MEDICAL AND BIOLOGICAL ASPECTS RELATED TO ASSESSMENT OF IMPACTS EXERTED BY RISK FACTORS

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Research article

INFORMATIVE VALUE OF TWO OBESITY MARKERS, BODY MASS INDEX (BMI) AND LIPID ACCUMULATION PRODUCT (LAP), FOR ASSESSING ATHEROGENIC RISKS IN LIPID PROFILE: COMPARATIVE ANALYSIS

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The obesity epidemic is a global concern nowadays since obesity is a major risk factor that can cause many serious diseases. A high risk of developing diseases in an obese person primarily occurs due to metabolic disorders. As a rule, dyslipidemia acts as an early sign of metabolic disorders in case of obesity.

Our research goal was to compare informative value of body mass index (BMI) and lipid accumulation product (LAP) for assessing atherogenic risks in lipid profile.

Two thousand and four hundred people aged 20–60 years took part in our study. We determined participants' anthropometric and clinical indicators and estimated lipid levels in blood serum.

As expected, LAP values had a strong correlation with BMI values. Spearman's rank correlation coefficient for LAP and BMI values amounted to 0.73 (< 0.001) in men (n = 1168) and 0.77 (< 0.001) in women (n = 1232). However, when we estimated agreement between these two indicators using Cohen's Kappa coefficient, we established that this agreement between LAP and BMI values was rather low (0.35 for men and 0.39 for women). Having compared samplings with quartiles that differed as per LAP and BMI values, we detected that lipid profiles tended to be more atherogenic in people with LAP values being higher than BMI values.

Given this established discordance in the quartiles, higher LAP values are associated with atherogenicity of lipid profile to a greater extent than values of BMI, the conventional obesity indicator. Using solely BMI to diagnose obesity may result in underestimating metabolic disorders in the body. To assess obesity and metabolic health correctly, it is advisable to determine LAP value together with traditional obesity indexes.

Keywords: *lipid accumulation product (LAP), body mass index (BMI), obesity, markers, waist circumference, triglycerides, atherogenicity, metabolism.*

At present, a great variety of indexes is used to assess obesity. These indexes primarily rely on anthropometric parameters and the best examples here are body mass index (BMI) [1], waist-to-height or waist-to-hip ratio [2], conicity index (CI) [3], abdominal volume index (AVI) [4], body adiposity index (BAI) [5], a body shape index (ABSI) [6] and many others. In addition, several combined indexes have been developed recently. Such indexes include not only anthropometric components but also biochemical indicators, primarily those related to lipid metabolism. The most widely spread combined indexes are visceral adiposity index (VAI) [7], cardiometabolic index (CMI) [8] and lipid accumulation product (LAP) [9].

Despite all this variety of indexes, Quetelet index, which is usually called BMI, remains the most widely used one. A for-

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mula to calculate it was developed by Adolphe Quetelet, a Belgian scientist, in 1832. More than a century later, A. Keys with colleagues from the Minnesota University made the index applicable for population studies and gave it a new name, BMI [1]. BMI evaluates a ratio of a person's weight to his or her height thereby giving an opportunity to conclude whether a person has underweight, normal weight or overweight. In 1997, the World Health Organization (WHO) developed the obesity classification as per BMI and recommended using it to assess risks of obesity-related diseases [10]. However, the classification the WHO offers to use has certain drawbacks. Thus, it does not consider sex, age and obesity phenotype. Recently, more research data have become available indicating that BMI does not provide sufficient information to determine health risks properly. This has motivated experts to try developing combined obesity indexes that would include both anthropometric parameters and biochemical indicators. LAP is the simplest to calculate among all combined indexes.

LAP as an obesity index was first introduced in 2005. It combines an anthropometric parameter and a biochemical indicator, namely, waist circumference and triglyceride concentration in blood. They reflect amounts of accumulated fat and circulating fat in the body accordingly [9]. Multiple studies have shown that LAP can be used to predict cardiovascular pathologies and to diagnose metabolic diseases [11–19].

Our research goal was to compare informative value of body mass index (BMI) and lipid accumulation product (LAP) for assessing atherogenic risks in lipid profile.

Materials and methods. There were 2400 participants in our study (1168 men and 1232 women aged 20–60 years). We measured participants' anthropometric parameters (height, weight, and waist circumference). Height and weight were measured with a standard height meter and scales in a standing position; a participant did not wear outer clothing or footwear during measuring. BMI was calculated as per the following formula: BMI (kg/m^2) = weight (kg) / height $(m)^2$. Waist circumference was measured with a centimeter band.

