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RESEARCH ARTICLE

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Are visceral adiposity index and lipid accumulation product reliable indices for metabolic disturbances in patients with type 2 diabetes mellitus?

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Background: Visceral adiposity index (VAI) and Lipid accumulation product (LAP) are novel visceral adiposity indexes, proposed for the evaluation of cardiometabolic risk in adult population. Considering contradictory results obtained from many studies so far, we aimed to examine the potential benefit of applicability of VAI and LAP, over simple anthropometric indices and traditional lipid parameters in individuals with type 2 diabetes mellitus (DM2).

Methods: A total of 180 DM2 (of them 50% females) and 119 controls who volunteered to participate in this cross-sectional study were enrolled. Anthropometric and biochemical parameters, as well as blood pressure were obtained. VAI and LAP were calculated.

Results: Multivariate logistic regression analysis showed that high-density lipoprotein cholesterol (HDL-c), (P<.001), waist circumference (WC), (P=.027), age (P=.001), hypolipemic therapy (P=.024), and LAP (P=.005) were independent predictors of DM2 in adjusted models.

In Receiver Operating Characteristic curve analysis, used to discriminate subjects with DM2 from those who did not have it, good accuracy of the applied procedures was only achieved with models which were consisted of parameters used in VAI (Body mass index, WC, HDL-c, triglycerides) and LAP (WC, triglycerides) indexes equations, respectively [Area under the curve (AUC)=0.819 and AUC=0.800, respectively], but not with VAI (AUC=0.781) and LAP (AUC=0.784) indexes themselves.

Conclusion: Visceral adiposity index and Lipid accumulation product may not be better than parameters that enter its equation in type 2 diabetes prediction.

KEYWORDS

lipid accumulation product, obesity, type 2 diabetes mellitus, visceral adiposity index

1 | INTRODUCTION

A growing proportion of individuals with type 2 diabetes mellitus (DM2) worldwide is attributed in large part to the increase in body fat mass, especially in intra-abdominal (visceral) region.[1] Visceral adipose tissue is regarded to be metabolically active endocrine organ, secreting a variety of pro-inflammatory adipokines, thus further leading to many cardiometabolic disorders.[1,2]

Simple anthropometric parameter of abdominal adiposity such as waist circumference (WC) is established and widely used in many investigations.[3-5] As early recognition and treatment of individuals with abdominal adiposity is of utmost importance in reducing cardiometabolic risk, some novel visceral adiposity markers, such as visceral adiposity index (VAI) and the lipid accumulation product (LAP) have been validated so far.[6,7]

The VAI is gender-specific mathematical model that uses both anthropometric indices [e.g., body mass index (BMI) and WC] and lipid parameters [e.g., high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG)] in its equation, and is highly correlated with visceral adiposity as measured with the gold standard method, such

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as magnetic resonance imaging.[6] The LAP is a gender-specific index based on a combination of WC and TG in its equation.[7] Both of these indexes are proposed as simple, accurate, and low-cost tools for the evaluation of visceral adipose tissue dysfunction and its associated cardiometabolic risk in adult population,[6-10] even superior than simple anthropometric parameters (e.g., BMI, WC).

These indexes were proposed as markers of insulin resistance and metabolic-associated disturbances in women with polycystic ovary syndrome (PCOS), implicating that VAI and LAP may be used as screening tool for young women who are susceptible to the development of diabetes and CVD.[11,12]

Furthermore, higher VAI[13] and LAP[14] were associated with metabolic syndrome (MetS), with the presence of DM2,[15,16] and with chronic kidney disease (CKD),[9] showing even better discriminative power in relation to cardiometabolic risk than anthropometric parameters alone.[7,12,17]

Even though a large number of studies in adult population indicate VAI and LAP as reliable markers of cardiometabolic risk advantageous over BMI and WC,[6-10,12,13,17] there are another ones that report the opposite.[18-22]

Considering contradictory results obtained from many studies so far, we aimed to examine the potential benefit of applicability of novel visceral adiposity indexes, such as VAI and LAP, over simple anthropometric indices and traditional lipid parameters in individuals with DM2.

