



## Clinical Research

# Identification of Patients at High Cardiovascular Risk

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## Abstract

**Objective:** To identify individuals at high cardiovascular risk (CVR) to check for an additional estimate of CVR with the use of the ESH/ESC Guidelines (2003, 2007) in patients earlier classified as being at low and moderate risk on «SCORE».

**Material and methods:** The study included 600 people (155 men and 445 women) with low and moderate cardiovascular risk on the SCORE scale. All patients were examined with duplex scanning of the carotid arteries (DSCA) to determine the thickness of the intima – media (IMT), the presence of atherosclerotic plaques (ASP); it has also been performed sphygmographic computer (SC) with automatic estimation of brachial-ankle pulse wave velocity (baPWV), biochemical analysis of blood lipid spectrum. **Results:** The frequency of ASP was 59.5% (357 out of 600), and a thickening of the complex "intima-media" (IMT) > 0.9 mm was detected in only 5% of the cases (28 persons out of 600), that indicated a slight contribution to the magnitude of the risk of such parameters as the IMT. The total number of patients with signs of preclinical lesions of the arterial wall (the presence of ASP and/or increased baPWV) was 337 (56% of 600). Our results showed that the presence of subclinical atherosclerosis is in itself a risk factor. **Conclusion:** The usage of instrumental methods of research (DSCA, SC) allowed to detect 32% of individuals with high CVR from 600 previously classified as low and moderate risk on SCORE scale. In our opinion, the proposed algorithm is convenient and easy to use for transfer of the patients into high-risk group. IJBM 2012; 2(2):102-107. © 2012 International Medical Research and Development Corporation. All rights reserved.

**Key words:** cardiovascular risk, risk stratification, high risk.

## Introduction

Since the late '40s of the 20th century the concept of risk factors (RF) was introduced in clinical practice and research, which is now universally accepted. To date, the overall assessment of cardiovascular risk (CVR) is essential to identify individuals with a high probability of adverse cardiovascular events in the next 5 -10 years. Currently, dozens of special scales are developed to stratify CVD risk. They are based on the conventional risk

factors (RF) such as gender, age, smoking, serum total cholesterol (TC), and blood pressure (BP). In 2003, a group of experts from the European Society of Cardiology and experts from other European societies presented the SCORE scale for estimating total cardiovascular risk [1]. The peculiarity of this model is because CVR is determined by calculating the absolute probability of developing a fatal cardiovascular event within the next 10 years. Moreover, the total risk can be determined by relatively simple screening. The disadvantage of this scale is that it can be applied only to persons who have no proven atherosclerosis, as it does not consider the totality of risk factors and target organ damage (TOD). In this regard, to clarify the risk scale Recommendations for the diagnosis and treatment of arterial hypertension of the European Society of Hypertension (ESH) and Society of Cardiology (ESC) (2003, 2007) [2] is used additionally. In this risk system stratification, in contrast to the SCORE

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scale, besides the conventional risk factors certain parameters are used, which characterize the state of the arterial wall (the thickness of the intima-media complex (IMT)), presence of atherosclerotic plaques (ASP), ankle-brachial index (ABI) and pulse wave velocity (baPWV), as well as the presence of diabetes mellitus (DM), metabolic syndrome (MS) and associated clinical conditions (ACC), which allow for a more accurate magnitude of risk.

## Objective

To identify individuals at high CVR to check for an additional estimate of cardiovascular risk with the use of the ESH/ESC Guidelines (2003, 2007) in patients earlier classified as being at low and moderate risk on «SCORE».

## Material

The study was carried out as part of the research: "Testing and introduction in outpatient clinics of new algorithms for the prevention, diagnosis and treatment of atherosclerosis as an example on WAD of Moscow City" (a contract #8/3-281n-10 of May 27, 2010 between the FGA RCRPC of the Ministry of Health and Social Development of the Russian Federation and the Department of Science and Industrial Policy of Moscow City)

Patient screening was performed at 12 outpatient clinics of Western Administrative District (WAD) of Moscow City. The study gradually (from August to December 2009) included patients between 30 - 65 years, who consulted the district physicians regarding various diseases and gave their consent to participate in the study.