Blood for biochemical analysis was taken from the ulnar vein into vacutainers; it was done in the morning on an empty stomach. We determined triglycerides, total cholesterol and high-density lipoprotein cholesterol (HDL-C) in blood serum. The test results were used to calculate the following:

♦ atherogenicity coefficient:

AC = (total cholesterol – HDL-C) / HDL-C;

♦ non-HDL-C:

non-HDL-C = total cholesterol – HDL-C;

♦ atherogenic index of plasma (AIP):

AIP = (log [triglycerides / HDL-C]) [20].

LAP index was calculated as per the following formulas:

♦ for men: LAP = (waist circumference – 65) × triglycerides;

♦ for women: LAP = (waist circumference – 58) × triglycerides [9].

All the results were statistically analyzed with MedCalc 19.5.1 software package (MedCalc Software Ltd, Belgium). Quantitative data in the tables are given as median, 25^{th} and 75^{th} percentiles; qualitative data are given as *n* (%). We assessed significance of differences between groups with Mann – Whitney test and used Spearman's rank correlation coefficient to reveal any correlations between indicators. To assess agreement between indicators, we calculated Cohen's Kappa coefficient.

Results and discussion. Overweight and obesity are a threat for health as they create elevated risks of several diseases caused by metabolic disorders. In comparison with traditional anthropometric parameters, LAP has a certain advantage since it simultaneously reflects both anatomic and biochemical outcomes of obesity and provides an opportunity to estimate how fat is distributed in the body and to reflect functional state of fat tissues.

Table 1

Anthropometric parameters and biochemical indicators in participants

Indicator	Men, n = 1168		Women, n = 1232		p
	Median (25 %; 75 %)	Minimum – maximum	Median (25 %; 75 %)	Minimum – maximum	
Age, years	42.0 (32.0; 50.0)	20.0–60.0	41.0 (32.0; 49.0)	20.0–60.0	0.437
Weight, kg	76.0 (69.0; 85.3)	44.0–150.0	66.0 (59.0; 76.0)	43.0–135.0	**<0.001**
Height, cm	175.0 (170.0; 180.0)	140.0–196.0	163.0 (158.0; 166.0)	141.0–184.0	**<0.001**
Waist circumference, cm	84.0 (78.0; 91.0)	66.0–136.0	77.0 (70.0; 88.0)	59.0–138.0	**<0.001**
BMI, kg/m^2	25.1 (22.9; 27.9)	16.4–46.7	25.3 (22.3; 28.8)	16.7–50.0	0.908
LAP, cm·mmol/l	23.0 (12.4; 40.8)	0.5–221.3	20.3 (9.7; 42.3)	0.4–262.2	**0.013**
Total cholesterol, mmol/l	5.41 (4.65; 6.32)	2.36–11.07	5.28 (4.51; 6.14)	1.65–14.24	**0.009**
Triglycerides, mmol/l	1.24 (0.90; 1.72)	0.40–9.50	1.06 (0.77; 1.55)	0.40–9.99	**<0.001**
HDL-C, mmol/l	1.23 (1.10; 1.34)	0.60–1.98	1.27 (1.13; 1.39)	0.58–2.42	**<0.001**
non-HDL-C, mmol/l	4.19 (3.43; 5.09)	1.17–10.11	4.01 (3.29; 4.84)	0.48–12.99	**<0.001**
Atherogenicity coefficient	3.41 (2.78; 4.22)	0.94–10.60	3.19 (2.55; 3.89)	0.41–10.39	**<0.001**
AIP	0.01 (-0.14; 0.16)	-0.52–0.96	-0.07 (-0.21; 0.09)	-0.51–0.83	**<0.001**

We detected significant differences between men and women as per almost all the analyzed indicators, apart from age and BMI (Table 1). All the indicators, HDL-C excluded, were higher in men than in women.

LAP values varied within quite a wide range in both men and women (from 0.5 to 221.3 cm·mmol/l in men and from 0.4 to 262.2 cm·mmol/l in women). However, having analyzed how the data were distributed, we established that the distribution was obviously left-handed (Figure). LAP values in 75 % of both men and women varied within a range from 0.4 to 40 cm·mmol/l. Average LAP values in men and women equaled 23.0 (12.4; 40.8) and 20.3 (9.7; 42.3) cm·mmol/l accordingly (Table 1).

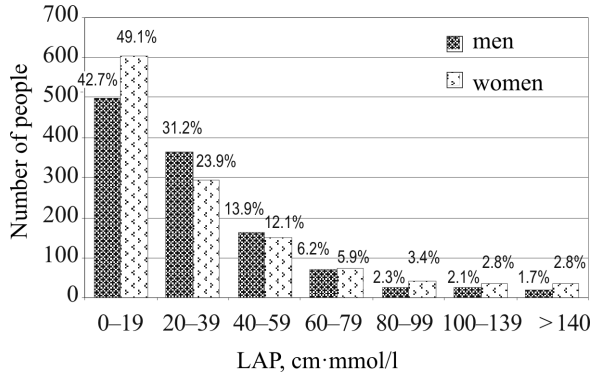

Figure. Distribution of LAP values in men (n = 1168) and women (n = 1232)

