ЗДРАВООХРАНЕНИЕ И ПРОФИЛАКТИЧЕСКАЯ МЕДИЦИНА

PUBLIC HEALTH AND PREVENTIVE MEDICINE

DOI: 10.12731/2658-6649-2025-17-3-1216 **EDN: NXRFOQ**
UDC 616-005

Original article

PROSPECTS FOR A COMPREHENSIVE ASSESSMENT OF SCLEROSTIN, ARTERIAL CALCIFICATION AND STIFFNESS IN THE CONTEXT OF CORONARY HEART DISEASE

I.A. Snimshchikova, M.O. Revyakina, N.A. Kabina, E.V. Mityaeva

Abstract

Background. Coronary heart disease is accompanied by increased calcification and vascular stiffness, which is associated with an increased risk of adverse cardiovascular events. This manuscript focuses on the contribution of sclerostin to the development of vascular calcification and arterial stiffness, which is a key aspect of coronary heart disease.

Purpose. To assess the possibility of developing a comprehensive approach to assessing the likelihood of vascular calcification, taking into account indicators of arterial stiffness and a marker of extraosseous calcification (sclerostin) to improve noninvasive diagnostics of cardiovascular risk.

Materials and methods. The study included patients with myocardial infarction and unstable angina. Arterial stiffness index and calcification were assessed taking into account coronary angiography data and 24-hour blood pressure monitoring. Serum sclerostin concentrations were measured using ELISA.

Results. An increase in sclerostin concentration was found in patients with coronary artery stenosis of more than 50% in combination with intravascular calcified atherosclerotic plaques. A strong correlation was found between serum sclerostin concentration and arterial stiffness index. Results on a significant increase in the arterial stiffness index against the background of coronary artery calcification were

obtained. The results of ROC analysis showed the possibility of using threshold value of arterial stiffness index in assessing the severity of coronary artery disease.

Conclusion. Understanding the relationship between sclerostin, calcification and vascular stiffness can help in the development of new strategies for the diagnosis, prevention and treatment of coronary artery disease.

Keywords: sclerostin; arterial stiffness; vascular calcification; coronary heart disease; myocardial infarction

For citation. Snimshchikova, I. A., Revyakina, M. O., Kabina, N. A., & Mityaeva, E. V. (2025). Prospects for a comprehensive assessment of sclerostin, arterial calcification and stiffness in the context of coronary heart disease. *Siberian Journal of Life Sciences and Agriculture*, *17*(3), 336-357. https://doi.org/10.12731/2658-6649-2025-17-3-1216

Научная статья

ПЕРСПЕКТИВЫ КОМПЛЕКСНОЙ ОЦЕНКИ СКЛЕРОСТИНА, АРТЕРИАЛЬНОЙ КАЛЬЦИФИКАЦИИ И ЖЕСТКОСТИ В КОНТЕКСТЕ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

И.А. Снимщикова, М.О. Ревякина, Н.А. Кабина, Е.В. Митяева

Аннотация

Обоснование. Ишемическая болезнь сердца сопровождается повышенной кальцификацией и жесткостью сосудов, что ассоциировано с увеличением риска неблагоприятных сердечно-сосудистых событий. В этой статье особое внимание уделяется вкладу склеростина в развитие сосудистой кальцификации и артериальной жесткости, что является ключевым аспектом ИБС.

Цель. Оценка возможности разработки комплексного подхода к оценке вероятности кальцификации сосудов с учетом показателей артериальной жесткости и маркера внекостной кальцификации (склеростина) для улучшения неинвазивной диагностики сердечно-сосудистого риска.

Материалы и методы. В исследовании участвовали пациенты с инфарктом миокарда и нестабильной стенокардией. Оценивались показатели артериальной жесткости (ASI) и кальцификации с учетом данных коронароангиографии и суточного мониторирования артериального давления. Измерение сывороточных концентраций склеростина проводилось методом ИФА.

Результаты. Установлено повышение концентрации склеростина у пациентов со стенозом коронарных артерий более 50% в сочетании с внутрисо-

судистыми кальцинированными атеросклеротическими бляшками. Выявлена прочная корреляционная зависимость сывороточной концентрации склеростина и ASI. Получены результаты о значительном повышении индекса артериальной жёсткости на фоне кальциноза коронарных артерий. Результаты ROC-анализа показали возможность использования порогового значения ASI в оценке тяжести течения ИБС.

Заключение. Понимание связи между склеростином, кальцификацией и жесткостью сосудов может помочь в разработке новых стратегий диагностики, профилактики и лечения ИБС.

Ключевые слова: склеростин; артериальная жесткость; сосудистая кальцификация; ишемическая болезнь сердца; инфаркт миокарда

Для цитирования. Снимщикова, И. А., Ревякина, М. О., Кабина, Н. А., & Митяева, Е. В. (2025). Перспективы комплексной оценки склеростина, артериальной кальцификации и жесткости в контексте ишемической болезни сердца. *Siberian Journal of Life Sciences and Agriculture*, *17*(3), 336-357. https://doi.org/10.12731/2658-6649-2025-17-3-1216

Introduction

Vascular calcification (VC) is a multifactorial pathological process that causes the progression of atherosclerosis, hypertension, diabetes mellitus, and also leads to the development of adverse cardiovascular events (ACEs) [7].

Meta-analysis of publications devoted to the assessment of coronary cardiovascular diseases (CVD) risk indicates an increase in the frequency of fatal and non-fatal cardiovascular events by 3-4 times in the presence of vascular calcification of any localization [19]. The most common sites of calcification deposition are the left coronary artery and the aortic arch [9; 11], while the features of their distribution and location in the arteries of the heart and main vessels can have different clinical manifestations and outcomes [9; 11]. Considering that VC is a slowly progressive process with a long asymptomatic course, the frequency of which increases significantly with age, reaching 80% by the age of 60–69 [9], it is necessary to develop screening methods aimed at early detection of calcification of the coronary arteries and aorta, especially in individuals with risk factors (arterial hypertension, hyperlipidemia, diabetes mellitus, etc.) to reduce the population burden of CVD.

