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The probabilistic calculator for prediction of coronary atherosclerosis risk in patients with obesity

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Summary

Objective

To create a method of coronary atherosclerosis prediction in patients with obesity.

Material and methods

This study involved 85 men, 39-65 years (average age of 47,68±6,65 years) with absence of clinical manifestations of coronary heart disease and atherosclerosis of other localizations. Patients had the obesity of the I-III degree, BMI 36,23±4,31 kg/m² and visceral obesity in case of epicardial fat tissue thickness≥7 mm. 2 groups of comparison were identified according with the performed coronary angiography or multislice spiral computer tomography of coronary arteries. Group I (n=35) included patients with existence of coronary atherosclerosis, Group II (n=50) included patients with absence of coronary atherosclerosis.

Results

As the result of comparison of two groups of an arterial hypertension the existence of carbohydrate violations, triglycerides, leptin, adiponectin and C -reactive protein have been identified as possible predictors of coronary

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atherosclerosis risk. Each predictor received its coefficient of importance after the regression analysis with optimal scaling importance. The size of right classifications as a result of logistic regression was 79,1% that indicates a good predictive ability of this regression model.

Conclusion

The created scale allows to estimate risk of coronary atherosclerosis in the absence of disease clinical manifestations, that is important in terms of well-timed preventive actions and the prevention of the disease progression.

Key words

visceral obesity, coronary risk, scale

It has been proved that neurohumoral activity of visceral fat including epicardial fat tissue has an important role in cardiovascular complications (CVC) development in patients with obesity [1, 2]. Due to this the identification of high coronary risk group considering the presence of normal obesity and in particular visceral one would allow to plan and perform prophylaxis interventions in order to prevent CVC with well timing.

At the same time existing scales of coronary risk stratification (Framingham, PROCAM, SCORE) do not take into account main pathogenetic mechanisms that connect obesity and CVC [3-7].

The aim of this study is to create probabilistic calculator for coronary atherosclerosis prognosis in patients with obesity.

Materials and methods

85 males of 38-65 years (average age 47,68±6,65 years) without clinical manifestations of stenocardia and atherosclerosis were included in this study. All patients had I-III grade obesity, body mass index (BMI) around 36,23±4,31 kg/m^2 and visceral obesity according with the epicardial fat tissue thickness (EFTS) >27 mm. Patients with severe concomitant diseases, diabetes mellitus 2 type (DM-2) and bad quality of echocardiography (EchoCG) visualization were excluded from this study.

During enrollment of the study we measured height and weight of patient, quantified BMI according with the formula (weight (kg)*height (m^2). When BMI was ⩾ 30 kg/m^2 patient was diagnosed with normal obesity. Total cholesterol (TC), triglycerides (TG), high density lipids cholesterol (HDLC), low density lipids cholesterols (LDLC) and glucose levels were measured in all patients. Lipoprotein A (LPA), apolipoprotein B (Apo B) and apolipoprotein A1 (apo A1) levels were measured with immune precipitation method. Leptin, adiponectin, resistin levels and interleukin-6 (IL-6) and tumor necrosis factor-α (TNFα) concentration in blood serum were identified using enzymoimmunoessay (EIE) kit (BioSource, Belgium). C-reactive protein (CRP) concentration was measured using highly sensitive latex-enhanced immune precipitation kit (Thermo Fisher Scientific, Finland). Epicardial fat tissue thickness was estimated with transthoracic EchoCG and Vivid 5 ultrasound machine (General Electrics, USA) with mechanical sector sensor 3,5 MHz. Three cardiac cycles in long parasternal position were registered. EFTS was measured behind free wall of the left ventricle in the end of systole. on the line that was maximally perpendicular to the fibrous ring of aortic valve used as an anatomic reference point [8, 9]. To estimate subclinical coronary atherosclerosis we performed selective coronaroangiography (CAG) with angiographic machine INNOVA 3100 (USA) or multislice computer tomography (MCT) of coronary arteries (CA) on Aquilion-64 ("Toshiba", Japan) tomography with the proceeding of data at the working station VITREA.

According with CAG and MCT results, we divided the patients with epicardial obesity into two groups: group 1 with the signs of coronary atherosclerosis (n=35) and group 2 (n=50) without signs of coronary atherosclerosis.

STATISTICA 10 and SPSS-21 software were used for statistical analysis. 0,05 was taken as the critical level of statistical significance during checking of the null hypothesis. Normality estimation for quantitative characteristics in compared groups was performed with Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistical values are present in the text of the article as M ± SD in case of characteristic's normal distribution, where M is an average value, SD – standard deviation, or as Med in case of not normal distribution. To compare central group parameters we used parametric and non-parametric methods: Student's T-test or Mann-Whitney U-test. To create the scale of coronary atherosclerosis prognosis and as a regression model we chose Regression with Optimal Scaling (CATREG) model that was performed with SPSS software.

