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Anthropometric indices and their relationship with poor prognosis in patients with coronary artery disease and obesity

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Aim. To assess the association of anthropometric indices in patients with coronary artery disease (CAD) and obesity and to study their predictive value in the development of adverse cardiovascular events.

Material and methods. The study included 229 patients with CAD (median age, 55±7,56 years). Depending on the presence of obesity according to the World Health Organization criteria (1999), patients were divided into 2 groups. The 1st group included 107 obese patients, while the 2nd group — those without obesity (n=122). The groups were comparable in age. We measured waist (WC) and hip circumference (HC), followed by waist-to-hip ratio and body mass index calculation. The lipid profile parameters were determined by the enzymatic colorimetric method. During the study, the following indices were calculated: body mass index, visceral adiposity index, insulin resistance index, body shape index (BSI), fasting triglyceride (TG)/plasma glucose index, waist-to-height ratio, lipid accumulation product, TG-to-high density lipoprotein cholesterol ratio.

Results. During the follow-up period, adverse cardiovascular events in the 1st group of patients were found in 37 (34,5%) patients, while in the 2nd group, the composite endpoint was revealed in 12,3% of patients. In order to develop a model for predicting the risk of an unfavorable CAD course in obese patients, we performed a logistic regression analysis, which showed that the following were the most significant predictors of unfavorable cardiovascular outcomes: TG/glucose index and BSI.

Conclusion. Thus, of all the considered anthropometric indices, only two were associated with unfavorable CAD course — TG/glucose index and BSI. The data obtained indicate the validity of the search for novel useful obesity indicators with a good predictive value.

Keywords: coronary artery disease, obesity, anthropometric indices, body shape index.

Relationships and Activities. Fundamental research topic (state assignment № AAAA-A20-120041090007-8).

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The high prevalence of overweight and obesity is a global public health problem, and are the main risk factors for coronary artery disease (CAD) [1]. The World Health Organization (WHO) estimates that >1,3 billion adults worldwide are overweight and another 600 million are obese. Over the past 40 years, the number of obese people has tripled, and if the current trend continues, the number will reach one billion by 2025.

In the presence of obesity, the risk of CAD increases by 2-3 times, which is based on coronary atherosclerosis with the subsequent development of fatal cardiovascular events [2]. The higher incidence of cardiovascular disease (CVD) in obese patients appears to be associated with endothelial dysfunction and subclinical inflammation [3].

Adipose tissue is now considered as a key organ in relation to excess dietary fats, which specify whether the body will maintain normal homeostasis (metabolically healthy obesity) or a state of inflammation, insulin resistance, with adverse cardiovascular effects. Obesity, especially visceral one, causes changes in the structure and function of adipose tissue, which is currently considered as an endocrine organ interacting with vital organs and tissues, such as the brain, liver, skeletal muscles, heart, and blood vessels [4].

It is now well known that metabolic risk correlates with the degree of visceral adiposity, while subcutaneous fat is a source of protective adipokines [5].

Recent data suggest that clinical practice should also include new indexes such as waist-to-height ratio (WHtR), visceral adiposity index (VAI), body shape index (BSI), lipid accumulation product (LAP), triglyceride-fasting plasma glucose (TyG) index. These novel indices are expected to be more sensitive and specific than conventional parameters such as waist circumference (WC) and body mass index (BMI) and may significantly improve CVD risk stratification in obese patients [6].

The aim was to assess the association of anthropometric indices in CAD patients and obesity and to study their predictive value in the development of adverse cardiovascular events.

Material and methods

The study included 229 patients who were hospitalized with a diagnosis of CAD in the period from May 18, 2015 to February 2, 2017 (median age, 55±7,56 years). Depending on the presence of obesity according to WHO criteria (1999), patients were divided into 2 groups. Group 1 included 107 obese patients, while group 2 — 122 non-obese patients. There were following inclusion criteria: CAD, indications for scheduled revascularization (stenting). Exclusion criteria included acute coronary or cerebrovascular events within prior 6 months, uncontrolled hypertension, cancer, hematological and immune diseases, acute inflammatory diseases. The groups were comparable in terms of age composition, myocardial infarction

