers are included in the equipment standard of the functional diagnostics department.

Concluding the discussion of the methods of vascular stiffness evaluation, we would like to emphasize that the above-mentioned markers of arterial rigidity do not substitute each other and have independent prognostic significance, and, consequently, their complex evaluation is necessary for more accurate evaluation of cardiovascular risk in concrete patient.

Clinical significance of evaluation of vascular stiffness

In general, evaluation of arterial stiffness may be used ad a screening approach for subclinical atherosclerosis detection and determination of the groups of high cardiovascular risk. Detection of subclinical lesions of vascular wall in patients without CVD aiming to modify lifestyle and to prevent further structural and functional lesions of target organs has a high value.

Arterial stiffness has an independent prognostic value in relation to fatal and non-fatal cardiovascular events in patients with AH [3, 25]. The results of arterial stiffness measurement demonstrated that a significant part of AH patients with moderate cardiovascular risk could be reclassified as high cardiovascular risk patients.

It has been established that decreased vascular elasticity indicates atherosclerosis progression and is associated with global severity of atherosclerotic process in patients with CHD and peripheral artery disease [26].

The brain is particularly sensitive to the decrease of vascular elasticity and, as a consequence, to a more pulsating blood flow [4]. Local circulation is connected with low resistance of microvessels which facilitates the transmission of excessive energy of the pulsating flow to the microvascular bed [27]. This may contribute to recurrent episodes of microvascular ischemia, tissue damage and is manifested as white matter tension, clinically unconfirmed focal brain infarction and tissue atrophy that contributes to the development of cognitive impairment and dementia. Aortic stiffness is also associated with increased risk of ischemic or haemorrhagic stroke [28].

Arterial stiffness is tightly related to decreased glomerular filtration rate and is a predictor of progressing kidney lesions up to terminal kidney insufficiency requiring dialysis [29]. Increased vascular stiffness is associated with higher risk of albuminuria and its progression [30]. High arterial rigidity is a potent independent predictor of total and cardiovascular mortality in the population of patients with chronic kidney disease [31].

The above-mentioned data suggest the high prognostic value of arterial stiffness markers for determination of total cardiovascular risk in different categories of patients. However, apart from solving the problems related to cardiovascular risk estimation, arterial rigidity markers can be used for therapy control. Even though nowadays there is no convincing evidence of improved prognosis associated with decreased arterial stiffness, it can be assumed by analogy with LVH, and these data will be available soon. In this regard, reduction of vascular stiffness should become a separate goal (intermediate endpoint) of therapy of patients with CVD together with reaching target levels of BP, cholesterol, cardio- and nephroprotection, etc.

Among the non-pharmacological approaches influencing vascular wall in a positive way, moderate physical activity, weight loss, low-salt diet, moderate

alcohol consumption, intake of garlic, fish oil, and α-lynoleic acid should be mentioned [32].

Pharmacological agents with a proved effect of decreased vascular remodelling include angiotensin-converting enzyme inhibitors, angiotensin receptor type II blockers, calcium channel blockers, several beta-blockers with vasodilating effects, indapamide, nitrates, and statins [33, 34, 35]. The results of our study [13] demonstrate a higher efficiency of a fixed combination of amlodipine and lisinopril comparing with metoprolol monotherapy.

Conclusion

Thus, nowadays practicing doctors have a sufficient number of methods evaluating arterial stiffness. These methods include some available markers (PP and ABI) and more sensitive and specific ones (AI, APWV, CAVI) requiring, however, additional equipment. The use of the above-mentioned vascular stiffness indicators in routine clinical practice for estimation of cardiovascular risk and therapy efficiency, undoubtfully, should contribute to increased quality of medical care for CVD patients.