Despite the fact that numerous clinical and epidemiological studies indicate the importance of vascular calcification as a pathomorphological indicator of CVD [6, 16, 23], and traditional imaging methods (computer tomography and computed tomography angiography) are successfully used to identify and assess the progression of vascular calcification; they are expensive, require special

equipment associated with radiation exposure to the patient, and do not always allow detection of the early stages of this pathological process.

At present time, the relationship between vascular calcification and increased arterial stiffness (AS) is studied [3; 22], as well as the possibility of using this indicator as a predictor of ACEs, along with VC.

However, numerous issues of diagnostics and a comprehensive understanding of the mechanisms responsible for AS and mineral dysregulation remain unresolved.

Significant progress in the study of pathological extraosseous calcification in the last two decades has been achieved due to the research of the role of the main multifunctional signaling pathways and molecular regulators that control the phenotypic modulation of vascular smooth muscle cells (VSMCs) in cardiometabolic diseases [15; 26].

Since canonical WNT signaling is a key regulator of bone metabolism, this signaling pathway has become one of the main areas of research in the area of pathological extraosseous calcification, which is involved in both the development of atherosclerosis and the process of myocardial and vascular remodeling [4; 8; 24].

In our previous study we demonstrated the importance of identifying sclerostin, on the one hand, as the main antagonist of the WNT signaling pathway, and on the other hand, as a regulator of bone tissue formation in acute forms of coronary heart disease [20].

In this regard, it was interesting to evaluate the possibility of developing an integrated approach to assessing the likelihood of calcification of vessels, taking into account indicators of arterial stiffness and a marker of extraosseous calcification (sclerostin) to improve non-invasive diagnosis of cardiovascular risk.

Materials and methods

This study was conducted at the cardiology departments (No. 1, No. 2) of the regional vascular center and the department of X-ray surgical methods of diagnostics and treatment of the State Health Institution of the Orel Regional Clinical Hospital (Russia).

A total of 58 patients admitted to the clinic for emergency indications with acute coronary syndrome were included in the study. According to clinical manifestations and the data of the spectrum of myocardial enzymes and electrocardiogram obtained in the emergency room, the patients were divided into 2 main categories: group 1 - with unstable angina (n = 28) and group 2 - with acute myocardial infarction (n = 30). The age of patients in group 1 was 49.14 ± 7.17 years, group 2 - 44.60 ± 8.57 years. No significant difference was found according to age ($p = 0.135$; method used: Student's t-test).

The distribution of patients in these groups was as follows: in group 1 - 16 men and 12 women, in group 2 - 28 and 2, respectively. Despite the apparent uneven distribution of patients in the groups according to gender, we were unable to identify statistically significant differences in patients ($p = 0.080$; method used: Fisher's exact test).

The diagnosis of patients with acute myocardial infarction (AMI) and unstable angina (UA) was established in accordance with the clinical guidelines of the Ministry of Health of the Russian Federation in the version current at the time of the study.

Sample collection

The scope of clinical examination of patients included determination of general blood test parameters, troponin levels in dynamics, cholesterol profile, C-reactive protein, electrolytes (potassium, sodium), glucose. General clinical laboratory tests were performed using the analyzers "Maxm Analyzer" (UK) and "Monarch chemistry system" (Italy).

Venous blood sampling (in volume of 5 ml) was carried out in patients on an empty stomach in the morning in the first 24 hours after hospitalization, subsequently the blood was centrifuged for 15 minutes at speed of 1500 rpm, the serum was aliquoted, frozen at temperature of - 24 ° C and stored for 1 to 2 months without repeated defrosting cycles before use.

ELISA

The serum concentration of sclerostin was determined in each sample in two repeats by enzyme immunoassay (ELISA). Optical density measurements were performed on STAT FAX 2100 photometer (Awareness Technology, USA) using a set of reagents from Sunlong Biotech Co (China), according to the manufacturer's protocol.

Electrocardiogram

The electrocardiogram (ECG) was recorded according to the generally accepted method in 12 leads on the ECG–9803 Medinova Industrial Co., Ltd.

Echo-KG

Ultrasound examination of the heart was performed on Toshiba Aplio 500 expert class device.

Coronary angiography

Coronary angiography was performed using Philips angiography units. After receiving the results of angiography and a comprehensive assessment of the affected arterial bed, according to the indications, the patients underwent revascularization of the affected artery using balloon angioplasty with its subsequent stenting.

The normal anatomy of the left and right coronary arteries according to coronary angiography data is shown in Figures 1, 2.

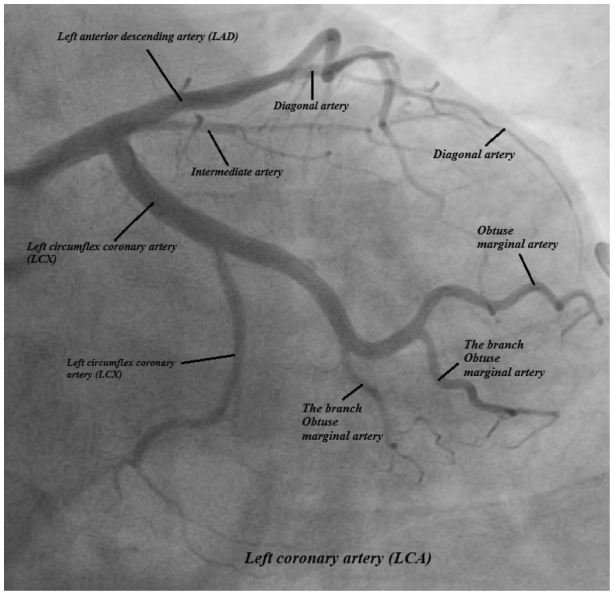

Figure 1. Coronary angiography of the left coronary artery (normal)

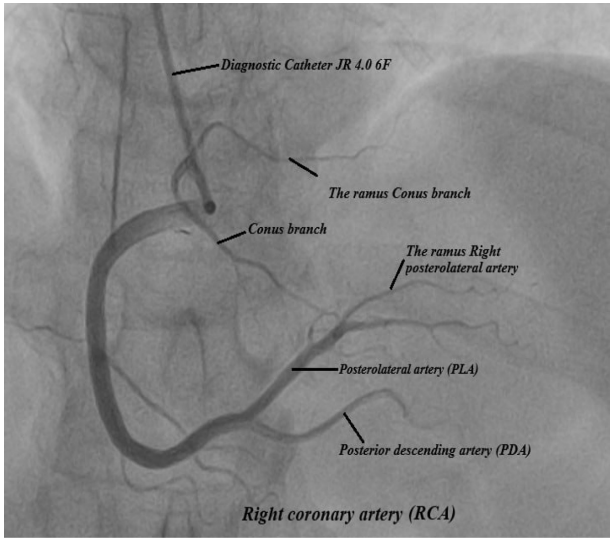

Figure 2. Coronary angiography of the right coronary artery (normal)

