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Visual Scale as a Non-Invasive Method for Evaluation of Risk and Severity of Coronary Atherosclerosis

Aim To evaluate quantitative and qualitative characteristics of atherosclerotic plaques (ASP) in carotid

arteries (CA) and femoral arteries (FA) and to use these data for developing a visual scale (VS) for

noninvasive diagnosis and determination of severity of coronary atherosclerosis.

Material and methods This study included 216 patients (115 men and 101 women) aged 24 to 87 years (mean age,

61.5±10.73 years). All patients underwent coronary angiography (CAG) for detecting and determining severity of CA atherosclerosis and duplex scanning (DS) for detecting atherosclerosis

of CA and FA.

Results Analysis of ultrasound parameters of ASP in CA and FA showed that the maximal ASP height,

moderate stenosis and maximal stenosis of the arterial bed had higher predictive values than other ultrasound parameters. These parameters were used for forming diagnostic complexes, on the basis of which two individual VSs for CA and FA were developed. Based on the high prognostic value of both scales, they were combined into one that was named VS_{COMB}. A ROC analysis determined cut-off points of the VS_{COMB} for diagnosis of CA atherosclerosis of various severity. VS_{COMB} scores >4 indicated pronounced CA atherosclerosis with sensitivity of 86.1% and specificity of 87.5% whereas VS_{COMB} scores \leq 4 excluded it. Thus, VS_{COMB} score 0–1 indicated the absence of CA atherosclerosis; score 2–4 indicated the presence of subclinical CA atherosclerosis; and score >4

indicated severe CA atherosclerosis.

Conclusion A VS_{COMB} was developed that includes a set of ultrasound parameters for CA and FA and is useful

for noninvasive diagnosis of CA atherosclerosis of various severity. Simple and convenient use of VS_{COMB} allows it to be used at the screening stage to detect subclinical CA atherosclerosis and

to prevent its progression.

Keywords Atherosclerosis; coronary arteries; carotid arteries; femoral arteries; visual scale; coronary angiography;

duplex scanning

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ost cardiovascular diseases (CVDs) are caused by atherosclerosis. Given the asymptomatic nature of the disease, this presents a challenge for early diagnosis [1]. There are cardiological scores to assess the total risk of cardiovascular complications (CVCs) in patients with CVDs of atherosclerotic origin, including asymptomatic patients. However, existing scores [Systematic Ceramic Coronary risk Evaluation (SCORE), AtheroSclerotic Cardio Vascular disease (ASCVD), Framingham Risk Score, PROspective Cardiovascular Munsterstudy (PROCAM), Assessment Scottish Intercollegiate Guidelines Network (ASSIGN)], which are based on a combination of conventional cardiovascular risk factors (RFs), are intended for the evaluation of total cardiovascular risk rather than for verifying the existence of coronary atherosclerosis. All attempts to use them in this context have been unsuccessful.

Coronary angiography (CAG), while representing the gold standard of invasive diagnosis of coronary atherosclerosis, is characterized by high cost, limited use in some groups of patients, possible complications, as well as adverse reactions during the diagnostic procedure, which makes its routine use for diagnosis of coronary atherosclerosis controversial [2]. Therefore, the proposal to using a complex of RFs and markers, combining the simplicity and convenience of a cardiac score, as well as the possibility of their application prior to hospitalization and in any hospital, reflects a rational approach to creating a score for predicting the presence and severity of coronary atherosclerosis [3].

Numerous epidemiological studies have revealed the association of carotid atherosclerosis with the presence and severity of coronary atherosclerosis [4–7]. Moreover, there is evidence of a high prognostic significance of peripheral



atherosclerosis (particularly, femoral atherosclerosis) in determining the presence and severity of coronary atherosclerosis [6–8]. The incidence of combined coronary, carotid, and femoral atherosclerosis varies between 10% and 65%, even reaching 90% according to some authors [7, 8]. Here the focus is on specific quantitative and qualitative characteristics of atherosclerotic plaques that allow the presence and the severity of coronary lesions to be verified.