2 | MATERIALS AND METHODS

2.1 | Study population

A total of 180 sedentary DM2 (of them 50% females), as well as 119 healthy controls (of them 71% females) who volunteered to participate in this cross-sectional study were enrolled. Diabetic patients were consecutively recruited by the endocrinologist in the Center of Laboratory Diagnostics of the Primary Health Care Center in Podgorica, Montenegro, for their regular check-up in a period from October 2015 to May 2016. All the participants completed a self-administered questionnaire including demographic characteristics, somatic illnesses, medication use, and lifestyle habits (e.g., information about cigarette smoking, diabetes duration, and physical activity). Medical history and clinical examinations were carried out on the same day.

Inclusion criteria for group of diabetic participants were as follows: DM2, sedentary patients (<90 minutes of weekly exercise), without acute inflammatory disease, with no history or the presence of malignancy, hypo- and hyperthyroidism. Diabetes cases were defined as self-reported diabetes, or with at least two elevated plasma glucose levels (fasting glucose ≥7.0 mmol/L, a random plasma glucose level of ≥11.1 mmol/L, or a plasma glucose level ≥11.1 mmol/L 2 h after an oral glucose tolerance test), or HBA1c ≥6.5% on two different occasions in the absence of symptoms; or treatment with hypoglycemia medication (insulin or oral hypoglycemic agents).[23]

For non-diabetics group, inclusion criteria were fasting glucose <7.0 mmol/L and glycosylated hemoglobin (HbA1c) ≤6%. In addition, all participants with fasting glucose ≥5.6 mmol/L, but <7.0 mmol/L, underwent a 2-h oral glucose tolerance test (OGTT). Participants with 2-h postload glucose ≥11.1 mmol/L were excluded from the control group.[23]

Exclusion criteria for all participants were as follows: type 1 diabetes mellitus, ethanol consumption >20 g/day, high-sensitivity C-reactive protein levels (hsCRP) >10 mg/L, liver disease, hypothyroidism or hyperthyroidism, patients on chronic dialysis, renal disease other than diabetic nephropathy, with a recent (6 months) history of acute myocardial infarction or stroke, pregnancy, usage of anti-inflammatory medications in the last 6 months, usage of insulin or hypoglycemic agents for controls, as well as participants who were unwilling to enter the study.

All participants who used lipid-modifying drugs (55.5%) in our study used statins (100% of them), whereas the smaller number of them used fibrates, also (3.3%).

All the participants provided written informed consent. The study protocol was approved by the Ethical Committee of Primary Health Care Center in Podgorica, Montenegro and the research was carried out in compliance with the Declaration of Helsinki.

2.2 | Anthropometric measurements

Basic anthropometric measurements: body height (cm), body weight (kg), and WC (cm) were obtained, and BMI was calculated, as described previously.[2]

Visceral adiposity index (VAI) was calculated using the formula: .[6]

$$\{[WC/36.58 + (1.89 \times BMI)] \times (TG/0.81) \times (1.52/HDL\text{-}c)\}$$

for females, and $\{[WC/39.68 + (1.88 \times BMI)] \times (TG/1.03) \times (1.31/HDL\text{-}c)\}$ for males

where WC is expressed in cm, BMI in kg/m^2, and TG and HDL-c in mmol/L.

Lipid accumulation product (LAP) was calculated by the following equation: [7]

$[(WC - 58) \times TG]$ for females, and $[(WC - 65) \times TG]$ for males,

where WC is expressed in cm, and TG in mmol/L.

2.3 | Biochemical analyses

The blood samples were taken between 7 and 9 hours a.m., after 12-14 hours of an overnight fast. Samples were left to clot for 30 minutes and then centrifuged at 3000 rpm for 10 minutes.

Serum samples were divided into aliquots and stored at −80°C, without prior thawing and re-freezing before analyses, except for glucose, which was determined immediately after the blood was drawn. Another aliquot was collecting as a whole blood in K_2EDTA for determination of HbA1c, and it was measured with immunoturbidimetric assay (Roche Cobas 400, Mannheim, Germany).

