The overall echogenicity (GSM) of carotid intima-media complex shows a positive correlation with arterial stiffness in hypertensive patients

Francesco Natale[1], Simona Covino[1, 2], Riccardo Molinari[1, 2], Mirella Limatola[1, 2], Noemi Mollo[1, 2], Roberta Alfieri[1, 2], Enrica Pezzullo[1, 2], Francesco Loffredo[1, 2], Paolo Golino[1, 2], Giovanni Cimmino[2, 3]

[1]Vanvitelli Cardiology and Intensive Care Unit, Monaldi Hospital, Naples, Italy
[2]Department of Translational Medical Sciences, University of Campania Luigi Vanvitelli, Naples, Italy
[3]Cardiology Unit, Azienda Ospedaliera Universitaria Luigi Vanvitelli, Naples, Italy

Abstract

Background: Arterial stiffness measurement still plays a role in prediction of future cardiovascular events, thus helping for quantification of patients' cardiovascular (CV) risk level. However, significant measurement difficulties still exist, making its widespread evaluation not routinary. At present indices of arterial stiffness have not been associated with qualitative morphological characteristics of intima-media complex. The intima-media thickness (IMT) measurement is no longer recommended in the cardiovascular disease (CVD) risk assessment due to lack of a standard acquisition protocol. The intima media gray scale median (IM-GSM) is a relatively simple measurement, acquirable during a conventional carotid color-Doppler ultrasound examination. This study aims at investigating the possible relationship between arterial stiffness and echogenicity of IM-GSM of the common carotid arteries, in patients already diagnosed with arterial hypertension.

Material and methods: A total of 421 hypertensive patients were retrospectively selected from our database of hypertension outpatients ambulatory. They were divided into two groups according to IM-GSM values (cutoff value: 30) and then subsequently compared.

Results: In our study population, subjects with IM-GSM > 30 showed a statistically increased arterial stiffness and left ventricle mass index. A weak positive correlation was also found between IM-GSM, systolic blood pressure and duration of hypertension.

Conclusion: The data presented here indicated that the variation of arterial stiffness observed in hypertensive patients is associated with structural modifications in carotid arterial wall.

Key words: carotid intima-media thickness; hypertension; arterial stiffness; echogenicity of intima-media complex; GSM; PWV

Arterial Hypertens. 2023, vol. 27, no. 4, pages: 232–239
DOI: 10.5603/ah.96896

Address for correspondence: Francesco Natale, MD, PhD, University of Campania Luigi Vanvitelli, e-mail: natalefrancesco@hotmail.com

Introduction

The latest guidelines for the management of arterial hypertension released by the European Society of Cardiology (ESC) in 2023, still describe arterial stiffening as a major causal factor of isolated systolic hypertension and age-related increase in pulse pressure [1]. It results from morphological modifications in large arteries, leading to a loss of vessel elasticity and the distending force resulting from the pressure exerted on the arterial wall [1]. Loss of elasticity seems to be an early manifestation of atherosclerosis and it is strictly related to the ageing process of the vasculature [2].

According to the more recent European Society of Cardiology (ESC) Guidelines on cardiovascular disease (CVD) prevention, published in 2021 [3], measurement of arterial stiffness (AS) is still recommended in CVD risk assessment. Previous studies show that, regardless of age, arterial stiffening is linked to CVD risk factors, such as hypertension, diabetes [4, 5] and cardiovascular target organ damage (TOD) secondary to arterial hypertension [6]. It has also been independently associated with higher risk of ischemic stroke and cardiovascular (CV) mortality [7].

Carotid-femoral pulse wave velocity (PWV) is currently considered the gold standard technique for evaluation of large arteries stiffness. A PWV value > 10 m/s is indicated as a reliable marker of significant alterations of aortic function in middle-aged hypertensive patients [8]. It may also be used to assess ventricular-arterial coupling and monitor therapy effectiveness in patients with arterial hypertension [9]. Randomized clinical trials and metanalysis indicate that angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) may improve PWV beyond the effect of BP lowering in the long-term [10, 11]. However, measurement difficulties and lack of distribution of appropriate devices averse its widespread use.

