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Prediction of Subclinical Coronary Atherosclerosis in Patients with High and Very High Cardiovascular Risk

Objective	To develop a diagnostic rule for detection of patients (pts) with high probability of subclinical atherosclerosis among those with high or very high cardiovascular (CV) risk.
Materials and Methods	This cross-sectional study enrolled 52 pts (32 men [62%]), aged 40 to 65 years [mean age 54.6±8.0]) with high or very high CV risk (5–9 and ≥10% by The Systematic Coronary Risk Estimation Scale [SCORE], respectively). All participants underwent cardiac computed tomography (CT) angiography and calcium scoring. Traditional risk factors (RFs) (family history of premature CVD, smoking, overweight/obesity and abdominal obesity, hypertension, type 2 diabetes mellitus, lipids parameters (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides) and lipids-related markers (apolipoprotein A1, apolipoprotein B, ApoB/ApoA1 ratio), biomarkers of inflammation (high-sensitivity C-reactive protein [hs CRP], fibrinogen), indicator carbohydrate metabolism (glucose), ankle-brachial index, stress-test, carotid plaques according to ultrasound were evaluated in all pts. Psychological RFs were evaluated using Hospital Anxiety and Depression Scale and DS-14 for type D personality.
Results	All pts were divided into 2 groups according to the CT angiography results: pts in the main group (n=21) had any non-obstructive lesions or calcium score >0, pts in the control group (n=31) had intact coronary arteries. The groups did not differ in age or gender. 26 multiple linear logistic models for any subclinical atherosclerosis were developed based on obtained diagnostic features. Taking into account R-square = 0.344 (p=0.0008), the best fitting model was follows: subclinical coronary atherosclerosis= –1.576 + 0.234 x SCORE ≥5% + 0.541 x hs CRP >2 g/l +0.015 x heart rate (bpm) +0.311 family history of premature CVD. The developed algorithm had sensitivity of 63% and specificity of 80%.
Conclusion	The created diagnostic model diagnostic model suggests the presence of subclinical coronary atherosclerosis in patients with high/very high CV risk with a high degree of probability. This easy-to-use method can be used in routine clinical practice to improve risk stratification and management choices in high-risk pts.

Keywords	Subclinical atherosclerosis; high cardiovascular risk; risk factors
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Atherosclerosis is the background of cardiovascular disease (CVD); specifically, of coronary artery disease (CAD) and cerebrovascular diseases – major contributors to the structure of cardiovascular mortality. Before the development of clinical manifestations, atherosclerosis remains symptom-free for a while, when atherosclerotic lesions begin to form, and the degree of narrowing of the coronary and peripheral vessels is not yet hemodynamically significant. At this stage, development of the disease can be significantly delayed through active preventive measures, which is particularly essential for patients with a high or very high CVR.

Various risk calculators are used to evaluate CVR. The most commonly used are SCORE (10-year risk of

fatal cardiovascular complications [CVCs]), ASCVD (10-year risk of death from CAD orcerebrovascular disease), Framingham risk score (FRS) (10-year risk of myocardial infarction or sudden cardiac death). Patients with SCORE >5%, ASCVD>20%, FRS >20%, diabetes mellitus (DM), and moderate-to-severe chronic kidney disease are considered to be at high risk of CVCs. They should promptly begininterventions to change lifestyle and correct cardiovascular risk factors (CVRFs), including drug therapy [1].

Following the European [2] and Russian [1] guidelines for the prevention of CVD, the SCORE scale is used in Russia to stratify the risk of fatal CVCs. This scale allows assessing the total CVR, which is calculated based on sex, age, smoking status, systolic blood pressure (SBP), and total cholesterol (TC). The resulting value is a percentage presenting the probability of cardiovascular death within the next 10 years. At the same time, in a significant number of cases, the actual CVR may be higher than calculated on the SCORE scale, such as when the patient has other CVRFs that are not included in the SCORE scale – for example, overweight, abdominal obesity (AO), low physical activity, psychosocial RFs, excessive alcohol consumption, orhistory of early-onset CVD in the immediate family. It should be noted that risk calculators (including SCORE, in which new options are being introduced) are in the process of being improved. In addition, various markers actively being studiedare associated with a high risk of clinical manifestations of atherosclerosis and its complications.