Results

In order to analyze the relation between coronary atherosclerosis with possible predictors we made preliminary comparative analysis of two comparison groups: group I (n=35) and group II (n=50) in major and additional metabolic, neurohumoral risk factors (RF) and vascular inflammation markers that after were used in current study.

We defined the list of characteristics that had statistical relation with dependent variable – the presence of coronary atherosclerosis, and after formed the list of variables for regression analysis.

Thus, the list of possible predictors included: presence of arterial hypertension (AH), presence of carbohydrate metabolism abnormalities (impaired fasting hyperglycemia or impaired glucose tolerance (IGT)), TG, leptin, adiponectin and CRP. We performed receiving operating characteristic (ROC) analysis to define threshold levels of quantitative predictors and interval variables' reduction.

Optimal level of TG that was taken as a cut-off point was 1,8 mmol/mL(sensitivity 72%, specificity 66,7%), for leptin – 12,8 ng/mL (sensitivity 80%, specificity 64%).

Cut-off point for adiponectin was 10 μmol/mL (sensitivity 84%, specificity 45%), for CPR cut-off point was 5 mg/mL (sensitivity 64%, specificity 76%).

After obtaining cut-off points we made regression analysis with optimal scaling to estimate significance of predictors. These importance coefficients were chosen as weight values for creating the scale. For each one of 6 predictors included in regression model we quantified the points by multiplying absolute value of appropriate importance coefficient and 100 and its rounding to integer (Table 1).

Thus we created preliminary version of this risk scale (Table 1). We tested if the created regression model was adequate by binary logistical regression. The value of true classifications was 79,1%, that is considered high enough and indicates of good prognostic ability of this regression model.

Using this equation, we quantified theoretical values of subclinical coronary atherosclerosis presence probability for each patient. Dispersion diagram that reflects this relation is present at Image 1.

Optimal cut-off value for sum of points according with the results of ROC-analysis that allowed to divide the patients into two groups was 58 points. Thus, if the probability of coronary atherosclerosis is ⩾40%, its risk can be considered as high (Image 1).

To make this risk calculator easier to use we created its version for MS Excel, MS Office 2010 software (Table 2).

Table 1. **Regression analysis results of coronary atherosclerosis predictor significance estimation**

Predictor	Cut-off values	Standardized coefficients		p-value	Partial correlation coefficient	Importance coefficient	Points
		Beta	Standard error				
TG	⩾1.8	0.262	0.105	0.015	0.314	0.234	+23
Leptin	⩾12.8	0.240	0.147	0.107	0.213	0.246	+25
Adiponectin	⩽10.0	0.060	0.087	0.493	0.063	0.043	+4
CRP	⩾5.0	0.233	0.128	0.074	0.251	0.222	+22
AH	Present	0.189	0.089	0.039	0.233	0.126	+13
Carbohydrate metabolism abnormalities	Present	0.236	0.102	0.024	0.278	0.129	+13

Comment: Beta-coefficient reflects summarized impact of predictor on response value, partial correlation coefficient reflects independent impact of predictor on response value.

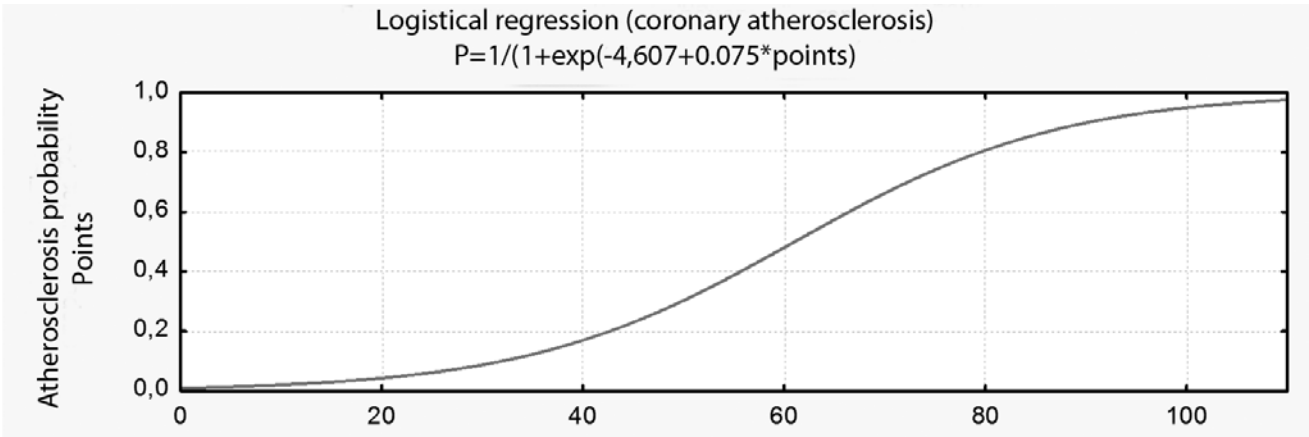

Image 1. Equation and logistic regression function plot that reflects the relation between the sum of points and probability of coronary atherosclerosis presence.

