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Original Research

Association of atherogenic indices with metabolically unhealthy obesity phenotype

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Abstract

Background and Aims: Obesity is a risk factor for diabetes and cardiovascular disease. Clinical studies have identified two subtypes of obesity: metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUHO), the latter being associated with an increased risk of mortality from any cause or cardiovascular (CV) events. Therefore, for better phenotyping, several atherogenic indices such as atherogenic index and lipid accumulation product have been used that can be calculated at the routine control in order to detect people at high cardiovascular risk. **Materials and Methods:** This was a retrospective study. A total of 163 obese participants (n = 118 metabolically unhealthy subjects with a mean ± SD body mass index (BMI) of 37.8 ± 5.7 kg/m²) took part in this study. Body composition was assessed by electrical bioimpedance; fasting blood glucose, lipid profile, creatinine, transaminases and serum insulin were obtained using standard protocols. **Results:** The frequency of metabolic syndrome was 72.8%. Patients with MUHO were significantly older, with a higher weight, BMI, waist circumference and waist-hip ratio compared to MHO. All atherogenic indices were statistically significantly higher in patients with MUHO. **Conclusions:** We described several clinical parameters that are accessible in medical offices, which can help the clinician in better phenotyping and identifying MUHO, in order to implement preventive measures to reduce cardiovascular risk.

Keywords: electrical bioimpedance, insulin resistance, metabolic syndrome, phenotyping

Background and Aims

Obesity has reached epidemic proportions and according to the World Health Organization (WHO), worldwide, over 650 million adults were obese in 2016 [1]. It is well-known that obesity is an independent risk factor for type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) [2, 3]. Clinical studies have identified two obesity phenotypes: "metabolically healthy obesity" (MHO), which includes obese persons with a lower risk of metabolic complications, and "metabolically unhealthy obesity" (MUHO), a group with an increased risk for all-cause mortality or cardiovascular (CV) events [4]. The concept of metabolic health has been recommended since 2000, especially to identify patients with obesity and insulin sensitivity [5]. To date, there is no clear definition of MHO. Therefore, according to the literature, depending on the parameters used, MHO prevalence ranges from 6% to 75% [6]. The most often used definition is the absence of any metabolic disorder and CV disease in patients with a body mass index (BMI) ≥30 kg/m² [7].

Also, some metabolic health definitions include insulin resistance indices, inflammatory markers, or cardiorespiratory fitness [8]. Regarding the pathophysiology of metabolic syndrome, it can be classified into 5 subtypes: lipid dominant, vascular dominant, adiposity dominant, insulin resistance dominant, and other risk factors [9].

For a better assessment of obesity phenotypes, and also to predict the risk of CVD, clinical studies have tried to introduce different indices that can be calculated with routinely assessed parameters. These parameters can be considered a plus in the daily practice of the clinician. Lipid accumulation product (LAP) is one of the validated markers of visceral obesity, and the atherogenic index (AI) can be used as a marker in the diagnosis of subclinical atherosclerosis [10, 11]. High levels of non-HDL cholesterol are associated with an increased risk of heart disease. Non-HDL cholesterol to HDL cholesterol (non-HDL-C/HDL-C) ratio is a suitable predictor for metabolic syndrome, insulin resistance, coronary heart disease, and non-alcoholic steatohepatitis (NASH) [12]. Also, total cholesterol/HDL-cholesterol ratio is correlated with ischemic heart disease risk [13]. LDL-C/HDL-C ratio can predict the progression of intima-media thickness (IMT) better than HDL-C or LDL-C alone [14]. Hypertensive waist (HW) is a concept of combination of clinical risk factors that could predict the presence of metabolic syndrome [15]. Although many studies have shown the association of the above mentioned indices with mortality and CVD, few studies have investigated them according to the obesity phenotype.

In this context, the objective of this research was to compare the atherogenic indices in MUHO and MHO and to assess their association with the MUHO phenotype.

Materials and Methods

This was a retrospective study in which were collected data from patients presenting for nutritional assessment in a private clinic. The participants included in this analysis presented for nutritional assessment and counseling for obesity (BMI ≥30 kg/m^2), age ≥18 years, and available laboratory investigations for plasma glucose, lipid profile, and insulinemia. The exclusion criteria included a previous diagnosis of diabetes mellitus and pregnancy. The final sample for the current analysis consisted of 163 obese participants fulfilling the inclusion criteria, without any exclusion criteria. The study followed the guidelines set by the Declaration of Helsinki.