Focusing on echographic images of the arterial wall, intima-media-thickness (IMT) measurement is the most studied parameter for evaluation of IM complex. However, its systematic use in the CVD risk assessment is no longer recommended due to lack of a standardized protocol and inability to reclassify the subjects toward higher CV risk [12, 13].

Recently, more attention has been paid on qualitative evaluation of echogenicity of IM complex and carotid plaques, using the Gray Scale Median (GSM) measurement [14]. Plaque echogenicity assessed by ultrasound has been found to reliably predict its morphology defining its soft content and the calcification degree [15, 16]. Moreover, GSM has been linked to most common CV risk factors [15, 16]. Intima-media GSM (IM-GSM) measurement is strictly related to GSM in atherosclerotic plaques, suggesting a similar histological correlation [17].

The study from Jashari et al. suggests that IM-GSM could be a better marker than IMT for evaluating multiple arterial district disease, since it could contrast the differences among several arterial territories affected by atherosclerosis [18]. Despite this evidence, the relationship between echogenicity of IM complex and carotid arterial stiffness remains, to date, less explored.

In the present study, we have evaluated simultaneously carotid-femoral-PWV and IM-GSM, in order to correlate these two parameters and trying to reinforce its possible role in arterial stiffness evaluation.

Material and methods

We have retrospectively analyzed the database of hypertensive outpatients admitted to our ambulatory, selecting data between October 2018 and December 2022. The following filter criteria have been applied:

- age between 35 and 65 years old;
- full clinical history and complete physical examination availability;
- lipid profile, creatinine, and fasting plasma glucose availability;
- carotid artery ultrasonography, 2D-ColorDoppler echocardiography, arterial stiffness measurement, IM-GSM measurement availability;
- diagnosis of grade I and II essential hypertension based on confirmation of systolic blood pressure (SBP) > 140 mm Hg and/or diastolic blood pressure (DBP) > 90 mm Hg on at least three visits, or in presence of antihypertensive treatment.

The following exclusion criteria were applied:

- patients with secondary hypertension;
- end-stage kidney disease;
- diabetes mellitus;
- atrial fibrillation;
- carotid plaques;
- severe valvular heart disease;
- inadequate echographic window.

The study complies with the principle of Good Clinical Practice and the Declaration of Helsinki. Local Ethics Committee approves this retrospective analysis. Informed consent was obtained from all subjects involved in the study. Once the above criteria were applied to the database, a final cohort of 421

Table 1. Characteristics of studied population

Study population (n)	
Patients	421
Male	232
Female	189
Smokers	105
HTN therapy	160

HTN — arterial hypertension; HCL — hypercholesterolemia

patients was identified for the final analysis. Population characteristics are summarized in Table 1. In our study population, 38% of our patients were previously treated for hypertension and only 7% for dyslipidemia. ACEIs, calcium antagonists and diuretics were the most used antihypertensive medications, while statins (mostly atorvastatin, rosuvastatin or simvastatin) were used for hypercholesterolemia.

As for standard procedure of our ambulatory, blood pressure was performed with a validated automatic sphygmomanometer of appropriate-sized rubber cuff around the non-dominant arm according the current guidelines [1] and international indications [19]. During each visit, three consecutive BP readings were obtained with the patient seated and at rest for at least 10 minutes. The mean of the three readings is subsequently used, rounded to the nearest 2 mm on the scale.

Arterial stiffness was analyzed using Complior SP (Complior II © — Fig. 1) to measure carotid-femoral-PWV. Carotid and femoral probes are put on the left side, respectively at carotid and femoral pulses; the distance between the two probes is automatically calculated by the device, based on each subject's height and weight. A PWV of 10 m/s is used as cutoff for normal values (calculating a real travelled distance of pulse wave as 80% of the direct anatomical distance between common carotid artery and femoral artery) [8]; a PWV value between 10 and 12 m/s is estimated mildly pathological; PWV values > 12 m/s (the cutoff value based on the 100% of distance between common carotid and femoral artery) [20] is estimated frankly pathological.