Serum levels of glucose, total cholesterol (TC), HDL-c, low-density lipoprotein cholesterol (LDL-c), TG, uric acid, bilirubin, aspartat aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamil transferase (GGT) were measured using standardized enzymatic

TABLE 1 Demographic characteristics of two study groups

	Control group	Diabetic group	*P*
N (male/female)	119 (34/85)	180 (90/90)	<.001
Age, years	55.00 (36.25-66.75)	63.00 (55.00-69.00)	<.001
BMI, kg/m^2	26.96 (23.26-30.46)	29.07 (26.80-32.28)	.003
WC, cm	96.00 (86.00-104.75)	106.00 (98.50-146.00)	<.001
SBP, mmHg	133.00 (127.00-141.75)	134.00 (126.00-142.00)	.801
DBP, mmHg	77.00 (70.00-80.00)	80.00 (70.00-85.00)	.102
Smoking habits, (Smoker/Non-smoker)	28/91	42/138	.969
Hypolipemics (Yes/No)	23/96	77/103	<.001
Statins (Controls/Diabetics, 23/77)			
Fibrates (Controls/Diabetics, 0/6)			
Antihypertensives (Yes/No)	58/61	129/51	<.001
ACE inhibitors (Controls/Diabetics, 51/116)			
Beta blockers (Controls/Diabetics, 36/31)			
Diuretics (Controls/Diabetics, 19/68)			
Antihyperglycemics (Yes/No)	-	0/157	<.001
Metformin (Controls/Diabetics, 0/149)			
Sulfonylurea (Controls/Diabetics, 0/8)			
Insulin (Controls/Diabetics, 0/31)	-	0/31	-
Duration of diabetes, years	-	4.00 (2.00-9.00)	-

Data are presented as median (interquartile range) and compared by Mann-Whitney test.
Categorical variables are presented as absolute frequencies and compared by Chi-square test.

procedures, spectrophotometrically (Roche Cobas 400). HsCRP) levels were determined using a nephelometric assay (Behring Nephelometer Analyzer, Marburg, Germany).

Glomerular filtration rate was estimated by using creatinine in the Modification of Diet in Renal Disease Study equation ($eGFR_{MDRD}$):[24]

$$eGFR_{MDRD}\,(mL/min/1.73\,m^2) = 186 \times [\text{serum creatinine}\,(\mu mol/L)/88.4]^{-1.154} \times [\text{Age}\,(\text{years})]^{-0.203} \times 0.742\,(\text{if female})$$

Blood pressure was measured as described previously.[2]

2.4 | Statistical analysis

Data are expressed as arithmetic mean±standard deviation for normally distributed variables, geometric mean [95% Confidence interval (CI) for the mean] for *log*-normally distributed variables, and as median (interquartile range) for skewed distributed variables. Differences in continuous variables between DM2 patients and control population were tested with Student's *t*-test for normally and *log*-normally distributed variables, and Mann-Whitney test for skewed distributed variables. Differences between categorical variables were examined with the Chi-square test. The associations among VAI, LAP index, and variables which entered VAI and LAP equations with other clinical parameters were assessed by Spearman's correlation analysis and presented as correlation coefficient (ρ). Using logistic regression analysis, we examined the associations and VAI, LAP index, and each parameter of VAI and LAP equations with risk for DM2 development. Multivariate logistic regression analysis was used to identify factors associated with risk for DM2 development. Multivariate analysis adjustment was made for all parameters which showed significant differences between two tested populations, exhibit significant correlations with other independent parameters, and associated with DM2 occurrence and development. Data were presented as odds ratio (OR) and 95% CI for odds. The explained variation in dependent variable was given by Nagelkerke R^2 value. Receiver Operating Characteristic (ROC) curve analysis was used to test the additional values of VAI, LAP index, single parameter used in VAI and LAP calculations and models to distinguish subjects that suffered from DM2 from those that did not. Differences between curve areas were also tested. All statistical analysis was carried out in the PASW® Statistic version 18 (Chicago, IL, USA) and the MedCalc® (Mariakerke, Belgium) Version 15.8. A *P* value <.05 was considered statistically significant in all analyses.

3 | RESULTS

In Table 1 are summarized demographic characteristics of studied groups. Diabetic patients were older (*P*<.001), had significantly higher BMI (*P*=.003) and WC (*P*<.001). Chi-square analysis showed unequal distribution of gender, subjects who used hypolipemic and antihypertensive therapy (*P*<.001 for all).