In the last decade, several new atherosclerosis (biochemical, structural, functional, genetic) markers haveemerged. However, there is still no consensus on the feasibility of extensive clinical use because their prognostic significance is unclear [3–7]. Coronary artery calcification (CAC), which is closely associated with the risk of CVCs, is one of the most reliable noninvasive diagnostic markers of subclinical atherosclerosis [8]. Other known markers are the carotid intima-media thickness (IMT) and pulse wave velocity (PWV), indicating the stiffness of arteries, though they exhibit low prognostic significance [9]. According to experts, use of circulating biomarkers reflecting different pathophysiological mechanisms of atherogenesis can improve the prediction of CVDonly slightly [4].

Given the limited prognostic value of these markers of atherosclerosis, it is relevant to study the multimarker approach for a more accurate assessment of CVR. For this reason, Melander,in assessing coronary lesions,suggested an «integrated biomarker» i-BIO, which includes the following parameters: sex, triglyceride levels, high-sensitivity C-reactive protein (hs-CRP), fibrinogen, adiponectin, glucose, IMT, number of atherosclerotic plaques, and extentof carotid lesions [10]. Similar approaches have been used in other studies that looked at various combinations of biochemical, genetic, and visual markers, includingthe Framingham Heart Study, Malmo Diet and Cancer Study, MORGAN, and the Cardiovascular Health Study [11–13].

Despite the complex approach, however, most of these intetratedbiomarkers exhibit limited effectiveness in the early diagnosis of atherosclerosis [14]. Moreover, these markers are not commonly used in real-world clinical practice, despite the clinical and economic imperatives of identifying atherosclerosis as early as possible. A more accurate and personalized examination of patients with a high risk of developing the clinical manifestations of atherosclerosis may be useful to avoid both over- and underuse of drug therapy, hypolipidemic therapy in particular.

Therefore, our analysis examined the relevance of further study of approaches for diagnosing subclinical atherosclerosis.

Materials and Methods

Thecross-sectional study included 52 patients aged 40–65 years with a high or very high cumulative CVR and without clinical manifestations of atherosclerosis. The absolute cumulative risk of developing CVD was estimated on the SCORE scale for the European countries with high cardiovascular mortality. Patients with SCORE <1% were classified as low cardiovascular risk;those with SCORE 1–4% were assigned to the moderaterisk category; those with SCORE 5–9% were assigned as high risk; and those with SCORE>10% were classified as at very high risk [1, 2]. Patients with DM were automatically considered to have high/very high risk (depending on the level of proteinuria) [1, 2].

Any clinical manifestations of atherosclerosis, decompensated chronic diseases, severe mental disorders, or drug or alcohol abuse issues were exclusion criteria.

Patients signed written informed consent forms and filled in a registration card, which included the main demographic (sex, age) and clinical characteristics, and information on whether a patient had any CVRFs: smoking, early-onset CAD orcerebrovascular disease in the immediate family (55 years or younger in males, 65 years or younger in females), hypertension (SBP and diastolic blood pressure [DBP] levels, antihypertensive therapy).

Height, weight, and waist circumference (WC) were measured in all subjects. Excess body weight was

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registered if body mass index (BMI) was 25.0–29.9 kg/m², obesity for weight >30 kg/m². WC >94 cm in males or>80 cm in females was interpreted as abdominal obesity and >102 cm in males or >88 cm in females as severe abdominal obesity. The office heart rate (HR) was determined at rest twice by a radial pulse (beats per minute). The mean value of the two measurements was calculated.

For the assessment of psychosocial CVRFs, all patients filled in the hospital anxiety and depression scale [15]; 8–10 points on the subscales of anxiety (HADS-A) and depression (HADS-D) were interpreted as subclinical, >11 points as clinically expressed anxiety and depression symptoms. The DS14 questionnaire was used to determine type D personality, which was determined if the score was >10 points on both scales (negative excitability and social inhibition) [16].

Venous blood was sampled on an empty stomach to determine levels of total cholesterol (TC), high-density lipoprotein (HDL), triglycerides (TG), low-density lipoprotein (LDL) using the Friedewald formula, apolipoproteins (APO) A1 and B, glucose, and hs-CRP. The analysis was carried out using the automatic biochemical ARCHITECT plus c8000 analyzer. Hypercholesterolemia was diagnosed atTC >5.0 mmol/L, hyperglycemia if glucose on an empty stomach was >6.1 mmol/L, and hypertriglyceridemia if the blood level of TG was >1.7 mmol/L. HDLs were considered low if <1.0 mmol/L in males and <1.2 mmol/L in females. The level of ApoA1 was considered low if <1.2 mg/dL in males and <1.4 mg/dL in females, and ApoB was considered elevated if >80 mg/dL in patients with very high CVR and >100 mg/dL in patients with high CVR. The hs-CRP level was considered elevated if >2 mg/L. Blood levels of fibrinogen were determined using the automatic ACL Elite 8/9/10000 system coagulometer. Fibrinogen was considered increased if >4 g/L.