Arterial stiffness

For non-invasive assessment of the arterial stiffness index (ASI) we used the method of indirect assessment of the properties of the main arteries based on the results of daily blood pressure monitoring using Schiller BR-102 plus device and SCHILLER MT-300 Holter-BPR software (Switzerland)

Statistical data processing

Statistical analysis was performed by StatTech v. 4.6.1 program (Russia, 2024). Shapiro-Wilk test was used to assess quantitative indicators for compliance with a normal distribution (if the patients' number was less than 50). Data are presented as the absolute number (%) of patients, as mean value and mean absolute error (M±m).

In the absence of normal distribution, quantitative data were described using the median (Me) and the first and the third quartiles (Q1; Q3). Student's t-test was used for the comparison of two groups according to the quantitative indicator with normal distribution on condition of equality variances; Mann–Whitney U test – for the comparison of two groups according to the quantitative indicator with abnormal distribution.

Kruskal–Wallis test was used for the comparison of three groups, and Dunn's test with Holm's correction was used for post hoc comparison. Spearman's rank correlation coefficient was used to assess the direction and strength of the correlation between two quantitative indicators (if the distribution of indicators was abnormal).

Pearson correlation coefficient was used to assess the direction and strength of the correlation between two quantitative indicators (with normal distribution).

The Chaddock scale is used to interpret correlation strength between two quantitative indicators. All statistical comparisons were two-sided, and $p<0.05$ was considered significant. To assess the diagnostic significance of quantitative characteristics in predicting a specific outcome, the ROC curve method was used.

Results

Analysis of clinical and laboratory data showed that there were no significant intergroup differences between the patients of the studied groups in almost all indicators, with the exception of creatine phosphokinase (CPK) and VLDL levels. Thus, the indicators of CPK released into the blood when the heart muscle is damaged, and serving as a marker for the identification of acute myocardial infarction, were 127.00 [113.00 – 171.50] units/l in patients of group 1, 215.00 [190.50 – 499.50] units/l in group 2 ($p = 0.006$; *method used: Mann U–test–Whit-*

ney), and the level of VLDL - 0.55 [0.41 – 0.79] mmol/l and 0.47 [0.38 – 0.63] mmol/l, respectively ($p<0.05$; *method used: Mann–Whitney U test*).

Moreover, the indicators of the number of red blood cells, hemoglobin, bilirubin, total protein, alkaline phosphatase, creatinine, HDL, sodium and potassium were within the normal range for both studied groups.

At the same time, patients with unstable angina were twice as likely to have a history of atherosclerotic heart disease at the time of hospital admission.

It should be emphasized that body mass index (BMI), systolic and diastolic blood pressure, total cholesterol, leukocytes, ESR, aspartate aminotransferase, alanine aminotransferase, LDL of patients with myocardial infarction exceeded the reference values.

ECG results

Myocardial infarction (MI) with ST segment elevation was observed in 24 patients of group 2. Pathological Q wave on the ECG was observed in 16 patients with MI.

ECG changes in 50% of patients with UA were characterized by minor deviations from the norm (in the form of supraventricular extrasystole, flattening of the T wave), normal ECG was recorded in half of the cases.

Results of coronary angiography (CAG)

In patients with MI stenosis of the middle section of the right coronary artery was most common (in 24 patients out of 30) with its degree varying from 20% to complete occlusion in 6 patients of this group. Stenosis (from 30% to 75%) of the anterior interventricular branch was found in 18 patients and of the posterolateral branch (stenosis 30-50%) - in 6 patients. It should be noted that stenosis of the posterior interventricular artery was not registered in patients of the study group.

In CAG stenosis of the left coronary artery was found in 6 patients with MI (stenosis degree 30-50%), 60% stenosis of the diagonal artery was detected in 2 patients of this group. More than that, stenosis of the left anterior descending artery was diagnosed in 6 patients with MI, the severity of which varied from 35 to 75 %, narrowing of the intermediary artery was recorded in 4 patients (stenosis of I and V degrees, respectively).

An example of CAG of a 49-year-old male patient with acute myocardial infarction is shown in Figure 3.

It should be noted that in patients with MI single-vessel coronary bed lesion was found only in 8 patients out of 30, and two-vessel lesion - in the majority of patients (14 people). Special attention should be paid to the data on the identified critical lesion of the coronary bed (100% stenosis) in 2 patients with single-ves-

sel and in 2 patients with two-vessel lesion of the coronary arteries. Stenosis of three coronary arteries was observed at once in 6 patients and simultaneous stenosis of four arteries was observed in 2 patients with AMI.

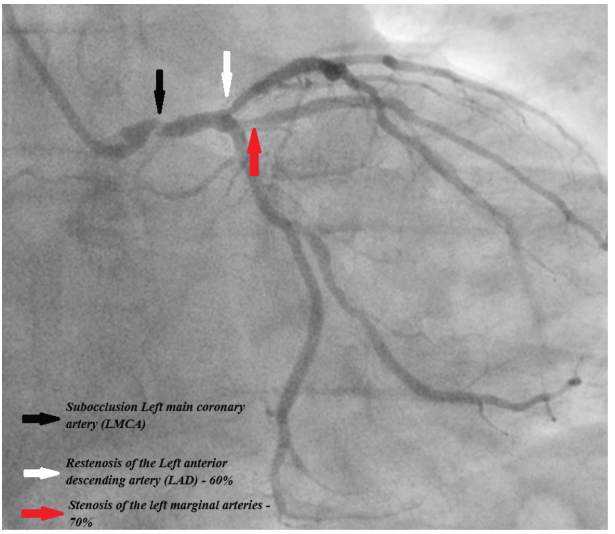

Figure 3. Variants of stenosis of the arteries of the left coronary artery basin.