IM-GSM was measured using a pre-specified software (RFA system, ALOKA© — Fig. 2). A region of interest (ROI) is placed manually surrounding the IM complex in a 10-mm area in the posterior wall of the common carotid artery. The ROI is considered from 5 mm proximal to the carotid bulb

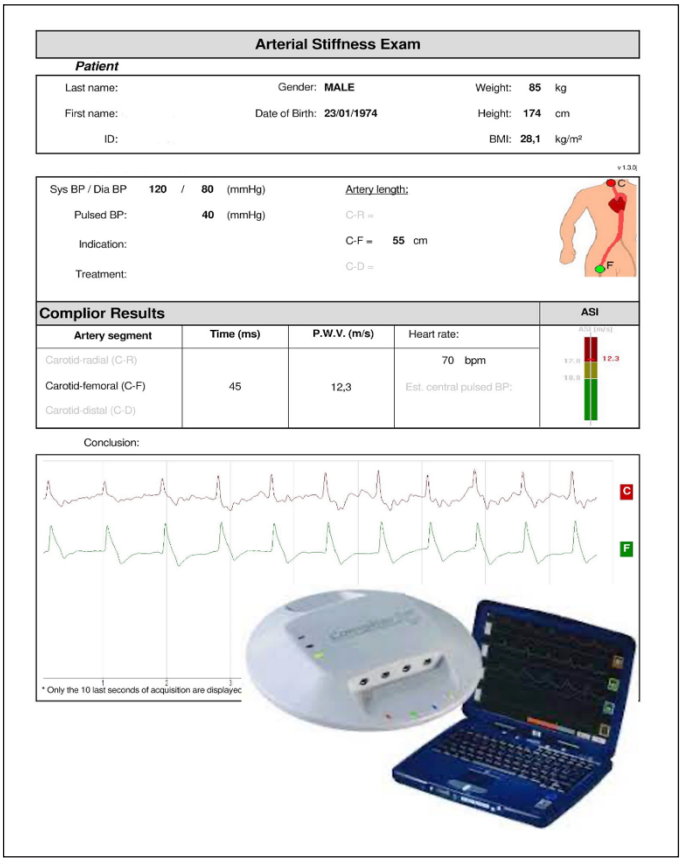

Figure 1. Arterial stiffness evaluation using carotid-femoral pulse wave velocity (cf-PWV) (Complior II©)