Data collected and measurements

From patients' medical charts, data on age, gender, anthropometric parameters (weight, height, waist circumference, hip circumference), results of body composition analysis, results of laboratory investigations for plasma glucose, lipid profile, and insulinemia were collected. The BMI was calculated as weight (kg)/ square of height (m), and the waist-hip ratio (WHR) as waist circumference/hip circumference [16]. The body composition analysis was performed by bioelectrical impedance analysis using an InBody 720 device (Biospace Co., South Korea). The parameters evaluated by bioelectrical impedance analysis were visceral fat area, percentage of body fat, skeletal muscle mass, and body fat mass (BFM). Plasma glucose, lipid profile (total cholesterol and HDL cholesterol, serum triglycerides [TG]), and insulinemia were assessed in fasting conditions in the institution's laboratory using a fully automated analyzer (Cobas Integra 400 Plus, Roche). In those with TG levels below 400 mg/dL, LDL cholesterol was calculated using the Friedewald formula: *total cholesterol–HDL cholesterol–TG/5*. Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR) formula = (*fasting insulin [μUI/mL] × fasting plasma glucose [mg/dL]*)/405. Metabolic syndrome (MS) was defined according to the International Diabetes Federation (IDF) criteria [17]. HTW was defined as the concomitant presence of systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg or a personal history of treated hypertension and the presence of an abdominal circumference ≥80 cm in women and ≥94 cm in men [15]. The following atherogenic indices were calculated: non-HDL cholesterol,

lipid accumulation product (LAP), atherogenic index (AI), total cholesterol/HDL cholesterol ratio, LDL cholesterol/HDL cholesterol ratio, and non-HDL cholesterol/HDL cholesterol ratio. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. LAP was calculated using the sex-specific formulas proposed by Kyrou et al.: *[Waist circumference (cm) – 65] × [TG (mmol/L)] for men and [Waist circumference (cm) – 58] × [TG (mmol/L)]* for women [18]. AI was assessed as *log [TG/HDL cholesterol]* [19].

The participants were classified into 2 cardiometabolic phenotypes based on the presence of metabolic syndrome: MHO (BMI ≥30 kg/m^2 and no metabolic syndrome) and MUHO (BMI ≥30 kg/m^2 plus metabolic syndrome).

Statistical analysis

For statistical analysis, SPSS-PC 20.0 (SPSS Inc., Chicago, IL, USA) was used. Data were presented as means and standard deviation for continuous variables with normal distribution, as median (quartile 1; quartile 3) for continuous variables with non-normal distribution, and as number (percentage) for categorical variables. To compare the variables between the MHO and MUHO groups, we used the Student t-test and the median test for continuous variables, and the chi-square test for frequencies. Unadjusted and adjusted logistic regression in the whole sample was employed to assess the variables associated with the presence of MUHO in our sample. A p value below 0.05 was statistically significant.

Results

This study evaluated 83 women and 80 men, with a mean age of 38.1 ± 11.2 years, a mean BMI of 37.2 ± 5.5 kg/m^2, and a mean visceral fat area (VFA) of 168.0 ± 46.6 cm^2. The frequency of metabolic syndrome was 72.8% and that of HW, 46.6%. Of the whole sample analyzed, 118 patients (72.4%) had MUHO. This phenotype was more frequent among men than women (p = 0.005). Patients with MUHO were significantly older and had a significantly higher weight, waist circumference, and WHR than those with MHO (p < 0.001 for all). For the lipid profile, as compared to patients with MHO, those with MUHO had lower HDL cholesterol levels (50.2 mg/dL vs. 40.8 mg/dL, p < 0.001) and higher triglycerides (102.0 mg/dL vs. 170.0 mg/dL, p < 0.001); no difference between groups was observed for total and LDL cholesterol. Also, patients with MUHO had significantly higher fasting plasma glucose (p < 0.001), fasting insulinemia (p = 0.016), HOMA-IR (p = 0.016), VFA (p = 0.002) (Table 1).

All atherogenic indices assessed were statistically significantly higher in patients with MUHO compared to those with MHO. In patients with MUHO vs. those with MHO, LAP was 106.5 vs. 55.4; atherogenic index was 3.9 vs. 2.4 (Table 2).

In the unadjusted logistic regression analysis, all indices were statistically significantly associated with the presence of MUHO. Also, these indices remained associated with MUHO after adjustment for age, gender, visceral fat area and HOMA-IR (Table 3).