The results of diagnostic CAG obtained in patients of group 1 did not allow us to identify signs of stenosis of the left coronary artery, diagonal branch, left anterior descending artery, intermediary artery, middle section of the right coronary artery, as well as the anterior interventricular and posterolateral branches of this artery.

It should be noted that in patients with unstable angina, stenosis of the anterior interventricular branch, disturbances of the lumen of the right coronary artery and the middle section of the circumflex branch of this artery were most often encountered.

Narrowing of one coronary artery was found in 8 patients, and two-vessel lesions - in 4 patients of this group. In addition, in 2 patients with UA, simultaneous narrowing of four coronary arteries of minor degree (stenosis) was registered (anterior descending artery; diagonal branch 1; obtuse marginal branch 1; posterior lateral branch).

A 53-year-old man with MI has calcification of the left main coronary artery and anterior interventricular artery visualized on CAG as a shadow (yellow oval in Figure 4).

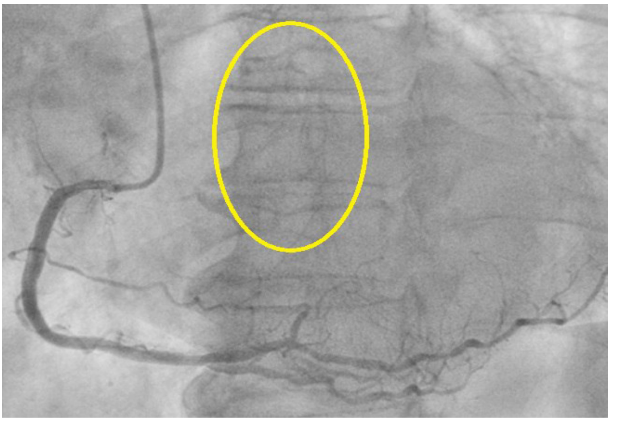

Figure 4. Calcification of the left main coronary artery and anterior interventricular artery

Figure 5 shows calcified atherosclerotic plaque of the right interventricular branch of the left coronary artery (marked with a red circle) in a 56-year-old male patient with acute myocardial infarction.

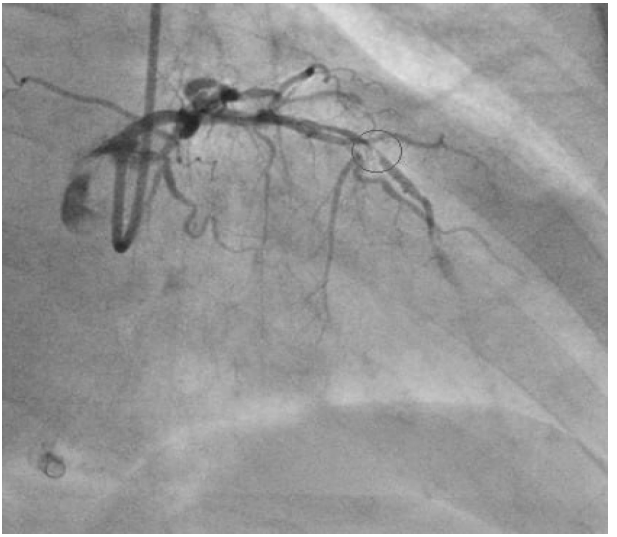

Figure 5. Calcified atherosclerotic plaque of the right interventricular branch of the left coronary artery

Results of determining serum sclerostin by ELISA

According to the results of the study the sclerostin level in patients with MI was 163 [148; 248] pg/ml, and in patients with UA - 224 [151 – 250] pg/ml (p= 0.498).

We performed an analysis of the serum level of sclerostin depending on the number of stenosed arteries, it was not possible to establish statistically significant differences (p = 0.970; *method used: Kruskal-Wallis test*). However, there is a tendency to decrease the concentration of sclerostin with an increase in the number of affected arteries according to CAG data (Table 1).

Table 1.

Serum sclerostin levels depending on the number of stenotic arteries

Categories	sclerostin (pg/ml)		p
	Me	$Q_1 – Q_3$	
no stenosis	229,00	150,00 – 250,00	0,970
stenosis of one artery	191,50	157,00 – 234,25	
stenosis of two arteries	154,00	151,75 – 268,50	
multivessel stenosis	150,00	145,00 – 215,00	

At the next stage of the analysis, we divided the patients into subgroups according to the severity of stenosis (degree of stenosis ≥ 50% and <50%), as a result of which we were unable to establish statistically significant differences (p = 0.312; *method used: Mann–Whitney U–test*). At the same time, it is worth noting a higher concentration of sclerostin in patients with degree of stenosis ≥ 50% (Table 2).

Table 2.

Serum sclerostin levels depending on the degree of arterial stenosis

Categories	sclerostin (pg/ml)		p
	Me	$Q_1 – Q_3$	
degree of stenosis <50%	156,50	148,50 – 226,75	0,312
degree of stenosis ≥ 50%	222,00	151,50 – 270,00	

Then having selected patients with degree of coronary artery stenosis ≥ 50% with existing atherosclerotic plaques, we estimated the concentration of sclerostin depending on the type of plaques, taking into account their echogenicity and homogeneity (calcified (CAP) and non-calcified (Table 3).

As a result of assessing the concentration of sclerostin in the blood serum of patients with a degree of coronary artery stenosis ≥ 50%, depending on the type of atherosclerotic plaque, statistically significant differences were identified (p <0.01; method used: Mann–Whitney U test).

Table 3.

Serum sclerostin level depending on the type of atherosclerotic plaque

Subgroup of patients	sclerostin (pg/ml)		p
	Me	$Q_1 – Q_3$	
Stenosis ≥50% without CAP	168,00	150,00 – 187,00	< 0,01*
Stenosis ≥50% with CAP	268,50	245,50 – 280,00	

Note: * – differences in indicators are statistically significant (p < 0.05)

Arterial stiffness index

The calculation indicators of the arterial stiffness index for the groups of examined patients are presented in Table 4.

Table 4.