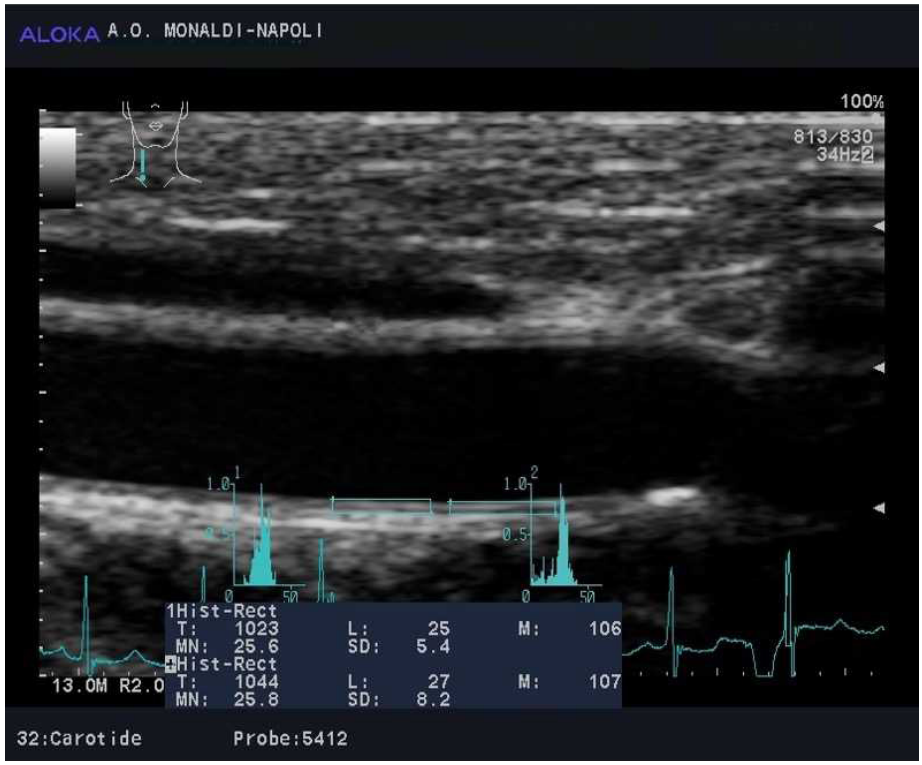

Figure 2. Intima-media gray scale median (IM-GSM) measurement (ALOKA©)

outside any atherosclerosis lesion. The GSM is calculated in the range 0 to 256 gray levels per pixel: black is used as reference for blood, as white for adventitia.

A cohort of non-hypertensive patients (n = 50) was randomly selected applying the same filtering criteria (with the exclusion of confirmed hypertension diagnosis). The 95% percentile reference range of IM-GSM for non-hypertensive patients was found to be 30 and coefficient of variation for IM-GSM was estimated around 3.5%.

Statistical analysis

Continuous variables are expressed as means ± standard deviation (SD) and discrete variables as counts and percentages. All statistical analyses were performed using GB-STAT version 6.50 (Dynamic Microsystems, Inc., Silver Spring, MD, United States). All the differences between the two groups were assessed using Student's t-test for unpaired data. Comparisons of categorical data were made using Fisher's exact test. The Pearson correlation coefficient was calculated to investigate the linear relationship between variables. Stepwise forward regression analysis was performed to assess which factors independently influence arterial stiffness, carotid IMT. The selected variables for inclusion in the models were those significant at univariate analysis. The $p < 0.05$ was considered statistically significant. K-statistic was used to assess inter- and intra-reader variability for echocardiographic and ultrasonographic parameters.

Results

The demographic and clinical parameters of our patients are shown in Table 2, where is reported each parameters at admission and according the IM-GSM values: group 1 (IM-GSM ≤ 30) and group 2 (IM-GSM >30). The correlation of IM-GSM values with age, gender, BMI and heart rate was not statistically significant, whereas a correlation in smokers (20% in group 1 VS 50% in group 2) was found. Subjects in group 2 (IM-GSM > 30) showed higher SBP and pulse pressure compared to those in group 1 (IM-GSM ≤ 30) ($p < 0.05$). A positive correlation was also found with time-duration of hypertension. Diastolic blood pressure values were mildly higher as well, but difference did not reach statistical significance.

Moreover, we did not find a significant differences in fasting plasma glucose, lipid profile [total cholesterol, high-density lipoprotein cholesterol (HDL-C) and triglycerides] or serum creatinine in these two

Table 2. Demographic and clinical parameters at admission and divided by intima-media gray scale median (IM-GSM) values

	Admission	IM-GSM ≤ 30 (Group 1)	IM-GSM > 30 (Group 2)	p-value
N°	421	354	67	
Age [years]	54 ± 11	53 ± 10	54 ± 8	NS
Male (%)	55 (232)	57 (204)	41 (28)	
BMI [kg/m^2]	28 ± 4	28 ± 3	28 ± 4	NS
Smokers (%)	25 (105)	20 (71)	50 (34)	< 0.05
Heart rate [bpm]	72 ± 11	72 ± 11	73 ± 10	NS
Duration of hypertension [years]	7 ± 6	6 ± 5	8 ± 6	< 0.05
Systolic blood pressure [mm Hg]	147 ± 14	146 ± 13	150 ± 15	< 0.05
Diastolic blood pressure [mm Hg]	92 ± 7	92 ± 7	93 ± 7	NS
Pulse pressure [mm Hg]	55 ± 5	54 ± 6	57 ± 8	< 0.05