Discussion

The gold standard of modern medicine is precise medicine. As a rule of thumb mainly in clinical practice, detailed phenotyping is the first stage of diagnosis. Considering these remarks, it is important to update the status of biomarkers/indices used in obesity and metabolic syndrome, which can help clinicians to decipher the above conditions. In this sense, here, we aimed to provide more details on the relationship between different indices and MUHO, for a detailed phenotyping analysis and individualization of the therapeutic approach.

In our research, we identified a high frequency of MUHO and metabolic syndrome (72%). This frequency is higher than the prevalence reported in the PREDATORR study, where the age and sex-adjusted overall prevalence of MUHO was 3.9% and that of metabolic syndrome was 38.5% [20]. This difference can be explained by the characteristics of the samples included – a sample representative of the Romanian population in the PREDATORR study and a selected

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Table 1: Clinical, metabolic, and anthropometric characteristics.

	Total n = 163	MHO n = 45	MUHO n = 118	p value
Women, n (%)	83 (50.9%)	31 (68.9%)	52 (44.1%)	0.005
Age	38.1 ± 11.2	34.5 ± 10.5	39.5 ± 11.3	0.013
Weight, kg	110.1 ± 19.5	103.0 ± 18.4	112.9 ± 19.4	0.004
BMI (kg/m^2)	37.2 ± 5.5	35.9 ± 5.1	37.8 ± 5.7	0.052
Waist circumference (cm)	115.3 ± 13.4	109.0 ± 10.6	117.8 ± 13.7	<0.001
WHR	1.0 (1.0; 1.1)	1.0 (1.0; 1.0)	1.0 (1.0; 1.1)	0.015
Medical history				
CVD (%)	46 (28.2%)	10 (22.2%)	36 (30.5%)	0.335
DLP (%)	51 (31.3%)	5 (11.1%)	46 (39.0%)	0.001
HTW (%)	76 (46.6%)	1 (2.2%)	75 (63.6%)	<0.001
Metabolic syndrome	118 (72.4%)	0 (0.0%)	118 (100.0%)	<0.001
Total cholesterol (mg/dL)	189.0 ± 40.8	183.0 ± 31.6	191.4 ± 43.7	0.182
HDL cholesterol (mg/dL)	43.3 ± 14.7	50.2 ± 12.6	40.8 ± 14.7	<0.001
LDL cholesterol (mg/dL)	112.8 ± 36.9	110.8 ± 28.6	113.6 ± 39.7	0.629
Triglycerides (mg/dL)	146.0 (102.0; 203.0)	102.0 (81.9; 127.5)	170.0 (115.0; 239.0)	<0.001
Creatinine (mg/dL)	0.8±.01	0.9 ± 0.2	0.9 ± 0.2	0.154
TGO (U/L)	26.7 (21.8; 35.0)	27.0 (19.9; 33.0)	26.4 (22.0; 36.0)	1.000
TGP (U/L)	32.0 (22.8; 50.9)	36.0 (19.8; 50.8)	36.0 (19.8; 50.8)	0.720
Glycemia (mg/dL)	99.5 ± 15.5	89.8 ± 12.6	103.3 ± 15.0	<0.001
Insulinemia (μU/mL)	18.4 (12.0; 28.2)	14.9 (10.6; 26.6)	19.9 (12.5; 28.5)	0.016
HOMA-IR	4.6 (2.7; 7.0)	3.2 (2.4; 6.0)	5.1 (3.2; 7.3)	0.016
Insulin resistance	129 (79.1%)	31 (68.9%)	98 (83.1%)	0.054
VFA (cm^2)	168.0 ± 46.6	150.4 ± 41.5	174.9 ± 46.9	0.002
SMM (kg)	36.3 ± 7.7	33.2 ± 6.8	37.5 ± 7.7	0.001
BFM (kg)	45.1 ± 13.2	43.7 ± 12.8	45.8 ± 13.4	0.360

Note: BMI – body mass index, VFA – visceral fat area, SMM – skeletal muscle mass, BFM – body fat mass, WHR – waist-hip ratio, HOMA-IR – homeostasis model assessment-insulin resistance, LAP – lipid accumulation product.

Table 2: Atherogenic indices in the whole sample and in patients with and without metabolically unhealthy obesity.