The established wide range of LAP values that amounted to 220.8 cm·mmol/l in men and 261.8 cm·mmol/l in women occurs due to its calculation being based on two indicators that have different dimensions (waist circumference and triglyceride concentration). The produced results correspond to data available in literature [16, 21–24]. The greatest range of LAP values was mentioned in a study by M. Bozorgmanesh with colleagues where it amounted to 569.64 cm·mmol/l in men and 619.83 cm·mmol/l in women [16]. Left-handed distribution of LAP values is in line with the data from our previously published study that concentrated on varying peculiarities, sex-related differences and age dynamics of LAP values in practically healthy people [24]. However, boundaries of a range within which LAP values varied turned out to be significantly lower in practically healthy people than the boundaries established in the present research where we did not exclude participants with diseases. The latter was due to the study design aimed at detecting any correlations between obesity indexes and lipid metabolism disorders.

LAP values had strong correlations with BMI values as confirmed by Spearman's rank correlation coefficient between LAP and BMI values. It amounted to 0.73 in men (< 0.001) and 0.77 in women (< 0.001). This strong correlation occurs due to BMI values being dependent on waist circumference value, which is also used to calculate LAP. Obviously, when body weight grows, its circumferences

also increase. According to data available in literature, there is a strong correlation (higher than 0.80) between BMI values and waist circumference. It is especially true for heterogeneous groups including both lean people and patients with obesity [25, 26]. Still, profound data analysis reveals that there can be a wide range of waist circumference values for each specific BMI value. Accordingly, people with the same BMI value but different waist circumference values can face substantially different risks of developing metabolic and cardiovascular disorders [26].

We estimated agreement between LAP and BMI values using Cohen's Kappa test. The estimation indicated that the agreement was rather low between them (Table 2). Quartiles of these two indicators were in agreement only for a half of the examined men and women (52 % and 54 % accordingly). Levels of this agreement in both men and women were higher (16–17 %) in the extreme quartiles and lower (9–11 %) in the middle ones.

Comparison between the samples with quartiles differing as per LAP and BMI values indicated that people with LAP values being higher than BMI values tended to have more atherogenic lipid profile (Table 3). Men who had disproportionately high LAP values against BMI values had significantly higher levels of total cholesterol and non-HDL-C and higher atherogenicity coefficient but HDL-C levels were the same in both groups under comparison. All the cholesterol metabolism indicators were significantly higher among women with LAP values being higher than BMI values. The established differences in triglyceride levels and AIP in the examined people occur due to a specific design used to create the compared groups.

A stronger association between high LAP values and lipid profile atherogenicity in comparison with BMI occurs due to this index is calculated using not only an anthropometric parameter (waist circumference) but also a biochemical indicator (triglyceride concentration). Thus, LAP indicates not only that a person is overweight but also that there is a risk of developing metabolic disorders. According to data available in literature, LAP values have a positive correlation with levels of total cholesterol, apolipoprotein-B and free fatty acids and a negative correlation with HDL-C concentrations. LAP values have also been established to be associated with quantity and size of high and low density lipoproteins [28].

An advantage that LAP has over BMI in predicting risks of metabolic and cardiovascular diseases has been outlined in multiple studies [14, 15, 29–31]. The reason for this advantage is that BMI describes only generalized obesity whereas waist circumference values used to calculate LAP reflect abdominal obesity. Meanwhile, simple measuring of waist circumference does not give a possibility to

Table 2

Agreement between quartiles of LAP and BMI values in men and women

Sex	Indicator	BMI, *n* (%)				Agreement as per Cohen's Kappa test (95 % CI)
	LAP	quartile 1	quartile 2	quartile 3	quartile 4	
Men, *n* = 1168	quartile 1	**192 (16.4)**	74 (6.3)	24 (2.1)	2 (0.2)	low, 0.35 (0.32–0.39)
	quartile 2	77 (6.6)	**108 (9.2)**	72 (6.2)	35 (3.0)	
	quartile 3	21 (1.8)	80 (6.8)	**119 (10.2)**	72 (6.2)	
	quartile 4	2 (0.2)	30 (2.6)	77 (6.6)	**183 (15.7)**	
Women, *n* = 1232	quartile 1	**206 (16.7)**	79 (6.4)	23 (1.9)	0 (0)	low 0.39 (0.35–0.42)
	quartile 2	78 (6.3)	**135 (11.0)**	80 (6.5)	15 (1.2)	
	quartile 3	17 (1.4)	73 (5.9)	**124 (10.1)**	94 (7.6)	
	quartile 4	7 (0.6)	21 (1.7)	81 (6.6)	**199 (16.2)**	

N o t e : Values of Cohen's Kappa test vary from 0 to 1 and show agreement between two variables. Agreement may vary from insignificant (from 0.0 to 0.20), low (from 0.21 to 0.40) and moderate (from 0.41 to 0.60) to significant (from 0.61 to 0.80) and almost ideal (from 0.81 to 1.00), according to J.R. Landis and G.G. Koch [27].