BMI — body mass index; NS — non significant

Table 3: Blood test results at admission and divided by intima-media gray scale median (IM-GSM) values

	Admission	IM-GSM ≤ 30	IM-GSM > 30	p-value
Fasting plasma glucose [mg/dL]	91 ± 11	90 ± 9	92 ± 3	NS
Serum creatinine [mg/dL]	0.92 ± 0.2	0.91 ± 0.2	0.92 ± 0.3	NS
Total cholesterol [mg/dL]	205 ± 35	202 ± 35	208 ± 36	NS
HDL-C [mg/dL]	48 ± 12	48 ± 11	47 ± 11	NS
LDL-C [mg/dL]	126 ± 31	128 ± 33	134 ± 28	NS
Triglycerides [mg/dL]	131 ± 57	128 ± 55	134 ± 57	NS

HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; NS — non significant

Table 4. Echocardiographic parameters and arterial stiffness results at admission and divided intima- media gray scale median (IM-GSM) values

	Admission	IM-GSM ≤ 30	IM-GSM > 30	p-value
IMT [mm]	0.72 ± 0.2	0.71 ± 0.2	0.73 ± 0.2	NS
PWV [m/s]	9.0 ± 2.4	8.0 ± 1.8	13.1 ± 1.4	< 0.05
LVMI [g/m^2]	112 ± 26	109 ± 21	117 ± 20	< 0.05

IMT — intima-media thickness; PWV — pulse wave velocity; LVMI — left ventricular mass index

groups, even though higher values of total cholesterol and triglycerides were detected in IM-GSM > 30 group as reported in Table 3.

Focusing on echocardiographic measurement, a positive correlation was found between IM-GSM values and left ventricular mass index ($p < 0.05$). IMT values between the two groups did not reach any statistical significance, suggesting that IMT and IM-GSM values are uncorrelated.

Conversely, a strong positive correlation was found between IM-GSM and arterial stiffness parameter ($r = 0.75$, $p < 0.001$): in group 1, PWV value was equal to or lower than admission value, while in group 2 the PWV value (13.1 ± 1.4 m/s) is clearly pathological. Regression analysis performed separately between IM-GSM or arterial stiffness with age, SBP, DBP, pulse pressure, left ventricular mass index (LVMI) as independent variables showed that only age, IM-GSM and SBP were independently correlated to arterial stiffness (Tab. 4).

Discussion

The present study highlights that carotid arterial stiffness and quality of carotid intima-media complex assessed by GSM, are significantly linked to hypertension as marker of disease. This may be explained by the underlying pathophysiological process leading to arterial stiffening such as connective

tissue accumulation in extracellular matrix (including collagen, proteoglycans, fibronectin)(21). It has been reported that fibrotic tissue is echo-rich at ultrasound evaluation, thus increasing GSM measurement values [14].

Stiffening of arterial wall leads to a loss in the elastic energy that normally helps to improve organ perfusion during diastole. The main consequences are intermittent flow and pressure, excessive pressure pulsatility at distal vessels and shorter capillary transit time [22], finally resulting in target organ damage (TOD) that especially affects brain, kidney and heart, strongly influencing the patient's prognosis [6]. While it is relatively simple to identify the stage of hypertension and the presence of other risk factors, evaluation of target organ damage is not immediate.

Focusing on cardiac damage, in our study an IM-GSM > 30 is associated to higher LVMI. Many other reports have suggested a connection between increased arterial stiffness and endothelial damage [23–25], that lead to higher peripheral resistances, increased left ventricular load as well as left ventricular hypertrophy (LVH) [26–28].

A strong association has been found between LVH and higher PWV values [28]. Recently, diastolic dysfunction and heart failure with preserved ejection fraction (HFpEF) have been associated to increased arterial stiffness, since it seems to impact on LV relaxation [37, 29]. It also has been directly related to brain vascular damage regardless of other cardiovascular risk factors [26].