	Total n = 163	MHO n = 45	MUHO n = 118	p value
Non-HDL cholesterol	145.6 ± 40.2	132.8 ± 29.6	150.0 ± 42.7	0.003
LAP	82.2 (57.7; 142.2)	55.4 (43.5; 69.1)	106.5 (68.7;162.1)	<0.001
Atherogenic index	3.5 (2.4; 4.8)	2.4 (2.1; 3.4)	3.9 (2.7; 5.2)	<0.001
Total cholesterol/HDL cholesterol	4.4 (3.4; 5.8)	3.4 (3.1;4.4)	4.9 (3.7; 6.2)	<0.001
LDL cholesterol/HDL cholesterol	2.5 (1.8; 3.7)	2.0 (1.7; 3.0)	2.9 (2.1; 3.9)	0.001
Non-HDL cholesterol/HDL cholesterol	3.4 (2.3; 4.8)	2.4 (2.1; 3.4)	3.7 (2.7; 4.9)	<0.001

Note: LAP – lipid accumulation product.

Table 3: Unadjusted and adjusted OR for atherogenic indices, lipid profile and body composition parameters as predictors of metabolically unhealthy obesity.

	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Non-HDL cholesterol	1.012 (1.003; 1.022)	1.012 (1.001; 1.022)
LAP	1.036 (1.021; 1.052)	1.036 (1.019; 1.052)
Atherogenic index	1.848 (1.370; 2.492)	1.837 (1.337; 2.525)
Total cholesterol/HDL cholesterol	1.848 (1.370; 2.492)	1.837 (1.337; 2.525)
LDL cholesterol/HDL cholesterol	1.549 (1.112; 2.139)	1.611 (1.132; 2.292)
Non-HDL cholesterol/HDL cholesterol	1.848 (1.370; 2.492)	1.837 (1.337; 2.525)

Note: *Adjusted for age, gender, visceral fat area, HOMA-IR. LAP – lipid accumulation product.

sample consisting of patients presenting for obesity counseling in our study. Also, in the PREDATORR study, prevalence was adjusted for age and sex, while in our sample we provide the crude prevalence.

Our study showed that MUHO participants were older and had a higher waist circumference and BMI compared to MHO subjects. This is in line with the observations in the Malmo diet cancer study, in which Korduner et al. found that MHO participants were younger, more likely to be men, had a lower BMI, and a lower waist and hip circumference [21]. It is well-known that waist circumference is a marker for cardiovascular risk and also for mortality and morbidity. A systematic review of >680,000 participants, with a follow-up of 24 years demonstrated that waist circumference was associated with increased all-cause mortality [6, 7]. In a consensus statement, the association between abdominal obesity and mortality of any cause, after adjustment according to BMI is highlighted [6]. A 10% larger abdominal circumference increases the risk of mortality 1.48 times. Nelms et al. demonstrated in a study with over 43,000 participants that waist circumference was related to non-fatal, fatal CVD and all-cause mortality in men, and only to fatal CVD and all-cause mortality in women, after adjustment for age and smoking status [8].

The main parameters that could be considered to help the clinician are hypertensive waist, atherogenic index and lipid accumulation product. In the present study, 46.6% of patients had a hypertensive waist. This is in line with a previous study conducted in the Romanian population, which included 1294 randomly selected persons and reported a 43.3% prevalence of hypertensive waist [17]. Since 2005, when LAP was introduced as a better atherogenic index than BMI in predicting CVD, numerous studies have shown that over 10 years of follow-up, LAP can be a useful index. In the ATTICA study, the mean LAP value at baseline was 69% higher in participants who developed a CV event [18]. LAP has a higher predictive accuracy for metabolic syndrome than other indices, as mentioned in a study on 15,490 participants [22]. Regarding the best independent predictor of hypertension, this was LAP (OR: 2.461 [95% CI: 2.277–2.660]) in a National Health Examination Survey study of 2009 (NHES-IV) [23]. In identifying the MHO phenotype, blood pressure measurement and LAP estimation are described as a useful method in postmenopausal women [24]. In our study, LAP and AI were significantly higher in patients with MUHO. Abolnezhadian F. et al. demonstrated that cardiovascular indices, including AI, were significantly higher in MUHO and metabolically unhealthy normal weight phenotype as compared to MHO and healthy normal weight phenotype [3]. AI is associated with a higher risk of subclinical coronary artery disease, beyond traditional risk factors [25]. Depending on the presence of metabolic factors, AI increases progressively and also, a score ≥2 is less common in metabolically normal phenotype than in metabolically unhealthy phenotype [26]. As for the lipid profile, we found that patients with MUHO