Using findings from carotid duplex scanning (DS), we developed a visual score [9] for assessing the presence and severity of coronary atherosclerosis according to the severity of carotid artery disease. The score includes intima-media thickness (IMT) (≤ 0.9 ; >0.9 mm), number of plaques ($\langle 3; \geq 3 \rangle$) and maximum carotid stenosis ($\leq 45\%$; >45%). Although this VS proved to be informative enough to diagnose severe coronary atherosclerosis, it had low sensitivity and specificity in diagnosing subclinical coronary disease. Such a visual score comprises an attractive tool for the non-invasive diagnosis of coronary atherosclerosis but needs to be developed to increase the statistical significance of defining coronary atherosclerosis and its severity. The evidence on combined coronary, carotid, and femoral atherosclerosis suggests the possibility of using ultrasonographic (US) parameters of femoral artery, both separately and in combination with US parameters of carotid arteries, to improve the prognostic significance of the visual score. At the same time, it seems reasonable to study other qualitative and quantitative characteristics of atherosclerotic plaques, which can be used in the diagnostic complexes of the visual score to more accurately demonstrate the severity of coronary atherosclerosis.

Objective

To evaluate quantitative and qualitative characteristics of carotid and femoral plaques and develop the corresponding visual score for the non-invasive diagnosis of coronary atherosclerosis and assessment of its severity.

Material and methods

The analysis included a cohort of patients admitted to and examined in the State Research Center of Preventive Medicine (currently National Medical Research Center of Internal and Preventive Medicine) from 2016 to 2019. The study was performed following the Declaration of Helsinki. The study protocol was approved by the ethics committee of the center (No. 09–05/19). All patients signed informed consent to be included in the study and on personal data processing.

Exclusion criteria: acute exacerbation of atherosclerosis within <6 months; any acute inflammatory disease; chronic kidney disease stage 3 or higher (glomerular filtration rate <60 mL/min/1.73 m²); decompensated diabetes mellitus

(fasting blood glucose >11 mmol/L); left ventricular ejection fraction <40%; malignancies; hematologic and immune diseases, pregnancy or lactation.

All patients underwent CAG [10] via radial and transfemoral access using the Philips Integris Allura and General Electric Innova 4100 angiography systems in the X-ray operating room. The quantification of stenosis was performed using General Electric Innova 4100 software.

The following causes for diagnostic CAG were identified in the analysis of medical records: retrosternal pain or left-sided chest pain (apparently of coronary origin) and inability to perform stress tests or undergo multislice computed tomography (MSCT) due to contraindications or patient refusal; positive or questionable stress test results (treadmill test or stress echocardiography) or the presence of coronary stenosis on MSCT; changes in the conventional electrocardiogram or Holter monitoring (apparently of ischemic origin), and inability to perform stress tests and MSCT due to contraindications or patient refusal; the need to undergo CAG due to the nature of patient's occupation (associated with increased risk to others).

All patients were subjected to DS and IMT measurement, determination of the presence of plaques, as well as their number and height, and the degrees of stenosis for assessing the condition of carotid and femoral arteries. The examination was performed in the supine position, B-mode with color flow mapping using a 9–11 MHz linear probe in a Vivid-7 ultrasound system. DS was performed to examine the common carotid artery (CCA), CCA bifurcation region, the internal and external carotid arteries on both sides; the common femoral artery, its bifurcation, deep and superficial femoral arteries on both sides.

IMT <0.9 mm was chosen as a reference proposed by the experts of European scientific societies. The criteria of the presence of plaques in carotid and femoral arteries comprised local vessel thickening by more than 0.5 mm or 50% compared to the surrounding areas or a thickening by more than 1.3 mm in carotid arteries and 1.5 mm in femoral arteries protruding into the vessel lumen [11]. The height of the plaque protruding furthest into the artery lumen (the height of the biggest plaque) was determined by measuring it three times and calculating the mean of three values. Stenosis of both arterial systems was assessed. The mean degree of stenosis was calculated as the arithmetic mean of all detected lesions in the arterial system of interest.

Statistical analysis

The data obtained were analyzed using the Statistica v.10 and SPSS v.20 software suites. ROC curve analysis was used to determine the sensitivity and specificity of the test in order to evaluate the cutoff points of the continuous parameters. The threshold level was determined by a combination of



sensitivity and specificity at the intersection of curves giving a total of 100%. In each group of patients, the odds were calculated as the probability of the presence of a feature of interest relative to the likelihood of its absence. The binary logistic regression model was used for the point estimation of odds ratio (OR) in the groups and 95% confidence interval (CI). The significance level used to test statistical hypotheses was p = 0.05.