The increase in arterial stiffness is a well-established marker of TOD as supported by several independent evidence [6, 23, 30–33]. In the present study, by reporting a correlation between PWV and carotid IM-GSM in hypertensive patients, we might speculate that this marker could be used for TOD evaluation as well. In line with previous articles already showing the role of IM-GSM as marker of plaque echogenicity [17, 34] and as surrogate of multisite atherosclerosis disease [35], our study support its role as simple and reliable marker of atherosclerosis, since carotid artery echography may be readily available at office visit and it could be routinely performed in hypertensive patients.

Limitations of our study are the small population size and exclusion of patients with common comorbidities like diabetes mellitus that is an independent factor of high cardiovascular risk. Further studies are needed to better evaluate whether the IM-GSM measurement can be used with this category of patients to estimate arterial stiffness.

Conclusions

This study shows a significant increase in carotid arterial stiffness indices in hypertensive patients with high IM-GSM. The increased stiffness in these subjects does not only depend on increased wall thickness, but could be related also to a change in arterial wall structure. Carotid-femoral pulse wave velocity (cf-PWV) and IM-GSM parameters as well might be used as reliable markers of target organ damage. In addition, they could give an additional information on disease progression and therapeutic response. Evaluation of arterial stiffness should be considered as part of the routine evaluation of cardiovascular risk in hypertensive patients.

Data availability statement

Data are available from the corresponding author upon request.

Ethics statement

The study complies with the principle of Good Clinical Practice and the Declaration of Helsinki. Local Ethics Committee approves this retrospective analysis. The study complies with the principle of Good Clinical Practice and the Declaration of Helsinki. Local Ethics Committee approves this retrospective analysis.

Author contributions

Conceptualization: N.F., data analysis: C.S., M.R., L.M., M.N., R.A., P.E., manuscript drafting: L.F., N.F., C.G., manuscript reviewing: C.G., P.G.

Conflicts of interest

None declared.

Funding

None declared.

Acknowledgements

None declared.

References

1. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension. J Hypertens. 2023; 41(12): 1874–2071, doi: 10.1097/hjh.0000000000003480, indexed in Pubmed: 37345492.
2. Arnett DK, Boland LL, Evans GW, et al. Hypertension and arterial stiffness: the Atherosclerosis Risk in Communities Study. ARIC Investigators. Am J Hypertens. 2000; 13(4 Pt 1): 317–323, doi: 10.1016/s0895-7061(99)00281-2, indexed in Pubmed: 10821330.