Arterial stiffness index

Group of patients	arterial stiffness index — ASI		p
	Me	$Q_1 – Q_3$	
Group 1 (unstable angina)	7,75	7,00 – 9,75	0,001*
Group 2 (acute myocardial infarction)	10,00	9,95 – 11,00	

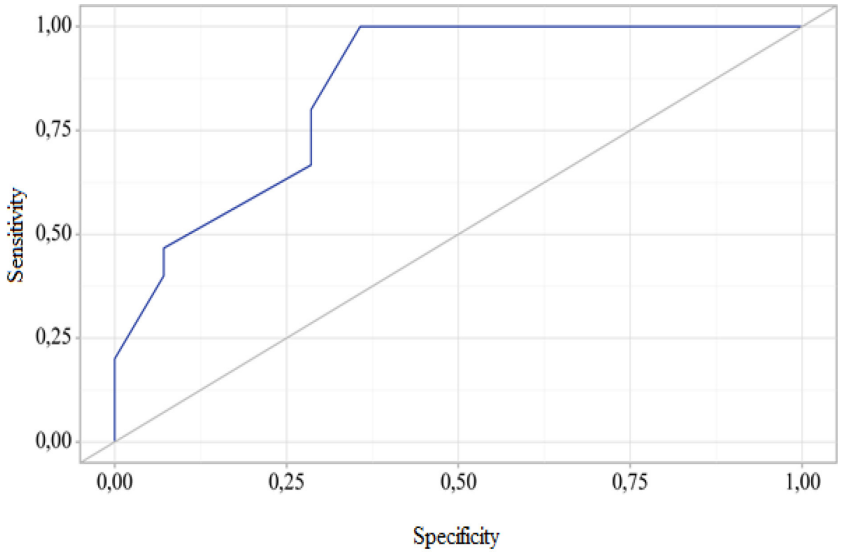

Figure 6. ROC curve characterizing the dependence of the probability of myocardial infarction and unstable angina on ASI

Correlation analysis of the relationship between serum sclerostin concentration and ASI allowed us to establish a highly statistically significant relationship (ρ=0.838; $p<0.05$). It is noteworthy that ASI>10 was recorded in patients with calcified arteries as well as an increase in this indicator with increasing age.

When assessing the dependence of the probability of acute myocardial infarction on ASI using ROC analysis, the following curve was obtained (Figure 6).

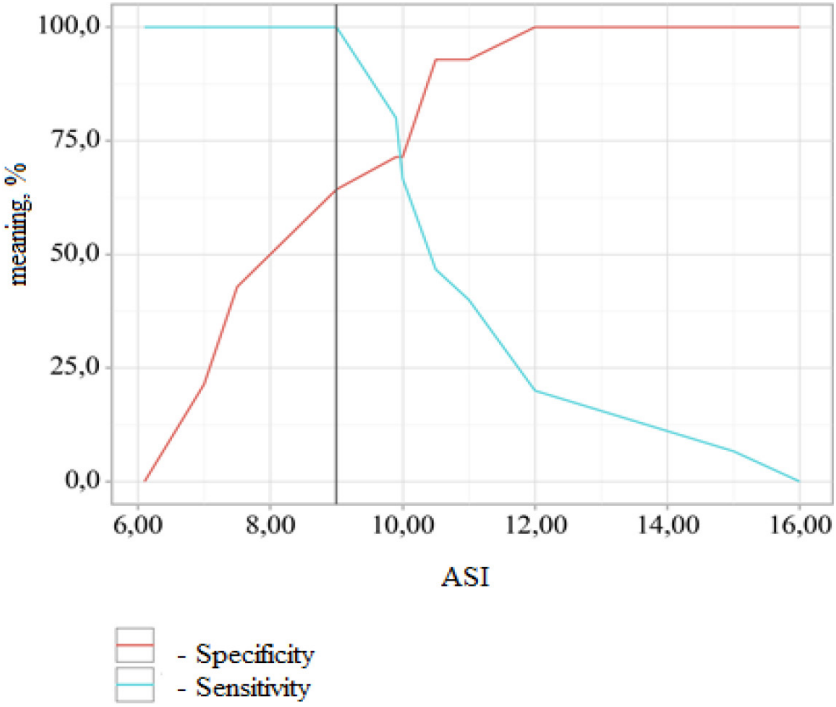

Figure 7. Analysis of sensitivity and specificity of the model depending on the ASI threshold values

Table 5.

ASI threshold values

Threshold	Sensitivity (Se), %	Specificity (Sp), %	PPV	NPV
10,00	**66,7**	**71,4**	**71,4**	**66,7**
9,90	80,0	71,4	75,0	76,9
9,00	100,0	64,3	75,0	100,0
8,00	100,0	50,0	68,2	100,0

The area under the ROC curve was 0.850 ± 0.073 with 95% CI: 0.707 – 0.993. The resulting model was statistically significant (p = 0.001).

The ASI cut-off value, which corresponded to the highest Youden index value, was 9.000. Myocardial infarction was predicted at an ASI value higher than or equal to this value. The sensitivity and specificity of the model were 100.0% and 64.3%, respectively.

Discussion

Increasing clinical and experimental data over the past two decades have demonstrated a close relationship between vascular calcification and aging and cardiovascular disease [3; 21]. Much attention is currently paid to the relationship between vascular calcification and arterial stiffness in association with the microenvironment, as well as with the underlying signaling pathways regulating both vascular and bone calcification [3; 17; 25].

It is well documented that AF is closely associated with structural and functional changes in arterial elasticity, which include processes such as extracellular matrix remodeling, elastin degradation, excessive collagen deposition, glycosylation, etc., which are of critical importance for the subsequent development of CVD [3; 4]. While endothelial cells, fibroblasts, macrophages, etc. contribute to arterial stiffness, vascular smooth muscle cells are necessary for maintaining vascular homeostasis, including arterial elasticity. Vascular calcification, currently recognized as an active process similar to osteogenesis [3; 14], leads to the formation of the osteogenic phenotype of VSMCs under the influence of both various extracellular and intracellular procalcification factors [2; 5].

In previous studies we focused on the role of sclerostin, one of the main morphogenic WNT signaling that regulates mineral metabolism and extraosseous calcification in acute forms of coronary heart disease, demonstrating the feasibility of its study as a biomarker of ectopic calcification of heart valves and great vessels [20].

Considering the fact that the combined assessment of arterial stiffness and vascular calcification biomarkers can improve noninvasive assessment of cardiovascular risk, allowing stratification of patients into CVD risk groups for preventive treatment or more regular medical examination, we conducted a comparative comprehensive assessment of arterial stiffness, serum sclerostin and coronary artery calcification according to CAG data in patients of the study groups.