Results

The study included 216 patients: 115 male patients and 101 female patients from 24 to 87 years old (mean age 61.5 ± 10.73 years), who were divided into the following groups: Group 1–73 patients with asymptomatic intact coronary arteries = coronary atherosclerosis is absent; Group 2–71 patients with asymptomatic hemodynamically insignificant coronary lesions (coronary stenosis <50%) = subclinical coronary atherosclerosis; Group 3–72 patients with clinically evident multiple coronary lesions with two or more coronary arteries involved, one of which is the left main coronary artery, and one coronary artery stenosis of $\geq 50\%$.

In order to develop VSNEW, various ultrasonographic characteristics of carotid and femoral plaques were evaluated to determine parameters having predictive value for the diagnosis of coronary atherosclerosis. In the previous VS [9], which was based on coronary DS, IMT was used as a parameter of interest. Following international guidelines, IMT ≤0.9 mm is used as a reference, while IMT> 0.9 mm is indicative of an artery wall thickening. However, since the significance of IMT as a risk factor for cardiovascular events has decreased [12–14], the «max plaque height» parameter was suggested for VS NEW. The ROC analysis allowed a definition of the cutoff point of the max plaque height for carotid arteries, which was equal to 2 mm. Furthermore, the max plaque height for femoral arteries was also established, which was also found to be 2 mm. Despite the statistically significant association of the degree of coronary lesions with both IMT and max plaque height, the model using max plaque height was more correlated with the degree of the coronary lesion.

Similarly, it was established that the «mean stenosis» parameter is of greater predictive value in determining coronary lesions than «number of plaques». Therefore, «mean stenosis» was included in VS NEW. The ROC analysis was used to obtain cutoff points for mean stenosis: 25% for carotid arteries and 30% for femoral arteries.

This study confirmed earlier results on the correlation of «max stenosis» with the presence of coronary atherosclerosis. The ROC-analysis allowed a determination of the cutoff point of this parameter for carotid and femoral

arteries, which was equal to 45% and the same as the cutoff point for the parameter used in the previous VS [9].

Thus, the new VS (VS NEW) included the following parameters: max plaque height (<2 mm; ≥2 mm), mean carotid stenosis (<25%; $\ge25\%$)/mean femoral stenosis (<30%; $\ge30\%$), max stenosis ($\le45\%$;> 45%). These parameters were used to develop the separate diagnostic complexes and scores for carotid and femoral arteries (Table 1 and Table 2). The presence and severity of coronary atherosclerosis can be determined based on the resulting score.

The statistical significance of carotid VS (VS_{carotid}) and femoral VS (VS_{femoral}) designed on the basis of VS [9] was evaluated in terms of the coronary atherosclerosis diagnosis. The ROC analysis was used to determine the cutoff points: 2 for VS_{carotid} and 1 VS_{femoral}. VS_{carotid} of >2 showed coronary atherosclerosis with the sensitivity of 84.7% and excluded it with a specificity of 85.4%. The sensitivity of VS_{femoral} >1 was 88.9%, while its specificity was 84.0%. Given the high accuracy of VS NEW based on carotid and femoral DS data, it was decided to merge these scores into VS_{GLOBAL}. VS_{GLOBAL} can vary from 0 to 14 (Table 1 and Table 2).

The ROC-analysis was used to analyze the statistical significance of VS_{GLOBAL} for the diagnosis of severe coronary atherosclerosis; the cutoff point was found to be equal to 4. Using this cutoff point, VS_{GLOBAL} was analyzed in groups A (Group 1 + Group 2) and B (Group 3). VS_{GLOBAL} score >4 showed severe coronary atherosclerosis with a sensitivity of 86.1% and excluded it with a specificity of 87.5%. When the cutoff point was reduced to 3, the sensitivity of the method increased to 91.7%, but specificity decreased to 81.3%. Thus, both cutoff points 3 and 4 gave reliable results. However, since the sensitivity/specificity ratio was optimal for the cutoff point of 4, this was used in further calculations.