TABLE 2 Laboratory and clinical parameters of two study groups

	Control group	Diabetic group	*P*
TC, mmol/L[a]	5.41 (5.20-5.63)	5.24 (5.08-5.41)	.227
HDL-c, mmol/L[a]	1.45 (1.37-1.53)	1.14 (1.09-1.23)	<.001
LDL-c, mmol/L[a]	3.16 (2.96-3.36)	3.10 (2.96-3.25)	.605
TG, mmol/L[a]	1.39 (1.27-1.52)	1.91 (1.77-2.06)	<.001
LAP[a]	44.34 (38.14-51.53)	82.87 (76.69-90.73)	<.001
VAI[a]	1.73 (1.53-1.96)	2.90 (2.61-3.21)	<.001
Glucose, mmol/L[b]	5.20 (4.90-5.77)	7.10 (6.20-8.90)	<.001
HBA1c, %[b]	4.90 (4.70-5.30)	6.60 (5.80-8.00)	<.001
AST, U/L[b]	19.00 (17.00-22.50)	19.00 (16.00-32.00)	.790
ALT, U/L[b]	20.00 (14.00-25.75)	22.00 (16.00-32.00)	.022
GGT, U/L[b]	14.00 (11.00-20.00)	19.00 (15.00-29.00)	<.001
Total bilirubin, μmol/L[b]	7.10 (6.12-9.90)	6.00 (4.60-8.15)	.028
Creatinine, μmol/L[b]	66.50 (59.00-78.00)	73.00 (64.00-86.00)	.001
Uric acid, μmol/L[b]	259.00 (213.75-330.50)	310.00 (249.00-357.00)	<.001
$eGFR_{MDRD,}$ mL/min/1.73 m²	90.04±22.20	82.82±22.42	.007
HsCRP, mg/L[b]	1.31 (0.49-2.68)	1.52 (0.90-3.64)	.004

Data are presented as arithmetic mean±SD and compared with Student's *t*-test.
[a]*Log*-normal distributed data are presented as geometric mean (95% CI) and compared with Student's *t*-test after logarithmic transformation.
[b]Skewed distributed data are presented as median (interquartile range) and compared with Mann-Whitney test.

Statistical analysis showed that diabetic patients had significantly higher TG, LAP index, VAI, GGT, uric acid (*P*<.001 for all), ALT (*P*=.022), creatinine (*P*=.001), $eGFR_{MDRD}$ (*P*=.007), and hsCRP (*P*=.004) than controls. Also, diabetic patients had significantly lower HDL-c and total bilirubin level than control group (*P*<.001, and *P*=.028, respectively) (Table 2).

Results of Spearman's correlation analysis were presented in Table 3. BMI and WC were highly positively correlated with ages, SBP, DBP, TG, glucose HbA1c, AST, ALT, GGT, uric acid, and hsCRP (*P*<.01), and negatively correlated with HDL-c (*P*<.01) and $eGFR_{MDRD}$ (*P*<.05). WC also showed significant correlation with creatinine (*P*<.05). HDL-c highly negatively correlated with TG, glucose, HBA1c, ALT, AST, GGT, uric acid, hsCRP, and creatinine (*P*<.01 for all). TG showed significant positive correlations with ages (*P*<.05), TC, LDL-c, glucose, HBA1c, ALT, AST, GGT, uric acid, hsCRP. and creatinine (*P*<.01 for all). Negative correlations were obtained between TG and $eGFR_{MDRD}$ (*P*<.05). LAP index was positively correlated with ages, BMI, WC, TC, TG, LDL-c, glucose HbA1c, AST, ALT, GGT, uric acid, hsCRP (*P*<.01 for all), and creatinine (*P*<.05), and negatively correlated with HDL-c (*P*<.01) and $eGFR_{MDRD}$ (*P*<.05). VAI was positively correlated with ages (*P*<.05), BMI, WC, TC, TG, LDL-c, glucose HbA1c, AST, ALT, GGT, uric acid, hsCRP (*P*<.01), and creatinine (*P*<.05), and negatively correlated with HDL-c, total bilirubin (*P*<.01 for both), and $eGFR_{MDRD}$ (*P*<.05).