Table 2. **MS Excel interface of the risk calculator for sublinical coronary atherosclerosis prognosis**

A	B	C	D	F	G	H	I	J	K	M
Predictors	TG	Leptin	Adiponectin	CRP	AH	IGT	A0–4.607	B 0.075	Sum of ponts	P (%)
Cut-off values	⩾1.8	⩾12.8	⩽10.0	⩾5	1 (0)	1 (0)				
Weight points	23	25	4	22	13	13				
Patient's characteristic										

Comments: 1. RF information of each patient should be put to the cells of the table. 2. Probability of coronary atherosclerosis presence (%) would appear in «M» cell.

This calculator contains the data of logistical regression. Numerical characteristics of analyzed prognostic criteria for each patient should be put into this calculator and the value of prognostic risk would automatically appear in percentage format in the "M" cell of this table.

Discussion

In this study coronary atherosclerosis in clinically unsuspected patients with visceral obesity was verified in 35 (41%) of patients. In other studies it was identified that 61% of patients of morbid obesity group and BMI ⩾40 kg/m² without coronary heart disease (CHD) clinical manifestations (average age 50,4±10,0 years, BMI 43,8±4,8 kg/m²) had stenosis at least of one CA [10]. Another study that was made in Latin American population, where 88,7% of participants had obesity and 53,2% of participants had metabolic syndrome, identified carotid arteries atherosclerosis signs in 34,8% of cases according with the results of Doppler ultrasound scanning [11]. Patients with metabolic syndrome that was diagnosed according with the ATP III classification and without CHD clinical manifestations had CA calcinosis in 24,7% of cases [12].

In one of Russian studies atherosclerosis plaques were found in 35% of patients of 30-55 years with abdominal obesity [13].

In our study coronary atherosclerosis predictors that are appropriate for risk prognosis were: AH presence, carbohydrate metabolism abnormalities – impaired fasting hyperglycemia or IGT, TG, leptin, adiponectin and CRP.

The correlation between CRP levels and intima-media complex thickness in carotid arteries was found in one study [14]. Previously the connection between CRP and atherosclerotic lesions of CA and other peripheral arteries was demonstrated in another study [15]. It was also proved that CRP and oxidized LDLC have direct relation to inflammatory lesions of arteries in CHD [16]. Another study identified the association of proinflammatory marker IL-6 and CA calcinosis [17]. Leptin levels were associated with CA calcinosis independently from weight and other RF that proves proatherogenic role of leptin [18]. It is known that CRP is one of the main chronic inflammation markers and it participates directly in CA atherosclerosis progression [19]. One study demonstrated that visceral fat tissue stimulates CRP synthesis [20].

Patients with CHD and low adiponectin levels have more prominent atherosclerotic CA lesions according with CAG results comparing with the patients with higher concentrations of this protein [21]. Low adiponectin concentrations in combination with high IL-6 levels in patients with obesity and metabolic syndrome were associated with the risk of cardiovascular disease development, and the highest risk of DM-2 and CHD development was found in patients with the combination of low adiponectin and HDLC levels [22]. Low adiponectin concentration had positive correlation with the degree of CA calcinosis and asymptomatic stenosis that was identified with angiography technique in patients with DM-2 or without it [23].

Conclusions

Investigation of neurohumoral and proinflammatory activity of visceral fat tissue proved the connection of these factors and coronary atherosclerosis. At the same time visceral obesity degree, adipokines and proinflammatory markers still haven't been used in any scale of coronary risk estimation that reduces significantly the precision of cardiovascular risk evaluation in patients with obesity.

Probabilistic calculator of coronary atherosclerosis risk prognosis in patients with visceral obesity that have been created by the authors of this study allows to take into account main pathogenetic mechanisms that link obesity and coronary atherosclerosis. Evaluation of TG, leptin, adiponectin, CRP, presence of AH and carbohydrate metabolism disorders in every single patient with visceral obesity allows to predict the presence or absence of subclinical coronary artery atherosclerosis with the probability of 79,1%,

that is particularly important for early prophylaxis and prevention of disease progression.

Conflict of interest: None declared

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