Table 1

Clinical and demographic characteristics of patients

Parameter	Group 1 (with obesity), n=107	Group 2 (without obesity), n=122
Male/female	77/30	118/4
Age, years	54 (51; 60)	58 (52; 64)
WC, cm	102 (95; 112)	102 (98; 108)
HC, cm	100 (93; 109)	98 (95; 105)
WHR	1,03 (1,02; 1,05)	1,04 (1,03; 1,05)
BMI, kg/m^2	31 (29; 34)	29 (27; 32)
Obesity, n (%)	70 (65%)	44 (36%)
Prior myocardial infarction, n (%)	65 (61%)	78 (64%)
Recurrent myocardial infarction, n (%)	9 (8%)	10 (8%)
Atrial fibrillation, n (%)	11 (10%)	7 (6%)
Hypertension, n (%)	106 (99%)	117 (96%)
Diabetes, n (%)	71 (66%)	46 (38%)
Smoking, n (%)	48 (45%)	61 (50%)
Positive family history for CVD, n (%)	43 (40%)	50 (41%)
GFR (CKD-EPI): ml/min/1,73 m^2	81 (74; 94)	84 (74; 96)

Note: data are presented as Me (Q25; Q75), n (%).

Abbreviations: BMI — body mass index, HC — hip circumference, WC — waist circumference, GFR — glomerular filtration rate, CVD — cardiovascular disease.

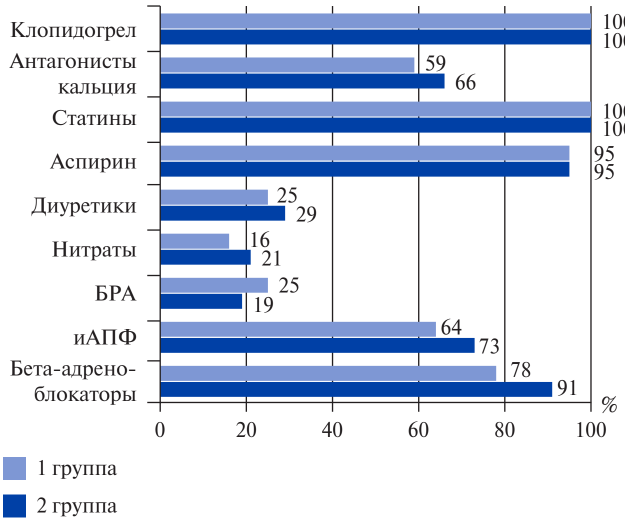

Figure 1. Drug therapy in the examined groups.

rate, comorbidities (Table 1). Drug therapy did not differ significantly between groups (Figure 1). Immediately before stenting, dual antiplatelet therapy was prescribed as follows: acetylsalicylic acid 75 mg, a loading dose of clopidogrel (600 mg/day), and then a maintenance dose of 75 mg/day at least 6-12 months after stenting.

All patients signed an informed consent to participate in the study and further prospective follow-up with data anonymization. The study was approved by the local ethics committee.

All patients underwent measurements of anthropometric parameters, including body weight (kg), height (m), WC (cm), hip circumference (HC) (cm), while waist-to-hip (WTH) ratio and BMI was calculated. The lipid profile parameters were determined by the enzymatic colorimetric method.

During the study, the following indices were calculated:

BMI = weight (kg)/(height (m))^2.

VAI was calculated using the followin formula:

(WC/(39,68 + (1,88 × BMI)) × (TG/1,03) × (1,31/HDL-C)) — for men,

(WC/(36,58 + (1,89 × BMI)) × (TG/0,81) × (1,52/HDL-C)) — for women.

Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) = fasting glucose (mmol/L) × fasting insulin (μIU/mL)/22,5. At a value >2,77, insulin resistance was diagnosed.

BSI was calculated as follows:

WC/BMI$^{2/3}$ × height$^{1/2}$.

TyG index (logarithmic ratio of TG levels and fasting plasma glucose) was calculated as followse: Ln (TG (mg/dL) × fasting plasma glucose (mg/dL)/2) [7].

WHtR=WC (cm)/height (cm).

LAP:

LAP for men = (WC (cm) — 65) × (TG (mmol/l)),

LAP for women = (WC (cm) — 58) × (TG (mmol/l)).

TG/HDL-C ratio was assessed in accordance with National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) III guidelines [8].

Statistical processing was carried out using the Statistica 10.0 and Medcalc 19.2.6 programs. Quantitative data were presented as Me (Q_{25}; Q_{75}) — median and interquartile range (Q_{25}; Q_{75} — 25th and 75th percentiles), while qualitative data — as absolute and relative frequencies (n (%)).