Logistic regression analysis was used to establish the associations of VAI, LAP index, and each parameter used in their equations with DM2 development (Table 4). Predictors were unadjusted and adjusted for other parameters significantly different between study groups (Table 2). Also, ages and hypolipemic therapy, which showed significant odds in univariate logistic regression analysis, were tested further in models to determine their independent predictions on DM2 development. WC kept independent predictions for DM2 development (Model 1 OR=1.050 *P*=.027; Model 3 OR=1.052, *P*<.001). As WC rose for 1 cm, risk for DM2 development got higher for 5% and 5.2%, respectively. HDL-c was also shown to be the independent predictor of DM2 development (Model 2 OR=0.142, *P*<.001). Rise in HDL-c by 1 mmol/L reduced the probability of DM2 development by 85.8%. VAI lost its independent predictive role (Model 2 OR=1.136, *P*=.053), but LAP kept its independent prediction of DM2 development (Model 4 OR=1.010, *P*=.005). TG was showed not to be the independent predictor of DM2 development (Model 1 OR=0.954, *P*=.730 and Model 3 OR=1.200, *P*=.155).

In all models, ages and hypolipemic therapy were shown to be the independent predictors of DM2 development. Usage of hypolipemic therapy presented around two times higher risk of DM2 development (all Models, Table 4). Also, as person got older by 1 year, the probability for DM2 development rose for 5.0% (*P*=.001, Model 1), for 6.4% (*P*<.001, Model 2), for 5.4% (*P*<.001, Model 3), and for 6.1% (*P*<.001, Model 4).

According to R^2 value, 41.1% variation in DM2 development could be explained by Model 1, 31.8% by Model 2, 35.6% by Model 3, and 33.3% by Model 4 (Table 4). Model 1 correctly classified 77%, Model 2 correctly classified 71%, Model 3 correctly classified 74%, and Model 4 correctly classified 72% of cases in group having DM2 (data were not presented in tables).

ROC analysis was used to discriminate subjects with DM2 from those who did not have it (Tables 5 and 6). The calculated AUCs for the measurement of single clinical parameter (ranking from 0.617 to 0.729) indicated that the clinical accuracy of the applied procedures containing single parameter was low.

TABLE 3 Associations among anthropometric, lipid parameters, VAI, and LAP with other clinical parameters

	BMI, kg/m^2	WC, cm	HDL-c, mmol/L	TG, mmol/L	LAP	VAI
Age, years	0.182**	0.238**	−0.036	0.140*	0.191**	0.127*
BMI, kg/m^2	–	0.829**	−0.297**	0.394**	0.659**	0.422**
WC, cm	0.289**	–	−0.405**	0.387**	0.696**	0.454**
SBP, mmHg	0.285**	0.215**	−0.007	0.049	0.147*	0.069
DBP, mmHg	0.275**	0.268**	−0.017	0.031	0.135*	0.031
TC, mmol/L	0.083	0.017	0.087	0.406**	0.337**	0.284**
HDL-c, mmol/L	−0.297**	−0.405**	–	−0.575**	−0.578**	−0.747**
LDL-c, mmol/L	0.080	0.060	−0.068	0.320**	0.280**	0.270**
TG, mmol/L	0.394**	0.387**	−0.575**	–	0.900**	0.932**
Glucose, mmol/L	0.328**	0.388**	−0.356**	0.379**	0.451**	0.415**
HbA1c, %	0.326**	0.398**	−0.466**	0.421**	0.488**	0.470**
AST, IU/L	0.222**	0.202**	−0.087	0.190**	0.219**	0.144**
ALT, IU/L	0.325**	0.340**	−0.254**	0.323**	0.370**	0.294**
GGT, IU/L	0.342**	0.405**	−0.350**	0.475**	0.503**	0.419**
Uric acid, μmol/L	0.344**	0.383**	−0.240**	0.322**	0.377**	0.283**
Total bilirubin, μmol/L	−0.028	−0.040	0.076	−0.096	−0.110	−0.159**
HsCRP, mg/L	0.509**	0.468**	−0.240**	0.267**	0.425**	0.320**
Creatinine, μmol/L	0.086	0.186*	−0.249**	0.171**	0.159*	0.120*
$eGFR_{MDRD}$, mL/min/1.73 m²	−0.131*	−0.126*	0.065	−0.148*	−0.168*	−0.147*

Data are presented as correlation coefficient Rho (ρ).
*P<.05.
**P<.01.