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had lower HDL cholesterol levels and higher triglycerides compared to MHO. No difference between groups was observed for total cholesterol and LDL cholesterol. Similar results were reported by Telle-Hansen et al., excepting the LDL cholesterol levels, which were found to be correlated with MUHO [27]. Regarding LDL cholesterol levels, the results of our study are consistent with the results of Catoi et al., which showed no statistically significant differences between MHO and MUHO [28]. Also, in our study, total cholesterol/HDL cholesterol ratio, LDL cholesterol/HDL cholesterol ratio, and non-HDL cholesterol/HDL cholesterol ratio were higher in the MUHO phenotype than in MHO. This is important as these indices have been associated with the risk of high carotid intima-media thickness in a prospective study of 13,612 participants followed for a two-year period. Also, there is a 31% reduction in the risk of major cardiovascular events with every 1% reduction in LDL-C/HDL-C ratio [29]. Another finding of our study is that all atherogenic indices were associated with the presence of MUHO even after adjustment for age, gender, visceral fat area and HOMA-IR, and therefore the risk of CVD is higher for these patients. The MUHO phenotype is characterized by ectopic fat and impaired adipose tissue function, leading to insulin resistance. The adipokine secretion pattern and pro-inflammatory status may also contribute to the MUHO phenotype [11]. Insulin resistance could explain many of the risks associated with metabolic syndrome, MUHO respectively (depending on the definition), and these data may help clinicians focus on the prevention of cardiometabolic diseases.

Although our goal was achieved, some limitations of the study should be mentioned. First, the sample included in the analysis was limited. Also, we collected data retrospectively and we included patients presenting for health evaluation regarding obesity and nutrition counseling.

Conclusions

In conclusion, in this study we described in patients with MUHO several clinical indices/parameters accessible in current practice, which can help clinicians to identify the MUHO phenotype, focus on cardiovascular risk, and to implement the required preventive measures. Knowledge of metabolic health can help the practitioner to take a stand and inform the patient about the benefits of lifestyle optimization to reduce cardiovascular risk. The modern approach means precise medicine based on detailed phenotyping. Even if precise medicine is a combination between genotyping and phenotyping, in medical practice, simple and useful parameters are needed to assess cardiovascular risk. The first step towards precise medicine within diagnosis should include accurate phenotyping for individualization of the therapeutic approach.

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Conflict of Interest

The authors declare no conflict of interest.

References

1. World Health Organization. Obesity and overweight. [online] Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight [Accessed 8th Apr 2021].
2. Piché, M. E., Poirier, P., Lemieux, I., Després, J. P. (2018). Overview of epidemiology and contribution of obesity and body fat distribution to cardiovascular disease: An update. *Prog Cardiovasc Dis*. 61(2): 103–113.
3. Abolnezhadian, F., Hosseini, S. A., Alipour, M., et al. (2020). Association metabolic obesity phenotypes with cardiometabolic index, atherogenic index of plasma and novel anthropometric indices: A link of FTO-rs9939609 polymorphism. *Vasc Health Risk Manag*. 16: 249–256.
4. Neeland, I. J., Poirier, P., Després, J. P. (2018). Cardiovascular and metabolic heterogeneity of obesity: Clinical challenges and implications for management. *Circulation* 137(13): 1391–1406.
5. Stefan, N. (2020). Causes, consequences, and treatment of metabolically unhealthy fat distribution. *Lancet Diabetes Endocrinol*. 8(7): 616–627.