The Mann-Whitney U-test was used to compare quantitative variables, and the Fisher's exact test and χ^2 test were used to compare qualitative data. Differences between the compared variables were considered significant at p<0,05.

Logistic regression was used to create predictive models. Odds ratio (OR) and 95% confidence interval (CI) were used as a quantitative measure of the influence of studied factors on the outcome.

To determine possible predictors, a ROC analysis was performed with the construction of ROC curves, the calculation of area under the curve (AUC), the determination of Youden's cutoff point, as well as its sensitivity and specificity.

Results

The mean follow-up period was 15,1 (6; 23) months. There were no cases of major or minor bleeding during the study. During the follow-up period, adverse cardiovascular events in the 1st group were established in 37 (34,5%) patients. Three (2,8%) cases of sudden death were registered, 7 (6,5%) — acute coronary syndrome, including 3 (2,8%) myocardial infarctions. In addition, 16 (15%) patients underwent repeated revascularization due to coronary atherosclerosis progression, while 11 (10,3%) patients had a stent restenosis-related angina.

In group 2, composite endpoint was recorded at 12,3% (n=15). In 1 case (0,8%), cardiovascular death was recorded due to heart failure progression and cardiac arrest. Some patients noted the recurrence of angina pectoris (n=14). However, angiographically confirmed stent restenosis was detected in 9 patients. One patient (0,8%) had a stroke.

In the group of obese patients, higher values of BMI, VAI, WHtR, TyG index, BSI, and LAP were found compared with group 2 patients (Table 2).

In order to develop a prediction model for unfavorable CAD course in obese patients, a logistic regression] was performed. The most significant predictors of adverse cardiovascular outcomes were the following parameters:

Table 2

Comparative characteristics of metabolic indices

Parameter	Group 1 (with obesity), n=107	Group 2 (without obesity), n=122	p
BMI, kg/m²	32,81 (31,25; 35,17)	24,62 (23,37; 25,86)	<0,001
VAI	2,84 (2,26; 3,52)	1,18 (0,71; 1,57)	<0,001
WHtR	0,75 (0,58; 0,92)	0,64 (0,47; 0,75)	0,030
TG-to-HDL-C ratio	1,53 (0,93; 2,10)	3,78 (2,74; 4,82)	<0,001
TyG index	8,97 (8,60; 9,16)	9,78 (9,50; 9,96)	<0,001
BSI	0,03 (0,02; 0,26)	0,04 (0,01; 0,07)	0,020
LAP	59,32 (37,60; 77,70)	116,84 (89,30; 149,43)	<0,001

Note: data are presented as Me (Q25; Q75), n (%).
Abbreviations: VAI — visceral adiposity index, BMI — body mass index, LAP — lipid accumulation product index, BSI — body shape index, WHtR — waist-to-height ratio, TG — triglycerides, TyG index — triglyceride-glucose index, HDL-C — high-density lipoprotein cholesterol.

1) TyG index: Wald χ^2 test =6,764; p=0,009; -95% CI =-1,05; +95% CI =-0,144. OR =0,550; χ^2 for the whole model =7,127; p=0,008; B0=5,315; B=-0,597.

2) WHtR: Wald χ^2 test =4,155; p=0,042; -95% CI =1,187; +95% CI =2716; OR =0,550; χ^2 for the whole model =4,332; p=0,037; B0=-3,387; B=5,188.

3) BSI: Wald χ^2 test =7,382; p=0,007; -95% CI =1,902; +95% CI =56,7; OR =10,3; χ^2 for the whole model =7,879; p=0,005; B0=-7,808; B=295,737.

Logistic regression allows not only to determine the predictors, but also to build a predictive model that takes into account several parameters. Taking into account that one prognostic model cannot include statistically related traits, before creating a mathematical model with more than one predictor, we tested predictors for collinearity by revealing correlations and associations between traits.

Correlation analysis showed that the WHtR correlates with the TyG index and BSI, so this index cannot be combined with these indices into one model (Table 3).

Therefore, the prognostic model included 2 predictors — TyG index and BSI. Next, the probability of belonging to a group of unfavorable or favorable CAD course was assessed as follows:

$$P=\frac{e^y}{1+e^y},$$

where p is probability of lethal outcome, e — a mathematical constant equal to 2,72 (exponent), y — natural logarithm.