3. Visseren FLJ, Mach F, Smulders YM, et al. ESC Scientific Document Group, ESC Scientific Document Group, ESC Scientific Document Group, ESC National Cardiac Societies, ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021; 42(34): 3227–3337, doi: 10.1093/eurheartj/ehab484, indexed in Pubmed: 34458905.
4. Cockcroft JR, Webb DJ, Wilkinson IB. Arterial stiffness, hypertension and diabetes mellitus. J Hum Hypertens. 2000; 14(6): 377–380, doi: 10.1038/sj.jhh.1001023, indexed in Pubmed: 10878698.
5. Christensen T, Neubauer B, Christensen T, et al. Increased arterial wall stiffness and thickness in medium-sized arteries in patients with insulin-dependent diabetes mellitus. Acta Radiol. 1988; 29(3): 299–302, indexed in Pubmed: 2968098.
6. Alonso-Domínguez R, Sánchez-Aguadero N, Patino-Alonso M, et al. Association between measurements of arterial stiffness and target organ damage in a general Spanish population. Annals of Medicine. 2021; 53(1): 345–356, doi: 10.1080/07853890.2021.1881812, indexed in Pubmed: 33533280.
7. Laurent S, Katsahian S, Fassot C, et al. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. Stroke. 2003; 34(5): 1203–1206, doi: 10.1161/01.STR.0000065428.03209.64, indexed in Pubmed: 12677025.
8. Van Bortel LM, Laurent S, Boutouyrie P, et al. Artery Society, European Society of Hypertension Working Group on Vascular Structure and Function, European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens. 2012; 30(3): 445–448, doi: 10.1097/HJH.0b013e32834fa8b0, indexed in Pubmed: 22278144.
9. Faconti L, Bruno RM, Ghiadoni L, et al. Ventricular and vascular stiffening in aging and hypertension. Curr Hypertens Rev. 2015; 11(2): 100–109, doi: 10.2174/1573402111666150529131208, indexed in Pubmed: 26022209.
10. Shahin Y, Khan JA, Chetter I. Angiotensin converting enzyme inhibitors effect on arterial stiffness and wave reflections: a meta-analysis and meta-regression of randomised controlled trials. Atherosclerosis. 2012; 221(1): 18–33, doi: 10.1016/j.atherosclerosis.2011.12.005, indexed in Pubmed: 22209214.
11. Ong KT, Delerme S, Pannier B, et al. investigators. Aortic stiffness is reduced beyond blood pressure lowering by short-term and long-term antihypertensive treatment: a meta-analysis of individual data in 294 patients. J Hypertens. 2011; 29(6): 1034–1042, doi: 10.1097/HJH.0b013e328346a583, indexed in Pubmed: 21519280.
12. Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. JACC Cardiovasc Imaging. 2014; 7(10): 1025–1038, doi: 10.1016/j.jcmg.2013.11.014, indexed in Pubmed: 25051948.
13. Den Ruijter HM, Peters SAE, Anderson TJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. JAMA. 2012; 308(8): 796–803, doi: 10.1001/jama.2012.9630, indexed in Pubmed: 22910757.
14. Huang X, Zhang Y, Meng L, et al. Evaluation of carotid plaque echogenicity based on the integral of the cumulative probability distribution using gray-scale ultrasound images. PLoS One. 2017; 12(10): e0185261, doi: 10.1371/journal.pone.0185261, indexed in Pubmed: 28977008.
15. Carotid artery plaque composition--relationship to clinical presentation and ultrasound B-mode imaging. European Carotid Plaque Study Group. Eur J Vasc Endovasc Surg. 1995; 10(1): 23–30, doi: 10.1016/s1078-5884(05)80194-7, indexed in Pubmed: 7633965.
16. Genkel VV, Kuznetsova AS, Lebedev EV, et al. Factors associated with atherosclerotic plaque echogenicity in patients aged 40-64 with carotid atherosclerosis. Kardiologiia. 2021; 61(6): 35–40, doi: 10.18087/cardio.2021.6.n1536, indexed in Pubmed: 34311686.
17. Lind L, Andersson J, Rönn M, et al. The echogenecity of the intima-media complex in the common carotid artery is closely related to the echogenecity in plaques. Atherosclerosis. 2007; 195(2): 411–414, doi: 10.1016/j.atherosclerosis.2007.03.029, indexed in Pubmed: 17462652.
18. Jashari F, Ibrahimi P, Johansson E, et al. Carotid IM-GSM is better than IMT for identifying patients with multiple arterial disease. Scand Cardiovasc J. 2018; 52(2): 93–99, doi: 10.1080/14017431.2018.1435903, indexed in Pubmed: 29402147.