The VS_{GLOBAL} and cutoff point of 4 was used to construct a binary logistic regression model, according to which the likelihood of finding severe coronary atherosclerosis increased 43.4-fold if VS_{GLOBAL} was >4 (95% CI 18.82–100.08; p <10⁻⁵). Thus, VS_{GLOBAL} , combined with a set of ultrasonographic parameters (max plaque height, mean stenosis, max stenosis) and the corresponding diagnostic complexes, demonstrated possibilities for identifying patients with severe coronary atherosclerosis.

The possibility of identifying subclinical coronary atherosclerosis using the proposed VS_{GLOBAL} was further analyzed. The comparison of patients with atherosclerosis of any degree (Group C combining Group 2 and Group 3) and patients without coronary arteriosclerosis (Group 1) was carried out. The ROC-analysis was used to establish the cutoff point of VS_{GLOBAL} , which was equal to 2 (<2; \geq 2). VS_{GLOBAL} of \geq 2 showed atherosclerosis of any degree with a sensitivity of 75.5% and excluded it with a specificity



Table 1. Visual score based on carotid DS data

Score	Diagnostic complex
0	Max plaque height < 2 mm, mean stenosis < 25%, max stenosis ≤45%
1	Max plaque height ≥ 2 mm, mean stenosis < 25%, max stenosis ≤45%
2	Max plaque height < 2 mm, mean stenosis ≥ 25%, max stenosis ≤45%
3	Max plaque height ≥ 2 mm, mean stenosis ≥ 25%, max stenosis ≤45%
4	Max plaque height < 2 mm, mean stenosis < 25%, max stenosis >45%
5	Max plaque height ≥ 2 mm, mean stenosis < 25%, max stenosis >45%
6	Max plaque height < 2 mm, mean stenosis ≥ 25%, max stenosis >45%
7	Max plaque height ≥ 2 mm, mean stenosis $\ge 25\%$, max stenosis >45%

DS – duplex scanning; max stenosis – maximum stenosis; max plaque height – maximum plaque height.

of 65.8%. The binary logistic regression model analysis showed that, if VS_{GLOBAL} is ≥ 2 , the likelihood of identifying atherosclerosis of any severity increases 5.9-fold (95% CI 3.19–11.00; p <10–5). Thus, VS_{GLOBAL} provided the criterion for distinguishing between patients with atherosclerosis of any degree and patients without coronary arteriosclerosis.

Next, we used VS_{GLOBAL} to separate patients without coronary atherosclerosis (Group 1) from patients with subclinical coronary atherosclerosis (Group 2). The ROC analysis was used to establish the cutoff point equal to 2 (<2; \geq 2). VS_{GLOBAL} \geq 2 points indicated the presence of subclinical coronary atherosclerosis with a sensitivity of 52.1% and specificity of 65.8%.

Thus, VS_{GLOBAL} is useful for non-invasive diagnosis of atherosclerosis and estimation of its severity. Table 3 shows the distribution of patients with coronary disease of varying severity depending on the total VS_{GLOBAL} score.

Discussion

The development of non-invasive diagnosis techniques for coronary atherosclerosis is a promising area of clinical medicine. Here a special focus is placed on the possibility of determining the presence and severity of coronary lesions based on the condition of carotid and femoral arteries.

Earlier, we proposed a VS [9] using the following ultrasonographic parameters of carotid arteries: IMT, number of plaques and maximum stenosis. However, since the VS did not produce statistically significant results for identifying patients with subclinical coronary atherosclerosis, we continued the analysis of ultrasonographic parameters of carotid and femoral arte-

Table 2. Visual score based on femoral DS data

Score	Diagnostic complex
0	Max plaque height < 2 mm, mean stenosis < 30%, max stenosis ≤ 45%
1	Max plaque height ≥ 2 mm, mean stenosis < 30%, max stenosis ≤45%
2	Max plaque height < 2 mm, mean stenosis ≥ 30%, max stenosis ≤45%
3	Max plaque height ≥ 2 mm, mean stenosis ≥ 30%, max stenosis ≤45%
4	Max plaque height < 2 mm, mean stenosis < 30%, max stenosis > 45%
5	Max plaque height ≥ 2 mm, mean stenosis < 30%, max stenosis > 45%
6	Max plaque height < 2 mm, mean stenosis ≥ 30%, max stenosis >45%
7	Max plaque height ≥ 2 mm, mean stenosis ≥ 30%, max stenosis >45%

DS – duplex scanning; max stenosis – maximum stenosis; max plaque height – maximum plaque height.

ries having greater predictive value for the diagnosis of subclinical coronary atherosclerosis.