Duplex (DS) scanning of the carotid arteries and estimation of IMT were carried out with the ultrasound Xario XG scanner in the B-mode using a linear sensor 8 MHz. DS of common carotid arteries (CCAs) and their bifurcations, internal carotid arteries, and subclavian arteries was carried out from three longitudinal views using direct, lateral, and posterior accesses, and cross-sectional view. CCA bifurcation IMT >0.9 mm was considered pathological [1]. Atherosclerotic plaque was identified as a focal thickening of the vascular wall by more than 50% as compared to other parts of the vessel wall, or as a local increase in CCA bifurcation IMT >1.5 mm protruding into the vessel lumen.

The stiffness of the vascular wall was evaluated by determining PWV and measuring the augmentation index (AI) using the Russian diagnostic hardware-software complex Angioscan-01. The threshold level of PWV was >10 m/s [17]. AI was calculated automatically by the carotid artery pressure curve as the ratio of a reflected wave (augmentation pressure) to pulse BP.

The state of the coronary bed and the coronary calcium score (CCS) were estimated using contrast-enhanced multislice computed tomography (MSCT) on the Siemens SomatomSensation CT scanner, which enabled a quantitative assessment of the CA calcification and the volume and density of the calcification foci. The method described in Agatstonet al. [19] was used, based on the quantitative calculation of the X-ray attenuation coefficient in the Hounsfield units. The CCS was interpreted as follows: CCS <10 corresponds to minimal CA calcification; 11–99 corresponds to moderate CA calcification; 100–400 corresponds to increased CA calcification; and >400 corresponds to extensive calcification.

Statistical analysis of the data obtained was carried out withthe SAS system using standard algorithms of variation statistics. The probability of detection and severity of coronary atherosclerosis was estimated using the calculation of multiple linear regression models for different combinations of the prognostic signs (quantitative, rank, and binary factors); significance of the prognostic signs was preevaluated using univariate risk analysis for the relevant contingency tables. In each patient group, the ratio of the presence/absence rate of a symptom was used as the odds ratio. The significance threshold for the statistical hypotheses was 0.05.

Results

Subjects were divided into two groups according to the presence or absence of stenosis and calcification of CAs on MSCT. Group 1 included 21 patients with stenosis and/or calcification of CAs; Group 2 included 32 patients with intact CAs.

Using the CCS index (Agatston score), patients in Group 1 were divided as follows: minimal calcification (33.3%); moderate calcification (19.1%); and elevated calcification (19.1%). Extensive calcification was not registered. Of Group 1 patients, 28.6% of patients had CA stenosis without calcification. Thus, the MSCT data demonstrate subclinical coronary lesions in this group.

Table 1 shows demographic characteristics and the main CVRFs in patients with or without coronary lesions, according to MSCT. The groups were comparable in terms of main demographic characteristics (sex, age, proportion of patients older than

60 years) and commonRFs (smoking, overweight and obesity, hypercholesterolemia, hypertension, DM).

Interestingly, in the group of patients with subclinical atherosclerosis of CAs, the proportion with very high CVR (SCORE >10%) was significantly higher than among those without lesions (42.9% vs. 16.1%; p<0.05). Despite the almost-equal proportion of patients with hypertension in both groups (57.1% and 45.8%, respectively), Group 1 included significantly more patients with a long history of hypertension (>5 years) and longer duration of antihypertensive drug therapy. More patients with subclinical coronary lesions had a higher heart rate at rest (87.20 ± 13.70 bpm vs. 77.20 ± 49.11 bpm; p<0.01).

Standard univariate risk analysis, based on the relevant contingency tables, was used to evaluate the statistical significance of associations between subclinical atherosclerosis, confirmed by contrast-enhanced MSCT, and the common and psychosocial RFs, as well as biochemical and morphofunctional markers of atherosclerosis. For that purpose, odds ratio (OR) with a 95% confidence interval (CI) was calculated for the development of subclinical atherosclerotic changes in CAs depending on the presence of the most probable signs identified during comprehensive examination of patients with high CVR. The most predictive and diagnostically significant RFs for the development of atherosclerotic lesions of CAs were taken into account and evaluated (Tables 2 and 3).