19. Flack JM, Adekola B. Blood pressure and the new ACC/AHA hypertension guidelines. Trends Cardiovasc Med. 2020; 30(3): 160–164, doi: 10.1016/j.tcm.2019.05.003, indexed in Pubmed: 31521481.
20. Mancia G, De Backer G, Dominiczak A, et al. ESH-ESC Task Force on the Management of Arterial Hypertension. 2007 ESH-ESC Practice Guidelines for the Management of Arterial Hypertension: ESH-ESC Task Force on the Management of Arterial Hypertension. J Hypertens. 2007; 25(9): 1751–1762, doi: 10.1097/HJH.0b013e3282f0580f, indexed in Pubmed: 17762635.
21. Stary HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation. 1995; 92(5): 1355–1374, doi: 10.1161/01.cir.92.5.1355, indexed in Pubmed: 7648691.
22. Laurent S, Boutouyrie P, Laurent S, et al. Pathophysiology of hypertension in the elderly. Am J Geriatr Cardiol. 2002; 11(1): 34–39, doi: 10.1111/j.1076-7460.2002.00857.x, indexed in Pubmed: 11773714.
23. Sun Y, Liu F, Zhang Y, et al. The relationship of endothelial function and arterial stiffness with subclinical target organ damage in essential hypertension. J Clin Hypertens (Greenwich). 2022; 24(4): 418–429, doi: 10.1111/jch.14447, indexed in Pubmed: 35238151.
24. Duprez DA. Arterial stiffness and endothelial function: key players in vascular health. Hypertension. 2010; 55(3): 612–613, doi: 10.1161/HYPERTENSIONAHA.109.144725, indexed in Pubmed: 20083729.
25. Anderson TJ. Arterial stiffness or endothelial dysfunction as a surrogate marker of vascular risk. Can J Cardiol. 2006; 22 Suppl B(Suppl B): 72B–80B, doi: 10.1016/s0828-282x(06)70990-4, indexed in Pubmed: 16498516.
26. Einarsen E, Gerdts E, Waje-Andreassen U, et al. Association of increased arterial stiffness with diastolic dysfunction in ischemic stroke patients: the Norwegian Stroke in the Young Study. J Hypertens. 2020; 38(3): 467–473, doi: 10.1097/HJH.0000000000002297, indexed in Pubmed: 31725075.
27. Namba T, Masaki N, Matsuo Y, et al. Arterial Stiffness Is Significantly Associated With Left Ventricular Diastolic Dysfunction in Patients With Cardiovascular Disease. Int Heart J. 2016; 57(6): 729–735, doi: 10.1536/ihj.16-112, indexed in Pubmed: 27829641.
28. Yucel C, Demir S, Demir M, et al. Left ventricular hypertrophy and arterial stiffness in essential hypertension. Bratisl Lek Listy. 2015; 116(12): 714–718, doi: 10.4149/bll_2015_140, indexed in Pubmed: 26924139.
29. Seeland U, Brecht A, Nauman AT, et al. Prevalence of arterial stiffness and the risk of myocardial diastolic dysfunction in women. Biosci Rep. 2016; 36(5), doi: 10.1042/BSR20160276, indexed in Pubmed: 27653526.
30. Urbina EM, Isom S, Dabelea D, et al. Association of Elevated Arterial Stiffness With Cardiac Target Organ Damage and Cardiac Autonomic Neuropathy in Young Adults With Diabetes: The SEARCH for Diabetes in Youth Study. Diabetes Care. 2023; 46(4): 786–793, doi: 10.2337/dc22-1703, indexed in Pubmed: 36730642.
31. Bai Y, Wang Q, Cheng Di, et al. Comparison of Risk of Target Organ Damage in Different Phenotypes of Arterial Stiffness and Central Aortic Blood Pressure. Front Cardiovasc Med. 2022; 9: 839875, doi: 10.3389/fcvm.2022.839875, indexed in Pubmed: 35497999.

32. Vasan RS, Short MI, Niiranen TJ, et al. Interrelations Between Arterial Stiffness, Target Organ Damage, and Cardiovascular Disease Outcomes. J Am Heart Assoc. 2019; 8(14): e012141, doi: 10.1161/JAHA.119.012141, indexed in Pubmed: 31303106.
33. Mitchell GF. Aortic stiffness, pressure and flow pulsatility, and target organ damage. J Appl Physiol (1985). 2018; 125(6): 1871–1880, doi: 10.1152/japplphysiol.00108.2018, indexed in Pubmed: 30359540.
34. Mellucci PL, Bertanha M, Jaldin RG, et al. Grayscale median (GSM) post-processing, posterizing, and color mapping for carotid ultrasound. J Vasc Bras. 2023; 22: e20220081, doi: 10.1590/1677-5449.202200811, indexed in Pubmed: 36794172.
35. Jashari F, Ibrahimi P, Johansson E, et al. Carotid IM-GSM is related to multisite atherosclerosis disease. Atherosclerosis. 2015; 241(1): e164, doi: 10.1016/j.atherosclerosis.2015.04.851.