Recent studies and meta-analyses [12–14] have shown that IMT has decreased significance as a cardiovascular marker and no useful effect on the prognosis of developing CVDs; thus, it is unreasonable to use IMT to reclassify the risk in patients with asymptomatic atherosclerosis. Currently, neither American nor European clinical guidelines recommend using IMT to clarify the cardiovascular risk (class of recommendation IIIA) [15, 16]. There is a growing body of evidence that qualitative and quantitative characteristics of plaques (such as, area and height, severity of stenosis, number of plaques) are more indicative of the risk of developing CVDs than IMT [17, 18]. In this regard, we replaced IMT with the «max plaque height» criterion. The analysis of IMT and max plaque height showed that it is reasonable to use this more statistically significant criterion in the VS.

The analysis of «mean stenosis» and «number of plaques» showed that that mean stenosis of an arterial system reflects the atherosclerotic load since it allows all stenotic lesions to be taken into account and is more statistically significant for the diagnosis of coronary atherosclerosis. In this regard, it was decided to use «mean stenosis» in the VS instead of «number of plaques».

The ultrasonographic «max stenosis» parameter was included in the VS NEW diagnostic complexes due to its statistical significance being confirmed for the detection of severe coronary atherosclerosis. Thus, the analysis of the ultrasonographic parameters of carotid and femoral plaques showed that the VS should include max plaque height, mean



and max stenosis (both carotid and femoral arteries). It should also be noted that the cutoff points of the above carotid and femoral parameters, which differ only in the mean stenosis, are the same for max plaque height and max stenosis.

Carotid and femoral DS showed promising results in terms of the non-invasive detection of coronary atherosclerosis. Therefore, given the reliability of the data of the two blood systems and the possibility that only one of the two arterial systems is involved, it was reasonable to develop a combined score VS_{GLOBAL} calculated as the sum of the two scores.

 VS_{GLOBAL} was developed based on a study cohort that had been non-randomly divided into groups. Given that one of the key study objectives was to find markers for non-invasive diagnosis of subclinical coronary atherosclerosis, it was necessary to stratify patients without coronary arteriosclerosis (Group 1) and patients with severe coronary atherosclerosis (Group 3) in order to identify most accurately a fine dividing line of the investigated parameters necessary for the diagnosis of subclinical coronary atherosclerosis.

Although the study is limited by the absence of a group of patients with moderate coronary atherosclerosis, the diagnosis and confirmation of the hemodynamic significance of which is possible using stress tests, VS_{GLOBAL} is a useful non-invasive diagnostic tool for the detection of subclinical and severe coronary lesions.

Conclusion

One of the most relevant focuses in cardiology is the search of markers for non-invasive diagnosis of coronary atherosclerosis. Thus, the development of a score to assess the risk of its presence and severity is a promising approach to solving this problem. The main advantage of scores is that they are easy to use both prior to and after admission to any

Table 3. Determining the severity of coronary atherosclerosis by VS_{GLOBAL}

Total score	Group
0–1	Intact coronary arteries (no coronary atherosclerosis)
2–4	Subclinical coronary atherosclerosis (coronary stenosis <50%)
>4	Severe coronary atherosclerosis (high probability of multivessel disease, including left main coronary artery, stenosis of one of the coronary arteries ≥50%)

VS_{GLOBAL} – global visual score.

hospital. Risk assessment carried out on the basis of such a score can su ppport using efficient allocation of treatment resources, as well as helping to standardize and evaluate the findings of randomized trials.