### Criteria for inclusion in the study

This included the presence of low and moderate risk on the SCORE scale in patients above 30 years, who sought medical help from the district physicians for various diseases and gave their consent to participate in the study.

### Exclusion criteria

Patients diagnosed with cardio-vascular diseases associated with atherosclerosis, diabetes, heart, kidney, respiratory and liver failure, cancer, mental illness and diffuse pathology of connective tissue were excluded.

The study included 600 people (155 men and 445 women) with low and medium cardiovascular risk on the SCORE scale. The study showed more women than men because women are more likely to seek treatment in clinics and more willing to participate in a research program. According to the study design, the patients were examined in a Cardiology center after one month of district physician treatment.

## Methods

### Systems of cardiovascular risk stratification

1. Screening of patients was conducted on the SCORE

scale, which permits the estimation of a 10-year risk of death from CVD (Systematic coronary risk evaluation, 2010). On this scale, a risk assessment is carried out based on sex, age, smoking status, systolic blood pressure and total cholesterol concentrations. The risk is considered low (<1%), moderate if the projection of patient data against the SCORE scale shows a risk of less than 5%, high if it is in the range 5-9% and very high if it equals or exceeds 10%.

2. Additional stratification of cardiovascular risk conducted using the Recommendations Scale of ESH/ESC (2003, 2007). Using this scale, all the patients, depending on the degree of increased blood pressure, presence of risk factors, TOD and associated clinical conditions (ACC) can be assigned to one of four risk groups: low, moderate, high and very high added risk. The term "added" in this system is used to emphasize that the cardiovascular risk in patients with hypertension is always higher than the average population.

It should be noted that according to the SCORE scale, 'low' and 'moderate' risk were combined into one group (5% or less). Based on the scale of Recommendations ESH/ESC (2003, 2007) the concept of "low" and "moderate" risk determines not only the risk of cardiovascular death, but the risk of such cardiovascular events like stroke and myocardial infarction, which are considered separately.

### Instrumental methods of research

1. Duplex scanning of the carotid artery (DSCA) was performed on the ultrasonic scanner Philips IE33 and Philips iU22, using the line sensor 9 11MGts. We determined the thickness of the intima - media in the automatic mode, the presence of atherosclerotic plaques (ASP) in the carotid arteries, based on the Recommendations of the American Society of Echocardiography and the Society for Vascular Medicine and Biology (2008) [3]. According to ESH/ESC (2003, 2007) a value of IMT < 0.9 mm was considered normal.
2. Sphygmographic Computer (SC) study was conducted on the VasEra (VS-1000) (Fucuda Denshi, Japan) with automatic estimation of brachial-ankle pulse wave velocity (baPWV) (goal<12 m/s) and ankle-brachial index (ABI) (goal>0.9).

Biochemical analyses were performed on the biochemical automatic analyzer Architect with Systems 8000 (Abbott, USA). Determined:

1. Lipid profile: total cholesterol (TC) (goal of  $\leq 5.0$  mmol/L), low-density lipoprotein cholesterol (LDL-C, goal of  $\leq 3.0$  mmol/L), high density lipoprotein cholesterol (HDL-C, goal of  $\geq 1.2$  mmol/L for women and  $\geq 1.0$  mmol/L for men), triglycerides (TG, goal of  $\leq 1.7$  mmol/l).
2. To determine the fasting plasma glucose level, the glucose oxidation method was used.
3. Serum creatinine was determined photometrically by Jaffe's method.
4. Creatinine clearance was calculated using the

Cockcroft-Gault formula (goal > 60 ml/min).

Biochemical parameters proposed in Recommendations ESH / ESC (2003, 2007) were used as the standards.