The same models were used in ROC analysis as in logistic regression analysis. Model 1 which included parameters that entered VAI equation showed higher ability to discriminate DM2 patients from controls than Model 2 which included VAI itself (AUC=0.819 and AUC=0.781, respectively, and AUC difference=0.038, P=.018). Also, difference between areas was significant between Model 1 and Model 4 which included LAP itself (AUC difference=0.035, P=.019). Good accuracy of the applied procedures was only achieved with Models 1 and 3 (AUC=0.819 and AUC=0.800, respectively) which were consisted of parameters used in VAI (BMI, WC, HDL-c, TG) and LAP (WC, TG) indexes equations, but not VAI and LAP indexes themselves (AUC=0.781 and AUC=0.784, respectively) (Figure 1). The highest sensitivity and specificity was achieved by Model 1 (82.20% and 70.60%, respectively) (Table 6).

4 | DISCUSSION

The main finding of our study reveals that neither VAI nor LAP are superior to simple anthropometric indices (e.g., WC) and lipid parameters (e.g., HDL-c) for DM2 prediction.

Logistic regression analysis showed that VAI lost its independent predictive role, but LAP kept its independent prediction of DM2 development, after adjustment for confounding factors (Table 4).

As more than 60%-70% of DM2 patients are affected by nonalcoholic fatty liver disease (NAFLD), and as that diabetic individuals with NAFLD have increased risk for long-term diabetes complications such as chronic kidney disease and CVD,[25] we determined liver enzymes activity in all participants. Moreover, we determined uric acid and total bilirubin levels, regarding that hyperuricemia and low total bilirubin levels are associated with increased risk of DM2 and its complications.[26] In addition, we determined creatinine levels and calculated eGFR in all subjects, as studies report the association of high creatinine levels, and low eGFR levels with an increased risk of DM2, as well as its complications.[27,28]

A ROC analysis was used to discriminate subjects with DM2 from those who did not have it and showed that good accuracy of the applied procedures was only achieved with models which were consisted of parameters used in VAI (BMI, WC, HDL-c, TG) and LAP (WC, TG) indexes equations, respectively (AUC=0.819 and AUC=0.800, respectively), but not with VAI and LAP indexes themselves (Table 6, Figure 1).

The majority of previous studies reported VAI and LAP to be reliable indices in prediction of many metabolic disturbances.[6-10,12,13,17]

Amato et al.[8] reported superiority of the VAI, to other anthropometric indices (BMI, WC, hip circumference, and waist/hip ratio) in relation to cardiometabolic risk and adipose tissue dysfunction in individuals with DM2. In addition, in their another study,[6] superiority of VAI than its individual components that entered equation (WC, BMI, HDL-c, and TG) with regard to discriminating cardio- and cerebrovascular events was reported, too. On the contrary, our results show that the highest sensitivity and specificity was achieved by model consisted

TABLE 4 Logistic regression analysis for the associations among VAI, LAP indexes, parameters used for indexes calculations, and DM2 development