Our study did not reveal statistically significant differences in sclerostin concentrations in the blood serum of patients with acute myocardial infarction and unstable angina, however, a decrease in sclerostin levels was found against the

background of an increase in the number of stenotic coronary arteries. Although the reason for this result is not well understood, one of the probable mechanisms explaining this fact may be osteogenic differentiation of VSMC and their calcification against the background of increased demand for sclerostin.

Despite the rather contradictory results of studies assessing the relationship between serum sclerostin levels and vascular calcification, most researchers show a direct correlation with a high probability of vascular calcification and atherosclerosis [1; 6; 10; 13; 18]. This is consistent with our statistically significant data on the highest sclerostin concentrations in patients with coronary artery stenosis ≥50% in combination with intravascular calcified atherosclerotic plaques.

At present, the question of the possibility of using serum sclerostin as a prognostic marker of adverse cardiovascular events and AF remains open, and the researches, made in this direction by many scientific teams, have not brought definite results [6, 18]. With the aggravation of clinical manifestations, ASI in the group of patients with myocardial infarction was significantly higher than in patients with unstable angina, which to a certain extent confirms the close relationship of ASI with coronary heart disease and its outcome, but requires further study.

The obtained results on the increase of the arterial stiffness index more than 10 against the background of coronary artery calcification may indicate a close relationship between vascular calcification and arterial stiffness and the possible formation of a vicious circle against the background of accelerated vascular calcification, an increase in AF, and, as a consequence, the development of ACEs, which is consistent with literature data [7].

In addition, the results obtained in our study on the increase in ASI with increasing patient age confirmed the existing data on vascular calcification as a marker of vascular aging and CVD risk.

In our study, we used ROC analysis to determine the diagnostic value of ASI in predicting myocardial infarction. The results of the ROC analysis showed that ASI can not only play a role in the predictive diagnosis of coronary heart disease, but also in assessing the severity of its course.

The threshold value of the ASI index at the cut-off point, which corresponded to the highest value of the Youden index, was 9.0. Taking this into account, the probability of unstable angina can be predicted at an ASI value below this value (the sensitivity and specificity of the model were 100.0% and 64.3%, respectively), and the ASI level above 9.0 can be used as a diagnostic marker of myocardial infarction, which is especially important in diagnostically complex expert cases.

Presenting our strong positive correlation between serum sclerostin concentration and ASI, it is possible to suggest that sclerostin plays an important role in this process via modulation and phenotypic switching of VSMC, which allows considering it as a therapeutic target and diagnostic biomarker in CVD, however, this requires additional clinical and laboratory studies.

We acknowledge several limitations of our study, including its cross-sectional nature, small sample size, and limited data describing vascular calcification and ASI. These limitations impact the establishment of a definitive causal relationship between sclerostin, ASI, and vascular calcification.

Furthermore, we did not use multivariate analysis to test parameters, thereby limiting our ability to make general statements regarding the associative data between the studied markers and vascular calcification.

Conclusion

Increased calcification and vascular stiffness are observed in coronary heart disease, which may lead to impaired blood flow and an increased risk of ACEs. Studies show that sclerostin may also affect vascular calcification, which is a key aspect of coronary heart disease. The use of multivariate analysis and the development of prognostic models to clarify the relationship between sclerostin, vascular stiffness and calcification will allow a better understanding of the pathophysiology of coronary heart disease and the development of more effective methods for screening diagnostics of cardiovascular diseases to stratify the risk of adverse outcomes at a pre-symptomatic or early stage of the pathological process. In addition, this may lead to the development of more effective strategies for the prevention and treatment of coronary heart disease, opening up new opportunities to improve the quality of life of patients.

Ethics committee conclusion. The study was carried out in accordance with GCP standards and the Declaration of Helsinki, the study protocol was approved by the local Ethics Committee of Orel State University named after I.S. Turgenev (Russia, Protocol No. 31 dated 06/27/2024).

Informed consent. All participants of the study signed informed consent for the use of their examination results for scientific purposes in an anonymous form.

Conflict of interest information. The authors declare no conflict of interest related to the publication of this manuscript.

Sponsorship information. The work was done at the Orel State University named after I.S. Turgenev (Russia) within the framework of the state assignment No. 075-00196-24-08 for 2024 and for the planning period of 2025

and 2026 since 08/23/2024, project № FSGN-2024-0014 (1024041900023-6-1.2.1;2.6.2;3.1.3;3.2.12;3.2.4).

Acknowledgments. The authors express their gratitude to all the staff of the cardiology departments (No. 1, No. 2) of the regional vascular center and the department of X-ray surgical methods of diagnostics and treatment of the Orel Regional Clinical Hospital (Russia).

References / Список литературы

1. Brandenburg, V. M., Kramann, R., Koos, R., Krüger, T., Schurgers, L., Mühlenbruch, G., Hübner, S., Gladziwa, U., Drechsler, C., & Ketteler, M. (2013). Relationship between sclerostin and cardiovascular calcification in hemodialysis patients: a cross-sectional study. *BMC Nephrology, 14*, 219. https://doi.org/10.1186/1471-2369-14-219 EDN: https://elibrary.ru/gzbmxs
2. Ceccherini, E., Cecchettini, A., Gisone, I., Persiani, E., Morales, M. A., & Vozzi, F. (2022). Vascular Calcification: In Vitro Models under the Magnifying Glass. *Biomedicines, 10*(10), 2491. https://doi.org/10.3390/biomedicines10102491 EDN: https://elibrary.ru/disuyh
3. Chen, Y., Zhao, X., & Wu, H. (2020). Arterial Stiffness: A Focus on Vascular Calcification and Its Link to Bone Mineralization. *Arteriosclerosis, Thrombosis, and Vascular Biology, 40*(5), 1078-1093. https://doi.org/10.1161/ATVBAHA.120.313131 EDN: https://elibrary.ru/dtcvyk
4. Demer, L. L., & Tintut, Y. (2008). Vascular calcification: pathobiology of a multifaceted disease. *Circulation, 117*(22), 2938-2948. https://doi.org/10.1161/CIRCULATIONAHA.107.743161 EDN: https://elibrary.ru/mmgbvr
5. Durham, A. L., Speer, M. Y., Scatena, M., Giachelli, C. M., & Shanahan, C. M. (2018). Role of smooth muscle cells in vascular calcification: implications in atherosclerosis and arterial stiffness. *Cardiovascular Research, 114*(4), 590-600. https://doi.org/10.1093/cvr/cvy010
6. Figurek, A., & Spasovski, G. (2018). Is serum sclerostin a marker of atherosclerosis in patients with chronic kidney disease-mineral and bone disorder? *International Urology and Nephrology, 50*(10), 1863-1870. https://doi.org/10.1007/s11255-018-1935-5 EDN: https://elibrary.ru/oanvkd
7. Gao, L., Lu, D., Xia, G., et al. (2021). The relationship between arterial stiffness index and coronary heart disease and its severity. *BMC Cardiovascular Disorders, 21*, 527. https://doi.org/10.1186/s12872-021-02350-6 EDN: https://elibrary.ru/hlxrmh
8. Golledge, J., & Thanigaimani, S. (2022). Role of Sclerostin in Cardiovascular Disease. *Arteriosclerosis, Thrombosis, and Vascular Biology, 42*(7), e187-e202. https://doi.org/10.1161/ATVBAHA.122.317635 EDN: https://elibrary.ru/jtlerh