Patients with very high CVR (SCORE >10%) are four times more likely to have subclinical atherosclerosis of CAs than those with intact CAs (OR 3.9; 95% CI, 1.07–14.16, p<0.04) (see Table 2). This reconfirms that the SCORE scale is one of the most effective and reliable tools for the evaluation of CVRs.

Interestingly, hypertension appears to be one of the most significant predictive markers of subclinical atherosclerosis. If the history of hypertension extends beyond5years, the probability of subclinical atherosclerosis is six times higher and, in the case of long-term antihypertensive drug therapy, four times higher (OR 6.14, 95% CI 1.53–23.79; p=0.007 and OR 3.97, 95% CI 1.23–13.91; p=0.02, respectively) than in subjects with intact CAs. Immediate family history of early-onset CVD is quite closely associated with the risk of subclinical atherosclerosis (OR 3.12, 95% CI 0.94–10.36; p=0.06).

Among the common CVRFs, AO also showed an association with the development of subclinical atherosclerosis in patients with high CVR; however, it was not significant (OR 3.89, 95% CI 0.75–20.25; p=0.08).

No significant associations were established between the main psychosocial RFs (clinically expressed anxiety or depression symptoms) and the presence of subclinical atherosclerosis.

Among the biochemical markers (see Table 3) of atherosclerosis, decreased HDL levels were close to having a significant association with subclinical atherosclerosis (OR 2.67, 95% CI 0.82–8.68; p<0.1).

It should be noted that in terms of instrumental examinations for the diagnosis of subclinical atherosclerosis, data on vascular wall stiffness were associated with the results of MSCT. PWV >10 m/s

Table 1. Clinical and demographic characteristics of patients with subclinical atherosclerosis of coronary arteries and intact vessels

Parameter	Group 1 (subclinical atherosclerosis of CAs)	Group 2 (intact CAs)	p
Males, %	38.10	61.29	ns
Age, years	56.29 ± 8.87	53.87 ± 7.50	ns
Age >60 years old, %	42.9	29.0	ns
Main CVRFs			
Smoking, %	14.3	22.6	ns
Overweight and/or obesity (BMI >25 kg/m2), %	80.7	66.7	ns
Obesity (BMI >30 kg/m2), %	28.6	19.4	ns
Abdominal obesity, %	90.5	70.9	ns
Severe abdominal obesity, %	52.4	41.4	ns
Family history of CVD, %	47.6	22.6	ns
Hypertension, %	57.1	54.8	ns
Duration of hypertension, years	5.43 ± 5.84	3.32 ± 5.66	ns
Duration of hypertension >5 years, %	47.62	12.9	<0.01
Long antihypertensive drug therapy, %	61.9	29.0	<0.05
HR at rest, bpm	87.20 ± 13.70	77.20 ± 10.40	<0.01
Type 2 diabetes, %	14.3	3.2	ns
Hypolipidemic therapy, %	14.3	9.7	ns
Very high CVR (SCORE >10%), %	42.9	16.1	<0.05
Very high CVR (SCORE >10%) taking into account HDL, %	23.8	9.7	ns

The data are expressed as the mean ± standard deviation unless specifiedotherwise. CAs, coronary arteries; BMI, body mass index; RFs, risk factors; CVD, cardiovascular disease; HR, heartrate; HDL, high-density lipoproteins; CVR, cardiovascular risk; ns, not significant.

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Table 2. Association between common and psychosocial cardiovascular risk factorsandsubclinical coronary lesions in patients with high cardiovascular risk according to regression analysis

Parameter	OR	95% CI	p
Male	0.39	0.12–1.21	ns
Age >60 years old	1.83	0.57–5.86	ns
Very high risk (SCORE >10%)	3.9	1.07–14.16	0.04
History of early-onset CVD in immediate family	3.12	0.94–10.36	ns
Hypertension	1.10	0.36–3.36	ns
Long duration of antihypertensive drug therapy, %	3.97	1.23–12.84	0.02
Duration of hypertension >5 years	6.14	1.53–23.79	0.007
AO (WC >80 cm in females and >94 cm in males)	3.89	0.75–20.25	ns
Overweight and/or obesity (BMI >25 kg/m2)	2.02	0.54–7.61	ns
Obesity (BMI >30 kg/m2)	1.67	0.45–6.12	ns
Smoking	0.57	0.13–2.52	ns
Type 2 diabetes	5.00	0.48–51.77	ns
Psychosocial risk factors			
Type D personality	3.73	0.82–17.09	ns
Negative affectivity	3.00	0.88–10.23	ns
Social inhibition	3.20	0.87–11.75	ns
Clinically expressed anxiety symptoms	1.56	0.28–8.57	ns
Clinically expressed depression symptoms	0.73	0.06–8.55	ns