6. Ross, R., Neeland, I. J., Yamashita, S., et al. (2020). Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol*. 16(3): 177–189.
7. Carmienke, S., Freitag, M. H., Pischon, T., et al. (2013). General and abdominal obesity parameters and their combination in relation to mortality: A systematic review and meta-regression analysis. *Eur J Clin Nutr*. 67(6): 573–585.
8. Nelms, M. W., Day, A. G., Sui, X., Blair, S. N., Ross, R. (2020). Waist circumference does not improve established cardiovascular disease risk prediction modeling. *PLoS One* 15(10): e0240214.
9. Sperling, L. S., Mechanick, J. I., Neeland, I. J., et al. (2015). The cardio metabolic health alliance: Working toward a new care model for the metabolic syndrome. *J Am Coll Cardiol*. 66(9): 1050–1067.
10. Caleyachetty, R., Thomas, G. N., Toulis, K. A., et al. (2017). Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. *J Am Coll Cardiol*. 70(12): 1429–1437.
11. Blüher, M. (2020). Metabolically healthy obesity. *Endocr Rev*. 41(3): 405–420.
12. Tsatsoulis, A., Paschou, S. A. (2020). Metabolically healthy obesity: Criteria, epidemiology, controversies, and consequences. *Curr Obes Rep*. 9(2): 109–120.
13. Ray, L., Ravichandran, K., Nanda, S. K. (2018). Comparison of lipid accumulation product index with body mass index and waist circumference as a predictor of metabolic syndrome in Indian population. *Metab Syndr Relat Disord*. 16(5): 240–245.
14. Won, K. B., Jang, M. H., Park, E. J., et al. (2020). Atherogenic index of plasma and the risk of advanced subclinical coronary artery disease beyond traditional risk factors: An observational cohort study. *Clin Cardiol*. 43(12): 1398–1404.
15. Niță, C., Hâncu, N., Rusu, A., Bala, C., Roman, G. (2009). Hypertensive waist: First step of the screening for metabolic syndrome. *Metab Syndr Relat Disord*. 7(2): 105–110.
16. World Health Organization. Obesity and overweight. [online] Available at: https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi [Accessed 8th Apr 2021].
17. Alberti, K. G., Zimmet, P., Shaw, J. (2005). Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Lancet* 366(9491): 1059–1062.
18. Kyrou, I., Panagiotakos, D. B., Kouli, G. M., et al. (2018). Lipid accumulation product in relation to 10-year cardiovascular disease incidence in Caucasian adults: The ATTICA study. *Atherosclerosis* 279: 10–16.
19. Dobiášová, M., Frohlich, J. (2001). The plasma parameter log (TG/HDL-C) as an atherogenic index: Correlation with lipoprotein particle size and esterification rate inapob-lipoprotein-depleted plasma (FERHDL). *Clin Biochem*. 34(7): 583–588.
20. Popa, S., Moța, M., Popa, A., et al. (2016). Prevalence of overweight/obesity, abdominal obesity and metabolic syndrome and atypical cardiometabolic phenotypes in the adult Romanian population: PREDATORR study. *J Endocrinol Invest*. 39(9): 1045–1053.
21. Korduner, J., Bachus, E., Jujic, A., Magnusson, M., Nilsson, P. M. (2019). Metabolically healthy obesity (MHO) in the Malmö diet cancer study – Epidemiology and prospective risks. *Obes Res Clin Pract*. 13(6): 548–554.
22. Shin, K. A., Kim, Y. J. (2019). Usefulness of surrogate markers of body fat distribution for predicting metabolic syndrome in middle-aged and older Korean populations. *Diabetes Metab Syndr Obes*. 12: 2251–2259.
23. Ngoc, N. H., Kriengsinyos, W., Rojroongwasinkul, N., Aekplakorn, W. (2019). Association of adiposity indices with hypertension in middle-aged and elderly Thai population: National Health Examination Survey 2009 (NHES-IV). *J Cardiovasc Dev Dis*. 6(1): 13.
24. Lwow, F., Jedrzejuk, D., Milewicz, A., Szmigiero, L. (2016). Lipid accumulation product (LAP) as a criterion for the identification of the healthy obesity phenotype in postmenopausal women. *Exp Gerontol*. 82: 81–87.
25. Won, K. B., Jang, M. H., Park, E. J., et al. (2020). Atherogenic index of plasma and the risk of advanced subclinical coronary artery disease beyond traditional risk factors: An observational cohort study. *Clin Cardiol*. 43: 1398–1404.
26. Ampuero, J., Aller, R., Gallego-Durán, R., et al. (2018). The effects of metabolic status on non-alcoholic fatty liver disease-related outcomes, beyond the presence of obesity. *Aliment Pharmacol Ther*. 48(11–12): 1260–1270.
27. Telle-hansen, V. H., Christensen, J. J., Formo, G. A., Holven, K. B., Ulven, S. M. (2020). A comprehensive metabolic profiling of the metabolically healthy obesity phenotype. *Lip Health Dis*. 19(1): 1–12.
28. Cătoi, A. F., Pârvu, A. E., Andreicuț, A. D., et al. (2018). Metabolically healthy versus unhealthy morbidly obese: Chronic inflammation, nitro-oxidative stress, and insulin resistance. *Nutrients* 10(9): 1–11.
29. Qin, P., Shi, J., Cao, L., et al. (2021). Low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio and carotid intima-media thickness: A cohort study in China. *Lipids* 56(1): 59–68.

 https://doi.org/10.46389/rjd-2021-1024