**Statistical processing** of data was carried out using a software package «Statistica 6.0». Data are presented as mean values (M±SD), median, lower and upper quartiles and the frequency of abnormalities (%). Comparative analysis of the quantitative traits was conducted with the

Mann-Whitney U-test.; differences were considered significant at  $p < 0.05$ . For comparison of proportions Fisher's exact test was used.

## Results and discussion

Characteristics of patients enrolled in the study are presented in Table 1.

As seen from Table 1, the average age of the female

**Table 1**

*The mean values of the cardiovascular risk factors and frequency of abnormalities in patients with low and moderate risk on SCORE scale*

Parameters	Females (n=445)		Males (n=155)		p
	mean values	%*	mean values	%	
Age, years	50.4±6.8	-	47.8±7.5	-	0.62
BMI	29±5.5	76	29±4.0	75	0.52
Waist circumference, cm	89.9±12.6	47	92±10.7	22	0.001
TC, mmol/L	5.9±1.1	73	5.7±1.2	67	0.52
LDL-C, mmol/L	3.6±0.8	64	3.5±0.9	61	0.34
HDL-C, mmol/L	1.4±0.3	35	1.2±0.3	24	0.61
TG, mmol/L	1.5±0.6	28	1.8±0.9	45	0.001
Fasting glucose, mmol/L	5.1±0.7	7	5.1±0.8	5	0.22
Serum creatinine, μmol/L	68±13.1	0	83±39	0	-
Creatinine clearance	128±37	0	130±38	0	0.62
SBP, mmHg	126.8±12.3	60	127.9±11.5	64	0.66
DBP, mmHg	82.6±7.8	52	83.5±8.2	51	0.65
Smoking, %	16%	-	45%	-	0.0001
Family history, %	14%	-	39%	-	0.0001
MS, %	43%	-	46%	-	0.56

**Note:** \* - the proportion of persons with a deviation of the level of the normal value;  
p – value for the two sided Fisher's exact test.

sample was 50.4±6.8 years, which is significantly higher than the average age of men 47.8±7.5 ( $p=0.0001$ ). An increasing body mass index (BMI) of over 25 was observed in both groups, at 76% and 75% respectively; therefore, overweight people dominated in the two groups. As mean values and frequency of abnormalities (%), BMI was not significantly different ( $p>0.05$ ) in the two groups. The average total cholesterol levels in women and men showed similar values ( $p>0.05$ ). No significant differences were noted at any level or in the frequency of abnormalities for LDL-C (64% vs. 61%,  $p=0.34$ ) and HDL-C (35% vs. 24%,  $p=0.61$ ). The mean values of TG and the frequency of abnormal TG (45% vs. 28%,  $p=0.001$ ) were seen to be significantly higher in men.

The sample included a small number of individuals with elevated fasting blood glucose, both among men and among women (7% and 5%,  $p=0.22$ ). Mean levels of creatinine and creatinine clearance remained within normal values, and individuals with the higher levels of parameters were excluded. The mean values of SBP and DBP were not significantly different. At the same time there was quite a large incidence of persons having high normal values of SBP (60% and 64%,  $p=0.66$ ) and DBP

(52% and 51%,  $p=0.65$ ) in both groups. The diagnosis of arterial hypertension (AH) was established in 220 (36.6%), women were 159 of 445 (35.9%), men - 61 of 155 (39.6%). Antihypertensive therapy according RMSAH and ARSSC recommendations previously was assigned to all patients with a diagnosis of hypertension. However, high blood pressure was marked in a substantial portion of those examined in the Cardiac center. In this connection, based on the blood pressure levels, the patients were divided into 3 groups: patients with hypertension (BP>140/90 mmHg), those with high normal blood pressure (BP=130-139/85-89 mmHg) and those with normal blood pressure (BP <130/85 mm Hg). The greatest number of patients was in the group with normal blood pressure (n=326; 54%), next in the group with hypertension (AH) - 153 (25%), and finally those with high normal blood pressure - 121 people (21%).