AO, abdominal obesity; CI, confidence interval; BMI, body mass index; CAs, coronary arteries; WC, waist circumference; OR, odds ratio; CVD, cardiovascular disease; RFs, risk factors; ns, not significant; SCORE, Systematic COronary Risk Evaluation.

increases the risk of subclinical coronary lesions 3.8-fold (OR 3.79, 95% CI 0.92–15.67; p<0.05).

Thus, univariate risk analysis established significant associationwith subclinical coronary lesions (presence of calcification and/or stenosis) confirmed by MSCT for the following factors:

1. Very high CVR (SCORE 10%);
2. Long history of hypertension >5 years;
3. Long duration of antihypertensive drug therapy;
4. Increased stiffness of vascular wall (PWV >10 m/s).

During multivariate linear regression analysis with the maximum R-square improvement, 26 models were developed and analyzed. Each model included various combinations of the following four prognostic variables: high and very high risk of CVD (SCORE >5% and >10%, respectively); family history of CVD; long history (>5 years) of hypertension; history of maximum SPB, hypolipidemic therapy, hypotensive and hypolipidemic therapy; HR at rest; AO;type D personality and its two individual components (negative affectivity and social inhibition); patient's global impression of their health; elevated hs-CRP levels; hypo-alpha-cholesterolemia; vascular wall stiffness with PWV >10 m/s; atherosclerotic plaque (right or left obstructive sleep apnea [OSA] bifurcation, IMT >1.5 mm).

All calculations in the linear regression analysis were based on the count, comparison, and evaluation of the statistical significance of individual prognostic signs according to the relevant analyses of variance (ANOVA), which were automatically integrated into the calculation procedure. Since ANOVA is a nonparametric method of statistical analysis, the applied method allowed combining different parameters (i.e., parameters measured on the different interval scales or ordinal scales, and binary parameters) within specific verified regression models.

The most informative linear regression model taking into account the R-square coefficient appeared to include the combination of parameters described here:

Multivariate linear regression model of the diagnosis of subclinical atherosclerosis: Subclinical atherosclerosis of CAs confirmed by MSCT = –1.576 + 0.234 x high and very high risk (SCORE >5%) + 0.541 xhs-CRP levels (>2 mg/L) + 0.015 x HR (bpm) + 0.311 x immediate family history of early-onset CVD; the probability of subclinical atherosclerosis is high when individual rate is >0.5.

The integrated significance of the whole model was p=0.0008. Total explanatory power of the regression model (coefficient of determination) was R-square =0.3443 – that is, this regression equation makes it possible to explain 34.43% of individual variability of the predicted sign (subclinical atherosclerosis of CAs) by measuring the individual values of the four parameters: presence/absence of a high or very high CVR (SCORE >5%), elevated hs-CRP levels, family history of early-onset CVD, and HR at rest in a specific patient. The contribution of individual parameters in the linear regression model is provided in Table 4.

The probability of subclinical coronary lesions was high if an estimated value of the binary parameter predicted using the multivariate linear regression

Table 3. Association between biochemical and structural markers and subclinical coronary lesions in patients with high cardiovascular risk according to regression analysis

Biochemical marker	OR	95% CI	p
Hypercholesterolemia (>5.0 mmol/L)	1.15	0.24–5.45	ns
Reduced HDL levels (<1 mmol/L in males;<1.2 mmol/L in females)	2.67	0.82–8.68	ns
Elevated apolipoprotein B	0.34	0.04–3.26	ns
Hypertriglyceridemia (>1.7 mmol/L)	1.5	0.47–4.86	ns
Elevated fibrinogen	2.11	0.49–9.02	ns
Increased stiffness of vascular wall (PWV >10 m/s)	3.79	0.92–5.67	<0.05

PWV, pulse wave velocity; CI, confidence interval; CAs, coronary arteries;
OR, odds ratio; CVD, cardiovascular disease; HDL, high-density lipoproteins; ns, not significant.

was >0.5 (i.e., the midinterval between actual measured numerical values of «0» and «1»). This threshold was used to transform estimated quantitative values into the predicted binary parameter (as the most likely prognosis for a given patient), after which the binary results were compared with actual data on the presence/absence of subclinical coronary lesions. This allowed performing standard calculation of the total explanatory value of the chosen multivariate linear regression model, including the parameters of integral sensitivity and specificity. The developed diagnostic algorithm for the presence/absence of subclinical atherosclerosis appeared to have a 63% sensitivity in identifying patients with subclinical coronary atherosclerosis and 80% specificity in excluding patients who did not have subclinical coronary lesions.