Predictors	Unadjusted OR (95%CI)	*P*	Nagelkerke R^2
BMI, kg/m^2	1.140 (1.079-1.205)	<.001	.115
WC, cm	1.068 (1.046-1.091)	<.001	.198
HDL-c, mmol/L	0.095 (0.046-0.198)	<.001	.209
TG, mmol/L	1.718 (1.295-2.279)	<.001	.083
LAP	1.016 (1.010-1.021)	<.001	.162
VAI	1.292 (1.133-1.474)	<.001	.092
Age, years	1.052 (1.033-1.071)	<.001	.142
Hypolipemics	3.120 (1.814-5.367)	<.001	.081
	Adjusted OR (95%CI)	***P***	**Nagelkerke R^2**
Model 1			
BMI, kg/m^2	0.963 (0.863-1.076)	.513	.411
WC, cm	1.050 (1.006-1.097)	.027	
HDL-c, mmol/L	0.142 (0.053-0.385)	<.001	
TG, mmol/L	0.954 (0.728-1.249)	.730	
Age, years	1.050 (1.021-1.086)	.001	
Hypolipemics	2.130 (1.150-4.108)	.024	
Model 2			
VAI	1.136 (0.998-1.295)	.053	.318
Age, years	1.064 (1.034-1.095)	<.001	
Hypolipemics	2.040 (1.020-3.770)	.023	
Model 3			
TG, mmol/L	1.200 (0.934-1.536)	.155	.356
WC, cm	1.052 (1.022-1.082)	<.001	
Age, years	1.054 (1.023-1.086)	<.001	
Hypolipemics	2.041 (1.086-3.840)	.027	
Model 4			
LAP	1.010 (1.003-1.017)	.005	.333
Age, years	1.061 (1.031-1.092)	<.001	
Hypolipemics	1.985 (1.065-3.698)	.031	

Model 1: age, *BMI*, *WC*, *HDL-c*, *TG*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 2: age, *VAI*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 3: age, *WC*, *TG*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 4: age, *LAP*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).

of parameters that enter VAI equation (82.2% and 70.6%, respectively) in discriminating subjects with DM2 from those who did not have it (Table 6).

Also, previous studies reported that LAP better than other variables (e.g., BMI and WC) predicted MetS,[14] DM2,[12,17] and CVD.[7,10]

However, our results are opposite, showing that visceral indexes, VAI and LAP, are not superior to WC and HDL-c in predicting DM2 occurrence. Our findings are similar to results obtained from a recent study,[19] which encompassed nearly 600 healthy Saudi children, showing superiority of BMI and WC relative to VAI in relation to cardiometabolic risk factors.

Similarly, some other investigations reported simple anthropometric measures, BMI and WC to be more accurate than VAI in prediction of the presence of MetS,[20] hepatic steatosis,[21] and incident CVD.[22]

In addition, it has been reported that although LAP was an independent predictor of cardiovascular events even in normal weight subjects, it had no advantageous capabilities over other anthropometrics indices.[18] Similarly, Dai et al.[9] showed that neither VAI nor LAP index

TABLE 5 ROC analysis for single parameter discriminatory abilities regarding DM2 development

Predictors	AUC (95%CI)	SE	Sensitivity (%)	Specificity (%)	*P*
BMI, kg/m^2	0.667 (0.603-0.732)	0.033	90.56	38.66	<.001
WC, cm	0.715 (0.653-0.777)	0.032	66.11	68.07	<.001
HDL-c, mmol/L	0.729 (0.670-0.787)	0.030	70.56	65.55	<.001
TG, mmol/L	0.671 (0.609-0.734)	0.034	68.89	60.50	<.001
LAP	0.716 (0.657-0.776)	0.031	86.11	50.42	<.001
VAI	0.707 (0.647-0.776)	0.030	59.44	73.95	<.001
Age, years	0.669 (0.605-0.733)	0.030	70.56	56.30	<.001
Hypolipemics	0.617 (0.553-0.681)	0.033	42.78	80.67	.001

SE, standard error.

TABLE 6 ROC analysis for model discriminatory abilities regarding DM2 development

Predictors	AUC (95%CI)	SE	Sensitivity (%)	Specificity (%)	AUC difference	*P*
Model 1	0.819 (0.771-0.861)	0.025	82.20	70.60	-	-
Model 2	0.781 (0.730-0.826)	0.027	66.11	79.00	0.038	.018
Model 3	0.800 (0.746-0.841)	0.027	80.00	66.40	0.019	.076
Model 4	0.784 (0.733-0.829)	0.027	69.44	76.47	0.035	.019

P, probability for AUC differences.
Model 1: age, *BMI*, *WC*, *HDL-c*, *TG*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 2: age, *VAI*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 3: age, *WC*, *TG*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).
Model 4: age, *LAP*, hsCRP, ALT, GGT, uric acid, bilirubin, creatinine, $eGFR_{MDRD}$ (continuous variables); gender, smoking status, hypolipemics, and antihypertensive therapies (categorical variables).

was superior for identifying individuals with CKD over BMI in the male gender.