9. Gui, Z., Shao, C., Zhan, Y., Wang, Z., & Li, L. (2024). Vascular calcification: High incidence sites, distribution, and detection. *Cardiovascular Pathology, 72*, 107667. https://doi.org/10.1016/j.carpath.2024.107667 EDN: https://elibrary.ru/qzdifq
10. Hampson, G., Edwards, S., Conroy, S., Blake, G. M., Fogelman, I., & Frost, M. L. (2013). The relationship between inhibitors of the Wnt signalling pathway (Dickkopf-1(DKK1) and sclerostin), bone mineral density, vascular calcification and arterial stiffness in post-menopausal women. *Bone, 56*(1), 42-47. https://doi.org/10.1016/j.bone.2013.05.010
11. Hata, Y., Mochizuki, J., Okamoto, S., Matsumi, H., & Hashimoto, K. (2022). Aortic calcification is associated with coronary artery calcification and is a potential surrogate marker for ischemic heart disease risk: A cross-sectional study. *Medicine, 101*(29), e29875. https://doi.org/10.1097/MD.0000000000029875 EDN: https://elibrary.ru/yhytxe
12. Kadıoğlu, A., & Bahadır, S. (2022). Breast arterial calcifications as an indicator of atherosclerotic cardiovascular disease: comparative analysis of coronary computed tomography scoring systems and carotid intima-media thickness. *Quantitative Imaging in Medicine and Surgery, 12*(1), 457-469. https://doi.org/10.21037/qims-21-98 EDN: https://elibrary.ru/yyftdo
13. Koos, R., Brandenburg, V., Mahnken, A. H., Schneider, R., Dohmen, G., Autschbach, R., Marx, N., & Kramann, R. (2013). Sclerostin as a potential novel biomarker for aortic valve calcification: an in-vivo and ex-vivo study. *The Journal of Heart Valve Disease, 22*(3), 317-325.
14. Lee, S. J., Lee, I. K., & Jeon, J. H. (2020). Vascular Calcification-New Insights Into Its Mechanism. *International Journal of Molecular Sciences, 21*(8), 2685. https://doi.org/10.3390/ijms21082685 EDN: https://elibrary.ru/joqymx
15. Mack, C. P. (2011). Signaling mechanisms that regulate smooth muscle cell differentiation. *Arteriosclerosis, Thrombosis, and Vascular Biology, 31*(7), 1495-1505. https://doi.org/10.1161/ATVBAHA.110.221135
16. Mozos, I., Malainer, C., Horbańczuk, J., Gug, C., Stoian, D., Luca, C. T., & Atanasov, A. G. (2017). Inflammatory Markers for Arterial Stiffness in Cardiovascular Diseases. *Frontiers in Immunology, 8*, 1058. https://doi.org/10.3389/fimmu.2017.01058
17. Ortega, M. A., De Leon-Oliva, D., Gimeno-Longas, M. J., Boaru, D. L., Fraile-Martinez, O., García-Montero, C., de Castro, A. V., Barrena-Blázquez, S., López-González, L., Amor, S., García-Honduvilla, N., Buján, J., Guijarro, L. G., Castillo-Ruiz, E., Álvarez-Mon, M. Á., Albillos, A., Álvarez-Mon, M., Diaz, R., & Saez, M. A. (2024). Vascular Calcification: Molecular Networking,

Pathological Implications and Translational Opportunities. *Biomolecules, 14*(3), 275. https://doi.org/10.3390/biom14030275 EDN: https://elibrary.ru/tbtxgc