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References

1. Maslennikova GYA, Oganov RG. Russian experience in reducing the burden of noncommunicable diseases and proposals for international cooperation. Preventive medicine. 2016;19(4):4-6. Russian
2. Health care in Russia. 2015: A statistical compilation. Rosstat. 2015:174. Russian
3. Consistent opinion of Russian experts on arterial stiffness in clinical practice. Cardiovascular therapy and prevention. 2016;15(2):4-19. Russian
4. Mitchell GF. Effects of central arterial aging on the structure and function of the peripheral vasculature: implications for end-organ damage. JAppl Physiol. 2008;105:1652-1660.
5. Madhaven S, Ooi WL, Cohen H. Relation of pulse pressure and blood pressure reduction to the incidence of myocardial infarction. Hypertension. 1994;23:395-401.
6. Franklin SS, Khan SA, Wong ND. Is pulse pressure useful for predicting coronary heart disease? The Framingham Study. Circulation. 1999;100:354-360.
7. Verdecchia P, Porcelatti C, Schulatti G. Ambulatory blood pressure an independent predictor of prognosis in essential hypertension. Hypertension. 1994;24:793-801.
8. Sharman JE, Fang ZY, Haluska B. Left ventricular mass in patients with type 2 diabetes is independently associated with central but not peripheral pulse pressure. Diabetes Care. 2005;28:937-939.
9. Recommendations of the European Society of Cardiology for the diagnosis and treatment of peripheral arterial disease (2011). Rational pharmacotherapy in cardiology (2011). 2012;4:4-73. Russian
10. Dzizinsky AA, Protasov KV. Arterial stiffness as a new factor in assessing the prognosis of arterial hypertension (literature review). Bulletin of the VSNC SO RAMN. 2006;6(52):209-215. Russian
11. Chirinos JA, Zambrano JP, Chakko S. Aortic pressure augmentation predicts adverse cardiovascular events in patients with established coronary artery disease. J Hypertens. 2005;45(5):980-985.
12. Broyak ON, Senchikhin VN, Lyamina SV. Arterial stiffness is a reliable marker of endothelial dysfunction in the early stages of the development of arterial hypertension, arterial hypertension. 2008;14(4):336-340. Russian
13. Drozdetsky SI, Kuchin KV, Tikhomirova YuR. Comparative assessment of the effects of two antihypertensive treatment regimens on arterial stiffness. Diary of Kazan Medical School. 2015;3(9):5-15. Russian
14. Recommendations for Improving and Standardizing Vascular Research on Arterial Stiffness. A Scientific Statement from the American Heart Association. J Hypertension. 2015;66(3):698-722.
15. Van Bortel LM, Laurent S, Boutouyrie P. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens. 2012;30:445-448.
16. Boutourie P, Tropeano AI, Asmar R. Aortic stiffness is an independent predictor primary coronary events in hypertensive patients (A longitudinal study). Hypertension. 2002;39:10-15.
17. Laurent S, Boutourie P, Asmar R. Aortic stiffness is an independent predictor all-cause and cardiovascular mortality in hypertensive patients. Hypertension. 2001;37:1236-1241.
18. Nichols WW, McDonald DA. Wave-velocity in the proximal aorta. Med Biol Eng. 1972;10:327-335.
19. Van Bortel LM, Duprez D, Starmans-Kool MJ. Applications of arterial stiffness, Task Force III: recommendations for user procedures. 2002;15:445-452.
20. Chiu YC, Arand PW, Shroff SG. Determination of pulse wave velocities with computerized algorithms. Am Heart J. 1991;121:1460-1470.
21. Isnard RN, Pannier BM, Laurent S. Pulsatile diameter and elastic modulus of the aortic arch inessential hypertension: a noninvasive study. J Am Coll Cardiol. 1989;13:399-405.
22. Laurent S, Cockcroft J, Van Bortel L. On behalf of European Network for Non-invasive Investigation of Large Arteries. Expert consensus document on arterial stiffness: methodolog-

ical issues and clinical applications. EurHeart J. 2006;27:2588-2605.

23. Park HE, Choi SY, Kim MK. Cardio-ankle vascular index reflects coronary atherosclerosis inpatients with abnormal glucose metabolism: Assessment with 256 slice multi-detector computed tomography. J Cardiol. 2012;60(5):372-376.
24. Izuhara M, Shioji K, Kadota S. Relationship of cardio-ankle vascular index (CAVI) to carotid and coronary arteriosclerosis. Circ J. 2008;72(11):1762-1767.
25. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010;55:1318-1327.
26. Mitchell GF, Parise H, Benjamin EJ. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. Hypertension. 2004;43:1239-1245.
27. Mitchell GF, van Buchem MA, Sigurdsson S. Arterial stiffness, pressure and flow pulsatility and brain structure and function. Brain. 2011;134(11):3398-3407.
28. Laurent S, Katsahian S, Fassot C. Aortic stiffness is an independent predictor of fatal stroke inessential hypertension. Stroke. 2003;34:1203-1206.
29. Ford ML, Tomlinson LA, Chapman TP. Aortic stiffness is independently associated with rate of renal function decline in chronic kidney disease stages 3 and 4. Hypertension. 2010;55:1110-1115.
30. Bouchi R, Babazono T, Mugishima M. Arterial stiffness is associated with incident albuminuria and decreased glomerular filtration rate in type 2 diabetic patients. Diabetes Care. 2011;34:2570-2575.
31. Blacher J, Guerin AP, Pannier B. Impact of aortic stiffness on survival in end-stage renal disease. Circulation. 1999;99:2434-2439.
32. Lopatin YuM., Ilyukhin OB. Control of vessel stiffness. Clinical significance and methods of correction. The heart. 2007;6(3):128-132. Russian
33. Kosheleva ON., Rebrov AP. Features of the processes of remodeling of the heart and blood vessels in patients with heart failure on the background of 6-month therapy with lisinopril. Rational pharmacotherapy in cardiology. 2010;6(3):323-328. Russian
34. Nedogoda SV, Chalyabi TA. Vascular rigidity and pulse wave velocity: new risk factors for cardiovascular complications and targets for pharmacotherapy. Topical issues of diseases of the heart and blood vessels. 2006;4:33-49. Russian
35. Oleynikov VE, Moiseev IYa, Melnikova ON. The clinical value of indicators of local and regional vascular rigidity, the possibility of pharmacological correction. Cardiovascular therapy and prevention. 2017;16(1):22-26. Russian