Table 3

Baseline characteristics in men and women with discordant quartiles as per LAP and BMI values

Indicator	Men		*p*	Women		*p*
	BMI quartile > LAP quartile, *n* = 279	BMI quartile < LAP quartile, *n* = 287		BMI quartile > LAP quartile, *n* = 291	BMI quartile < LAP quartile, *n* = 277	
	Median (25 %; 75 %)	Median (25 %; 75 %)		Median (25 %; 75 %)	Median (25 %; 75 %)	
Age, years	44.0 (33.0; 51.0)	42.0 (34.0; 50.0)	0.598	40.0 (31.0; 48.5)	44.0 (37.0; 50.0)	**<0.001**
Weight, kg	79.0 (74.0; 88.0)	74.0 (68.0; 80.0)	**<0.001**	71.0 (64.0; 78.0)	62.0 (56.0; 69.0)	**<0.001**
Height, cm	173.0 (169.0; 178.0)	176.0 (170.0; 180.0)	**<0.001**	162.0 (158.0; 166.0)	163.0 (158.0; 167.0)	0.115
Waist circumference, cm	85.0 (78.0; 91.0)	84.0 (79.0; 88.0)	0.230	79.0 (70.0; 87.0)	77.0 (72.0; 85.0)	0.746
BMI, kg/m^2	26.5 (25.0; 28.6)	24.0 (22.4; 25.4)	**<0.001**	26.9 (24.6; 29.8)	23.7 (21.6; 25.8)	**<0.001**
LAP, cm·mmol/l	17.71 (10.23; 23.58)	31.20 (22.47; 46.69)	**<0.001**	16.0 (8.4; 26.9)	29.6 (18.4; 54.6)	**<0.001**
Total cholesterol, mmol/l	5.23 (4.58; 5.97)	5.78 (4.99; 6.63)	**<0.001**	5.03 (4.36; 5.94)	5.61 (4.93; 6.54)	**<0.001**
Triglycerides, mmol/l	0.89 (0.70; 1.12)	1.72 (1.38; 2.25)	**<0.001**	0.77 (0.61; 0.97)	1.60 (1.15; 2.17)	**<0.001**
HDL-C, mmol/l	1.24 (1.08; 1.34)	1.24 (1.11; 1.34)	0.498	1.25 (1.13; 1.36)	1.30 (1.17; 1.46)	**<0.001**
non-HDL-C, mmol/l	4.00 (3.36; 4.76)	4.49 (3.76; 5.46)	**<0.001**	3.82 (3.12; 4.62)	4.27 (3.59; 5.20)	**<0.001**
Atherogenicity coefficient	3.34 (2.76; 3.99)	3.66 (3.07; 4.47)	**<0.001**	3.02 (2.48; 3.75)	3.26 (2.61; 4.08)	**0.012**
AIP	-0.14 (-0.24; -0.02)	0.15 (0.05; 0.28)	**<0.001**	-0.21 (-0.31; -0.10)	0.08 (-0.04; 0.25)	**<0.001**

differentiate visceral and subcutaneous fats; this drawback, however, is compensated with introducing triglyceride levels into the formula since these levels are associated with visceral fat tissue. It is excessive visceral fat that induces a cascade of metabolic disorders leading to dyslipidemia, hyperglycemia, hyperinsulinemia and insulin resistance [32].

Many researchers admit that BMI is useful in population studies due to being widely recognized as a screening tool to detect obesity. However, its use at an individual level has rather limited prognostic value. BMI is a good diagnostic instrument for revealing obesity when its values are high but as some studies have revealed people with average BMI values are a heterogeneous group regarding fat contents in the body. Another established point is that excessive visceral fat content is associated with metabolic regulation disorders regardless of body mass [33]. In this case, LAP can become a useful tool applied in clinical practice to detect and predict personified risks of metabolic disorders.

Conclusion. Obesity is a global concern nowadays since it creates elevated risks of many serious diseases. Adverse effects produced by obesity on health are primarily associated with concomitant metabolic diseases. It is necessary to detect metabolic disorders as early as possible and to apply correction therapy in due time in order to prevent negative outcomes of obesity for the body. Our research results indicate that LAP as an up-to-date index to estimate obesity has certain advantages over traditional BMI when it comes to detecting atherogenic changes in lipid profile. Developing atherogenic disorders in case of obesity result from

dysfunction of visceral fat tissue. If LAP is introduced into clinical practice as a complex indicator showing functional state of visceral fat tissue, this will bring about substantial improvements in diagnostics and assessing risks of metabolic disorders associated with obesity.

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