18. Popovic, D. S., Mitrovic, M., Tomic-Naglic, D., Icin, T., Bajkin, I., Vukovic, B., Benc, D., Zivanovic, Z., Kovacev-Zavisic, B., & Stokic, E. (2017). The Wnt/β-catenin Signalling Pathway Inhibitor Sclerostin is a Biomarker for Early Atherosclerosis in Obesity. *Current Neurovascular Research, 14*(3), 200-206. https://doi.org/10.2174/1567202614666170619080526 EDN: https://elibrary.ru/yhxvlc
19. Rennenberg, R. J., Kessels, A. G., Schurgers, L. J., van Engelshoven, J. M., de Leeuw, P. W., & Kroon, A. A. (2009). Vascular calcifications as a marker of increased cardiovascular risk: a meta-analysis. *Vascular Health and Risk Management, 5*(1), 185-197. https://doi.org/10.2147/vhrm.s4822 EDN: https://elibrary.ru/nakwvx
20. Snimshchikova, I. A., & Plotnikova, M. O. (2023). Role of morphogenic proteins of the WNT signaling pathway in coronary artery disease. *Medical Immunology (Russia), 25*(4), 985-990. https://doi.org/10.15789/1563-0625-ROM-2835 EDN: https://elibrary.ru/ppgrow
21. Sutton, N. R., Malhotra, R., St Hilaire, C., Aikawa, E., Blumenthal, R. S., Gackenbach, G., Goyal, P., Johnson, A., Nigwekar, S. U., Shanahan, C. M., Towler, D. A., Wolford, B. N., & Chen, Y. (2023). Molecular Mechanisms of Vascular Health: Insights From Vascular Aging and Calcification. *Arteriosclerosis, Thrombosis, and Vascular Biology, 43*(1), 15-29. https://doi.org/10.1161/ATVBAHA.122.317332 EDN: https://elibrary.ru/jscdmh
22. Toussaint, N. D., Lau, K. K., Strauss, B. J., Polkinghorne, K. R., & Kerr, P. G. (2008). Associations between vascular calcification, arterial stiffness and bone mineral density in chronic kidney disease. *Nephrology, Dialysis, Transplantation, 23*(2), 586-593. https://doi.org/10.1093/ndt/gfm660 EDN: https://elibrary.ru/ixuljd
23. van der Toorn, J. E., Bos, D., Arshi, B., Leening, M. J. G., Vernooij, M. W., Ikram, M. A., Ikram, M. K., & Kavousi, M. (2021). Arterial calcification at different sites and prediction of atherosclerotic cardiovascular disease among women and men. *Atherosclerosis, 337*, 27-34. https://doi.org/10.1016/j.atherosclerosis.2021.10.009 EDN: https://elibrary.ru/bogovk
24. Wang, X.-R., Yuan, L., Zhang, J.-J., Hao, L., & Wang, D.-G. (2017). Serum sclerostin values are associated with abdominal aortic calcification and predict cardiovascular events in patients with chronic kidney disease stages 3-5D. *Nephrology, 22*(4), 286-292. https://doi.org/10.1111/NEP.12813
25. Yang, S., Zeng, Z., Yuan, Q., Chen, Q., Wang, Z., Xie, H., & Liu, J. (2023). Vascular calcification: from the perspective of crosstalk. *Molecular Biomedicine, 4*(1), 35. https://doi.org/10.1186/s43556-023-00146-y EDN: https://elibrary.ru/vivgbl

26. Yu, Q., Li, W., Xie, D., Zheng, X., Huang, T., Xue, P., Guo, B., Gao, Y., Zhang, C., Sun, P., Li, M., Wang, G., Cheng, X., Zheng, Q., & Song, Z. (2018). PI3Kγ promotes vascular smooth muscle cell phenotypic modulation and transplant arteriosclerosis via a SOX9-dependent mechanism. *EBioMedicine, 36*, 39-53. https://doi.org/10.1016/j.ebiom.2018.09.013

AUTHOR CONTRIBUTIONS

The authors contributed equally to this article.

ВКЛАД АВТОРОВ

Все авторы внесли эквивалентный вклад в подготовку рукописи.

ДАННЫЕ ОБ АВТОРАХ

Снимщикова Ирина Анатольевна, ведущий научный сотрудник лаборатории новых медицинских технологий, заведующий кафедрой иммунологии и специализированных клинических дисциплин, директор Медицинского института, доктор медицинских наук, профессор
Федеральное государственное бюджетное образовательное учреждение высшего образования «Орловский государственный университет имени И.С. Тургенева»
ул. Комсомольская, 95, г. Орёл, 302026, Российская Федерация
snimshikova@mail.ru

Ревякина Мария Олеговна, старший научный сотрудник лаборатории новых медицинских технологий, доцент кафедры иммунологии и специализированных клинических дисциплин, кандидат медицинских наук
Федеральное государственное бюджетное образовательное учреждение высшего образования «Орловский государственный университет имени И.С. Тургенева»
ул. Комсомольская, 95, г. Орёл, 302026, Российская Федерация
revyakina_masha@mail.ru

Кабина Наталья Александровна, старший преподаватель кафедры фармакологии, клинической фармакологии и фармации
Федеральное государственное бюджетное образовательное учреждение высшего образования «Орловский государственный университет имени И.С. Тургенева»

ул. Комсомольская, 95, г. Орёл, 302026, Российская Федерация
apt53boss@mail.ru

Митяева Екатерина Вячеславовна, доцент кафедры внутренних болезней, кандидат медицинских наук
Федеральное государственное бюджетное образовательное учреждение высшего образования «Орловский государственный университет имени И.С. Тургенева»
ул. Комсомольская, 95, г. Орёл, 302026, Российская Федерация
orel_rel@mail.ru

DATA ABOUT THE AUTHORS

Irina A. Snimshchikova, Leading Researcher of the Laboratory of New Medical Technologies, Head of the Department of Immunology and Specialized Clinical Disciplines, Director of the Medical Institute, Doctor of Medical Sciences, Professor
Orel State University named after I.S. Turgenev
95, Komsomolskaya Str., Orel, 302026, Russian Federation
snimshikova@mail.ru
SPIN-code: 2728-3520
ORCID: https://orcid.org/0000-0002-4258-963X
ResearcherID: X-6716-2019
Scopus Author ID: 57194214547

Maria O. Revyakina, Senior Researcher, Laboratory of New Medical Technologies, Associate Professor, Department of Immunology and Specialized Clinical Disciplines, Candidate of Medical Sciences
Orel State University named after I.S. Turgenev
95, Komsomolskaya Str., Orel, 302026, Russian Federation
revyakina_masha@mail.ru
SPIN-code: 4921-7530
ORCID: https://orcid.org/0000-0003-1593-5290
Scopus Author ID: 57326361600

Natalia A. Kabina, Senior Lecturer, Department of Pharmacology, Clinical Pharmacology and Pharmacy
Orel State University named after I.S. Turgenev
95, Komsomolskaya Str., Orel, 302026, Russian Federation

apt53boss@mail.ru
ORCID: https://orcid.org/0009-0007-6915-9035

Ekaterina V. Mityaeva, Associate Professor of the Department of Internal Medicine, PhD in Medicine
Orel State University named after I.S. Turgenev
95, Komsomolskaya Str., Orel, 302026, Russian Federation
orel_rel@mail.ru
SPIN-code: 9917-8471
ORCID: https://orcid.org/0000-0001-9964-7549
ResearcherID: LRC-5828-2024
Scopus Author ID: 57204703234

Поступила 13.11.2024 Received 13.11.2024
После рецензирования 13.12.2024 Revised 13.12.2024
Принята 16.12.2024 Accepted 16.12.2024