In the group of male smokers were significantly more than among women (45% vs. 16%,  $p=0.0001$ ). No significant differences were observed in the frequency of detection of the metabolic syndrome (43% and 46%,  $p=0.56$ ).

As noted above, the SCORE scale does not account

for the totality of the risk factors and TOD, which may affect the underestimation of the value of the CVR and therefore the method of treatment selected for these patients. In this regard, we have additionally applied the Recommendations scale of ESH/ESC (2003, 2007) to clarify the value of CVR. At the same time, data from the duplex scanning of carotid arteries and the parameters baPWV was used. ABI parameter characterizing the stenosing lesions of the arteries of the lower extremities was also estimated. However, in our study group, the number of people with an ABI value  $<0.9$  was seen in only 29 people out of 600 (5%). Moreover, all of them have had either ASP in the carotid arteries or increased baPWV; therefore, this parameter was not used by us in this study.

Duplex scanning of the carotid arteries allows for detection of signs of subclinical carotid atherosclerosis using two parameters: the IMT and the presence of ASP. The frequency of ASP was 59.5% (357 out of 600), and a thickening of the complex "intima-media" (IMT)  $> 0.9$  mm was detected in only 5% of the cases (28 persons out of

600), that indicated a slight contribution to the magnitude of the risk of such parameters as the IMT.

The total number of patients with signs of preclinical lesions of the arterial wall (the presence of ASP and / or increased baPWV) was 337 (56% of 600); they are as follows:

1. The number of persons showing only the increased value of baPWV and without ASP was 24 people (4%).
2. The number of persons having only the presence of ASP and a normal baPWV value was 360 (60%).
3. The number of persons regarding the presence of ASP, and with a higher baPWV was 216 people (36%).

Thus, the presence of ASP in the carotid arteries compared with the other parameters has the greatest diagnostic value for determining the magnitude of risk. The results clarify the magnitude of risk in the group of patients studied and are presented in Table 2.

The data presented in Table 2 shows that 210 (35%)

**Table 2**

*The results of the patient distribution into risk groups on Recommendations scale of ESH/ESC (2003, 2007) according to data of duplex scanning and the values of PWV (n=600)*

Groups of risk	Number of patients	%
<b>Low added risk</b>	n=210 (35%)	
Arterial hypertension	12	6**
High normal BP	44	21
Normal BP	154	73
<b>Moderate added risk</b>	n=198 (33%)	
Arterial hypertension	24	12
High normal BP	0	0
Normal BP	174	88
<b>High added risk</b>	n=192 (32%)	
Arterial hypertension	107	56
High normal BP	85	44
Normal BP	0	0

**Note:** \*- percentage of total number (n=600)

remained in the low-risk group, - 198 (33%) in the moderate-risk group and 192 (32%) transferred in the high-risk group. Individuals with normal blood pressure (73%) were predominant in the low-risk group, while the number of people with hypertension was 6%. Individuals with normal blood pressure (88%) were predominant in the group of moderate risk, as well as in the low-risk group, while people with high normal blood pressure were absent. No person with normal blood pressure was found in the high-risk group; on the contrary, most individuals had hypertension (56%), and the number of persons with high normal blood pressure was 44%.

Our results showed that the presence of subclinical

atherosclerosis (i.e., visualization of ASP in the carotid artery, in the absence of complaints and clinical symptoms) is in itself a risk factor. This is confirmed by the works of foreign authors. Thus, the CAFES-CAVE study evaluated the risk of cardiovascular complications in people with low risk depending on the atherosclerotic changes in the bifurcation of the carotid and femoral arteries [4]. It was demonstrated that the risk of cardiovascular events during 10 years increased by 9% with a thickening of the intima-media by 39%, with the presence of ASP hemodynamically non stenosing of carotid artery lumen, and 81% by the presence of ASP, which narrows the carotid artery by 70% or more. In 2009,

Cournot and colleagues revealed that the relative risk of complications in patients with no complaints, depended on the results of physical and instrumental examination. If the patient had a positive result on the stress test (treadmill, bicycle ergometry) the relative risk was 3.7, when listening to the sound over the femoral artery - 3, with the presence of ASP in the carotid artery - 3.8, and with thickening of the intima-media - 2.3 [5].