In our study, logistic regression analysis reported WC to be the independent predictor of DM2 development both in unadjusted and adjusted model. As WC rose for 1 cm, the risk for DM2 development got higher for 5% (Model 1) and 5.2% (Model 3), respectively (Table 4). Our results are in line with previous findings[1,29] suggesting that visceral adiposity is the independent risk factor for DM2. Visceral adipose tissue is significant source of variety of pro-inflammatory adipo- and cytokines which reach the liver, thus impairing insulin signaling, with consequent insulin resistance occurrence, lipid accumulation, and metabolic disorders.[1,2]

Although Computed Tomography (CT) represents the "gold standard method" for evaluating the quantification of visceral adipose tissue, it is not suitable diagnostic procedure in routine clinical practice due to its high cost and radiation exposure. Therefore, WC is regarded to be simple, easily obtained anthropometric parameter that can estimate visceral obesity in primary care settings.[30]

Furthermore, HDL-c was also shown to be the independent predictor of DM2. Rise in HDL-c by 1 mmol/L reduced the probability of DM2 development by 85.8% (Model 1) (Table 4).

Other studies also showed low HDL-c to be the independent risk factor for DM2.[31,32]

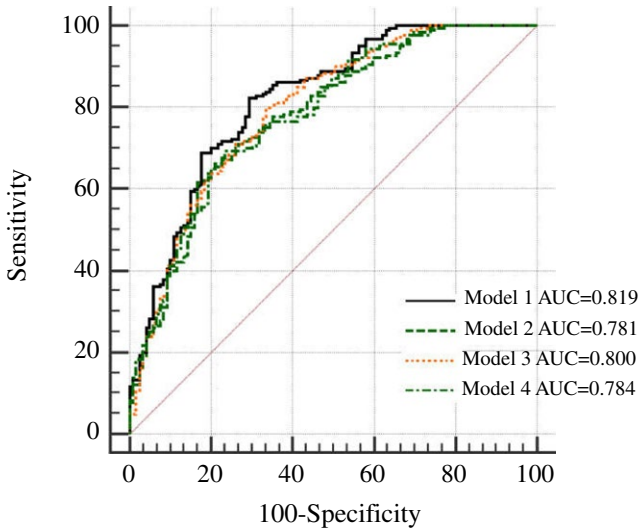

FIGURE 1 ROC curves for Models discriminative ability for DM2 development

Gupta et al.[31] found that increase in HDL-c by 1 mmol/L decreased the probability of DM2 by 28%. Favorable properties of HDL-c, such as antioxidative, anti-inflammatory, and antiapoptotic actions, are well established, thus explaining its protective roles in DM2.[33]

Another important finding of our study was that in all models, ages and hypolipemic therapy were shown to be the independent predictors of DM2 development. Relationship between ages and DM2 was also reported previously.[29] In our study, as person got older by 1 year, the probability for DM2 development rose for 5.0% in unadjusted and for 6.4% in adjusted model.

In this study usage of hypolipemic therapy presented around 3.12 time higher risk of DM2 development in unadjusted model, and 2 times higher risk of DM2 occurrence in adjusted model. It is important to note that all participants in our study who used hypolipemics, used statins. Our results are in line with recent studies which also showed an increased risk of DM2 with statins usage.[34,35] Cederberg et al.[34] in a large study comprised of about 9,000 non-diabetic participants, during a 6-year follow-up showed that statin treatment increased the risk of DM2 by 46%, mainly due to decrease in insulin sensitivity (by 24%) and insulin secretion (by 12%), compared with individuals without statin treatment.

Although this study has cross-sectional design which precludes causal inferences, we speculate that novel visceral adiposity indexes, such as VAI and LAP, have no advantages over simple anthropometric indices or lipid parameters in prediction of DM2 risk. Large longitudinal studies are needed to further examine the potential benefits of VAI and LAP in DM2 prediction.

5 | CONCLUSION

Visceral adiposity index and Lipid accumulation product may not be better than parameters that enter its equation in type 2 diabetes prediction.

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