The developed VS_{GLOBAL} score comprises a set of ultrasonographic parameters of carotid and femoral arteries to permit the non-invasive diagnosis of coronary atherosclerosis of varying severity in the study cohort. The simplicity and ease of use of the score justify its use at the screening stage to detect subclinical coronary atherosclerosis and promptly initiate preventive measures for slowing down the progression of atherosclerosis and thereby reduce the risk of cardiovascular complications. Non-invasive diagnosis of severe coronary atherosclerosis allow the timely referal of patients to additional investigations for assessing the need for surgical treatment, thus reducing the incidence of cardiovascular complications.

No conflict of interest is reported.

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«КАРДИОЛОГИЯ НА МАРШЕ 2021»

Ежегодная Всероссийская научно-практическая конференция и 61-я сессия ФГБУ «НМИЦ кардиологии» Минздрава России

УВАЖАЕМЫЕ КОЛЛЕГИ!

Приглашаем Вас принять участие в работе Ежегодной Всероссийской научно-практической конференции «КАРДИОЛОГИЯ НАМАРШЕ 2021» и 61-й сессии ФГБУ «НМИЦ кардиологии» Минздрава России. Конференция состоится 7–9 сентября 2021 года в ФГБУ «НМИЦ кардиологии» Минздрава России (г. Москва, ул. 3-я Черепковская, 15А). На Конференции будут представлены фундаментальные аспекты кардиологии, самые последние научные достижения и клинические подходы в области профилактики, диагностики, лечения и реабилитации сердечно-сосудистых и коморбидных заболеваний, в том числе в условиях пандемии СОVID – 19. Участниками Конференции станут ведущие ученые, клиницисты и организаторы здравоохранения из России и зарубежных стран. Конференция будет проводиться при поддержке Министерства здравоохранения Российской Федерации, Департамента здравоохранения города Москвы, Российского кардиологического общества, Национального медицинского общества профилактической кардиологии, Российского научного медицинского общества терапевтов. Часть мероприятий Конференции будет аккредитована в соответствии с требованиями к образовательным мероприятиям и рекомендациями Координационного совета по развитию непрерывного медицинского и фармацевтического образования (НМО) Минздрава России.

ОСНОВНЫЕ НАУЧНО-ПРАКТИЧЕСКИЕ НАПРАВЛЕНИЯ

- Фундаментальные аспекты кардиологии
- Первичная и вторичная профилактика сердечно-сосудистых заболеваний
- Организационные подходы к лечению сердечно-сосудистых заболеваний
- Новая коронавирусная инфекция COVID-19 и сердечно-сосудистые заболевания
- Ведение пациентов высокого и очень высокого сердечно-сосудистого риска
- Артериальная гипертония
- Легочная артериальная гипертензия
- Дислипидемии
- Острые коронарные синдромы
- Атеротромбоз
- Кардиореанимация
- Кардиохирургия: открытая, гибридная, микрохирургия
- Интервенционные методы лечения сердечно-сосудистых заболеваний
- Визуализация в кардиологии
- Хронические коронарные синдромы
- Фибрилляция предсердий и другие нарушения ритма и проводимости сердца
- Сердечная недостаточность
- Проблема приверженности кардиологических пациентов к лечению
- Ожирение, сахарный диабет и сердечно-сосудистые заболевания
- Профилактика мозговых инсультов
- Вопросы коморбидности заболеваний: лечить пациента, а не болезнь
- Кардиоонкология
- Психическая дезадаптация у кардиологических больных
- Сердечно-сосудистые заболевания и здоровье женщин
- Сердечно-сосудистая система и проблемы старения
- Кардиореабилитация
- Социально-экономические аспекты сердечно-сосудистых заболеваний

Научная программа Конференции будетвключать пленарные заседания, научные симпозиумы, научные сессии «Завтрак в Кардиоцентре», сателлитные симпозиумы, встречи с экспертами, круглые столы, телеконференции, мастер-классы, кардиологические «баттлы», постерные доклады, а также Конкурс молодых ученых, Конкурс на лучший постерный доклад, Конкурс на лучшие клинические практики в кардиологии, Конкурс на лучший волонтерский проект для пациентов с сердечно-сосудистыми заболеваниями. Победители Конкурсов будут награждены дипломами и ценными призами. Научная программа Конференции будет размещена на сайтах www.cardioweb.ru, www.cardioprevent.ru и www.scardio.ru в августе 2021 года.

РЕГИСТРАЦИЯ И ФОРМЫ УЧАСТИЯ

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