Table 3

Spearman's rank correlations

	TyG index	WHtR	BSI
TyG index	1,000000	0,256135*	-0,113857
WHtR	0,256135*	1,000000	0,287733
BSI	-0,113857	0,287733*	1,000000

Note: * — p<0,05.
Abbreviations: BSI — body shape index, WHtR — waist-to-height ratio, TyG index — triglyceride-glucose index.

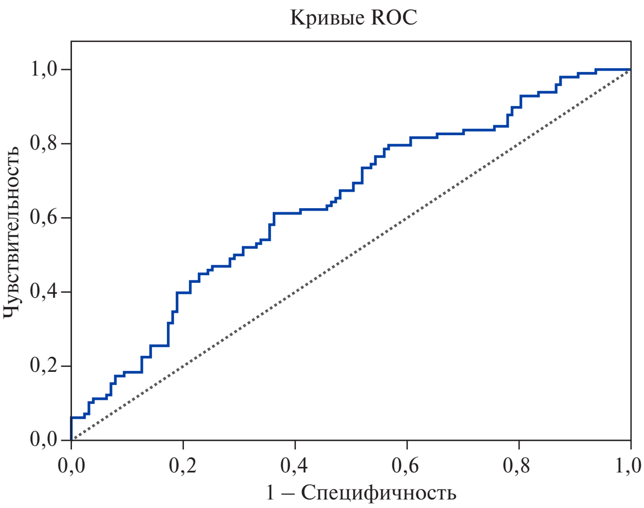

Figure 2. ROC-curve for predicting the risk of adverse cardiovascular events.

Table 4

Logistic regression results: OR

Variables	Equation coefficients	OR	p	χ^2 for whole model	p for whole model
X_1 — TyG index	B_1=-0,564	0,159	0,016	14,002	0,001
X_2 — BSI	B_2=279,070	9,102	0,011		

Abbreviations: BSI — body shape index, OR — odds ratio, TyG index — triglyceride-glucose index.

Discriminant function was determined as follows: y=B0-B1*TyG index+B2*BSI,
where B0 is a constant equal to -2,118; B1 is the coefficient of the equation, equal to 0,564; B2 is the coefficient of the equation, equal to 279,07.

The regression model parameters are presented in Table 4.

Thus, we got the following equation:
y=-2,118-0,564*TyG index+279,07*BSI.

At a p>0,366, a high risk of unfavorable outcome is predicted. The performed ROC analysis showed AUC of 0,639 with a sensitivity of 86,1% and a specificity of 39,4% at a cut-off of 0,366 (Figure 2).

Discussion

This study confirmed that obesity is an important risk factor for adverse cardiovascular events in CAD patients. It was found that the TyG index, WHtR and BSI were most associated with these events. It should be noted that only 2 indices (TyG index and BSI) were included in the multifactorial model, while BMI and VAI were not included in the model.

BSI is a novel index proposed in 2012 by Krakauer NY, et al. [5]. BSI was developed to quantify the risk associated with abdominal obesity (ratio of WC to height and BMI). The United States National Health and Nutrition Examination Survey (NHANES) showed that BSI has a stronger relationship with CVD, cancer, and all-cause mortality, regardless of age, sex, and body weight, compared with traditional anthropometric parameters [9]. In a cohort of Spanish men, BSI also showed its prognostic value in relation to cardiovascular risk prediction, in contrast to women, in whom the WC had higher predictive value [10].

Several studies have confirmed the practical value of BSI [11, 12].

Recently, data have appeared that the TyG index has an advantage for use in clinical and epidemiological studies due to its high availability and inexpensive biochemical markers required for calculation [13]. It has been established that this index can be used to identify subjects at risk of type 2 diabetes [14]. In addition, recent results have demonstrated a positive correlation between the TyG index and the frequency of cardiovascular events [15].

A Chinese study showed that rural residents with a higher TyG index had an increased risk of type 2 diabetes [16].

BSI and TyG index are currently practically not used by Russian specialists for the diagnosis of obesity. Our results indicate that these indices can be easily applied in routine practice. Thus, BSI and TyG index can be useful tools in everyday clinical practice to assess the risk of type 2 diabetes related to abdominal obesity.

Conclusion

Of all the considered anthropometric indices, only two were associated with unfavorable CAD course — TyG index and BSI. The data obtained indicate the validity of the search for novel useful obesity indicators with a good predictive value.

Relationships and Activities. Fundamental research topic (state assignment № AAAA-A20-120041090007-8).

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