The thickness of the intima-media also has a significant impact on risk stratification. The analysis of several studies (Atherosclerosis Risk in Communities study, n=12841, Cardiovascular Health study, n=5858, Rotterdam study, n=8000) showed that the increase of IMT on 0.2 mm leads to an increased risk of myocardial infarction by 33% and stroke by 28%. Meta-analysis of

eight studies (37197 patients) confirmed these data - the increase of IMT on 0.1 mm leads to the increased risk of myocardial infarction from 10% to 15% and stroke from 13% to 18% [6].

The results of our study led to the recommendation for risk stratification of the index of subclinical atherosclerosis which was determined on the basis of duplex scanning of the brachiocephalic arteries. The frequency of ASP was 59.5% (357 patients out of 600): in 253 (56.8%) women out of 445 and in 104 (67%) men out of 155. Table 3 shows the proportion of patients (%) with identified ASP in the carotid arteries in different age ranges. The data presented in Table 3 shows that the proportion of persons with ASP significantly increased in men over the age of 40 years compared with younger

**Table 3**

*The frequency of identify of ASP in the carotid arteries in different age ranges*

Age	Females (n=445)			Males (n=155)			p
	N	number of individuals with ASP	%	N	number of individuals with ASP	%	
from $\leq 30$ to $< 40$	28	5	17.8	25	8	32.0	0.331
from $\geq 40$ to $< 45$	58	17	29.3	24	13	54.1	0.044
from $\geq 45$ to $< 50$	104	57	54.8	38	26	68.4	0.179
from $\geq 50$ to $> 55$	131	81	61.8	39	31	79.5	0.033
$\geq 55$	124	93	75.0	29	26	89.6	0.134

*Note: p – value for the two sided Fisher's exact test*

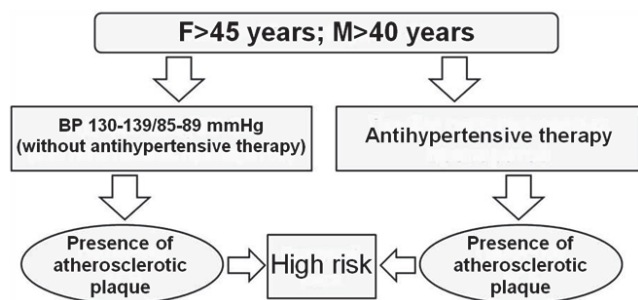
patients. Differences with the women same age (40-45 years) were statistically correct. Statistically significant increasing of plaques was determined in women of the age of 45 and especially after age of 50, when the probability of detection of plaques was 61.8%. Moreover, 79.5% men over the age of 50 had plaque, and a similar proportion of ASP (75%) in women was detected only in the age group over 55 years. Differences between the proportion of persons with plaques in men and women of age 50-55 were a statistically highly significant ( $p=0.033$ ).

Thus, if during duplex scanning of the brachiocephalic arteries ASP is determined in men older than 40 years of age or in women above 45 years with a blood pressure level of 130-139/85-89 mmHg without the use of antihypertensive drugs or in patients with any blood pressure and those taking antihypertensive drugs, such patients from the category of low or moderate risk were transferred to the high risk category, as shown in Fig. 1.

Thus, after an additional stratification of cardiovascular risk with the use of instrumental methods (duplex scanning of carotid arteries, computer sphygmography) from 600 people assigned to a group of low and moderate risk on the SCORE scale, 32% patients were transferred to the high-risk group, and only 35% were remained in low-risk group. In our opinion proposed algorithm for the transfer of patients to the high-risk group is convenient and easy to use.

**Figure 1**

*Potential algorithm of transfer of females (F) and males (M) with low to moderate risk according by the SCORE to the high-risk category.*



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