Discussion

Currently, CVR is predicted based on well-studied common CVRFs such as age, gender, blood pressure, cholesterol levels, and smoking status, all of which are included in the well-established SCORE scale – considered the gold standard for determining total CVR [1, 2]. However, examination of only those RFs included in the SCORE scale may underestimate the patient's CVR. It is evident that additional CVRFs and atherosclerosis markers should be considered to improve the accuracy of prediction.

We developed a multivariate linear regression model for the diagnosis of subclinical atherosclerosis, which is of sufficiently high sensitivity and specificity to determine whether a patient has subclinical atherosclerosis of CAs.

The study shows key factors that should be taken into account in examining patients at high risk in order to detect subclinical atherosclerotic lesions in the vascular bed. In addition to high risk as determined by the SCORE scale (>5%), of all common and psychosocial CVRFs, biochemical markers, and data from noninvasive instrumental examinations, the final model included elevated levels of hs-CRP (>2 mg/L), HR rate at rest, and history of early-onset CVD in the immediate family.

It should be noted that among five additional RFs taken into account when a treatment decision is made, the new risk calculator of the American College

Table 4. Contribution of individual parameters in the multivariate linear regression model for the diagnosis of subclinical atherosclerosis

Parameter	Partial p (model factor coefficient)	Fisher's test	p
High and very high CVR (SCORE >5%);	0.23	3.78	0.06
Elevated hs-CRP levels (> 2 mg/L)	0.54	4.57	0.04
HR	0.02	10.44	0.002
Family history of early-onset CVD	0.31	5.68	0.02

hs-CRP, high-sensitivity C-reactive protein; CVD, cardiovascular disease;
CVR, cardiovascular risk; HR, heart rate; SCORE, Systematic COronary Risk Evaluation.

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of Cardiology and the American Heart Association (ACC/AHA), the ASCVD scale, includes two parameters, which are used in our algorithm,specifically: family history of early-onset CVD (<55 years inmales and <65 years in females) and elevated levels of hs-CRP (>2 mg/L).

It should be noted that contrast-enhancedcoronary MSCT is one of the most informative but also one of the most expensive techniques for evaluatingthe presence of subclinical atherosclerosis. In addition to the high cost, it is necessary to take into account a considerable radiation exposure for a patient, which averages 1 mSv per procedure. Therefore, MSCT cannot be considered a first-line diagnostic method to detect subclinical lesions of CAs in large patient cohorts.

By contrast, parameters included in the developed regression model for the diagnosis of subclinical atherosclerosis can be assessed at outpatient visits. The collection of family history of early-onset CVD and measurement of HR at rest are standard procedures of the medical examination, and TC levels are also routinely tested. The only nonroutine test, the determination of hs-CRP levels, does not involve challenges around time expenditures and costscomparable with those of coronary MSCT.

The following steps for identifying and managing patients with subclinical atherosclerosis can be used in real-world clinical practice:

1) identification of patients with a high or very high CVR (SCORE >5%);
2) assessment of subclinical atherosclerosis risk using the developed regression model in patients with a high or very high CVR (SCORE >5%);
3) implementation of the most active preventive measures for patients with a high risk of subclinical atherosclerosis (>0.5 according to the regression model) to prevent disease progression and onset of CVCs, as well asperformance of additional examinations (MSCT, assessment of the severity of carotid atherosclerosis, etc.) if necessary.

Conclusion

To support the timely diagnosis of subclinical atherosclerosis, we suggest a diagnostic algorithm as part of a stepwise approach,given limited feasibility of expensive diagnostic techniques (specifically, multislice computed tomography) and grounded in a set of well-known and less expensive diagnostic examinations. A multivariate linear regression model forthe diagnosis of subclinical atherosclerosis was developed within this study. It is an affordable, easy-to-use method – feasible in everyday clinical practice, including the outpatient setting – of improving risk stratification, which makes it possible to select the most effective prevention and care interventions for patients with a high or very high risk to prevent cardiovascular complications.

No conflict of interest is reported.

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