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Novel anthropometric parameters in the adult population with prediabetes

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Abstract. – OBJECTIVE: Although it is assumed that novel-derived anthropometric indices can better reflect cardiometabolic risk than traditional ones, the results are conflicting. Previous studies have mainly focused on patients with type 2 diabetes mellitus. However, studies conducted on populations with prediabetes are scarce. The present study aimed to examine the potential relationship between prediabetes and novel anthropometric parameters [that is, cardiometabolic index (CMI), visceral adiposity index (VAI), lipid accumulation product index (LAP), body roundness index (BRI), and body adiposity index (BAI)] and traditional parameters [that is, waist circumference (WC), hip circumference (HC), body mass index (BMI), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR)] in adults with prediabetes.

PATIENTS AND METHODS: This case-control cross-sectional study included 177 patients with prediabetes and 609 control subjects. Biochemical and simple anthropometric parameters were measured (WC, HC, body weight, and height), whereas the other parameters were calculated.

RESULTS: WC, CMI, VAI, and LAP independently correlated with prediabetes. Principal component analysis (PCA) was used to extract several factors that correlated with prediabetes. Significant predictive capability was demonstrated for non-traditional anthropometric/lipid-related factors and WHipR-related factors for prediabetes (OR=1.334 and OR=1.202, respectively). However, only non-traditional anthropometric/lipid-related factors (i.e., VAI, CMI, and LAP) demonstrated an independent significant positive relationship with prediabetes in multivariate binary regression analysis.

CONCLUSIONS: CMI, VAI, and LAP could be superior to BAI, BRI, and conventional anthropometric parameters for discriminating patients with prediabetes in the adult population. Prospective trials are needed to confirm our results.

Key Words:
Anthropometric, Inflammation, Obesity, Visceral adipose tissue.

Introduction

A broad spectrum of metabolic abnormalities occurs even before the onset of type 2 diabetes (T2D)[1,2]. Owing to the high prevalence of prediabetes and increased risk of T2D progression, it is of utmost importance to act in a timely manner by reducing obesity and promoting physical activity and healthy dietary patterns[3,4]. The recognition of high-risk obesity phenotypes plays a significant role in the identification of individuals with a high cardiometabolic burden[5].

The link between obesity and cardiovascular disease is well-established since visceral adipose tissue has proatherogenic and prothrombotic properties due to its large number of proinflammatory adipocytokines that modify signaling pathways[6,7].

The most frequently used parameter that reflects general obesity is the body mass index (BMI), but it cannot differentiate fat storage from muscle mass[8]. BMI is also limited by information on adipose tissue distribution and body shape[8]. Waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR) can provide better insights into central/abdominal

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obesity than BMI, but the differentiation between subcutaneous and visceral fat by these traditional parameters is limited[8].

To gain a deeper insight into these limitations, efforts are being made to discover anthropometric indicators that best reflect cardiometabolic disorders. In the last few decades, several novel nontraditional anthropometric indices[5] have emerged.

Some include a combination of traditional anthropometric measurements [e.g., body roundness index (BRI) and body adiposity index (BAI)][9,10], whereas others include conventional anthropometric indices and lipid parameters [that is, lipid accumulation product index (LAP), visceral adiposity index (VAI), and cardiometabolic index (CMI)][11-13].

BRI combines WC and height data and reflects body shape and distribution of body fat[7]. BAI includes measurements of height and hip circumference (HC) and reflects the subcutaneous adipose compartment and the percentage of body fat stronger than BMI[10].

New indicators of abdominal obesity (i.e., LAP, VAI, and CMI) combine WC and lipid parameters to differentiate visceral from subcutaneous adipose tissue[11-13].

Although a large number of investigations[11-13] have demonstrated that these novel, derived anthropometric indices can better reflect cardiometabolic risk than traditional ones, numerous studies[14-16] have shown the opposite, since the latter ones did not confirm the superiority of non-traditional anthropometric parameters over traditional ones.

Furthermore, previous studies[14,16,17] have mainly focused on patients with T2D.

However, studies conducted on populations with prediabetes are scarce. Hence, the present study aimed to examine the potential relationship between prediabetes and novel anthropometric parameters (e.g., CMI, VAI, LAP, BRI, and BAI) and traditional parameters (e.g., WC, HC, BMI, WHtR, and WHR) in the adult population with prediabetes.

Patients and Methods

Subjects

The current case-control cross-sectional study included 177 patients with prediabetes and 609 subjects as the control group. Participants were recruited in a consecutive manner when visiting the Primary Health Care Center in Podgorica, Montenegro, for metabolic evaluation by performing laboratory analyses between April and June 2022. The Institutional Ethics Committee of the Primary Health Care Center, Podgorica, Montenegro, approved the study procedures, and all examinees signed an informed consent form.

Each examinee completed a questionnaire related to demographic characteristics, somatic illnesses, and lifestyle habits (e.g., cigarette smoking and alcohol consumption).

The inclusion criteria for participants with prediabetes were based on the 2020 American Diabetes Association Standards of Diabetes Care[4].

Participants were regarded with prediabetes if they were not taking any medications for diabetes, if they had glycated hemoglobin (HbA1c) levels between 5.7% and 6.4%, if they exhibited fasting glucose levels between ≥5.6 mmol/L and <7.0 mmol/L, or if 2 hours after oral glucose tolerance test (with 75 g anhydrous glucose dissolved in water) had serum glucose levels between 7.8 mmol/L and 11.1 mmol/L.

Diabetes-free participants who were not taking any antihyperglycemic medications, with fasting glucose <5.6 mmol/L and with HbA1c levels <5.7%, were included in the control group. A stable body weight in the last three months was another criterion for inclusion.

Participants with type 1 or type 2 diabetes mellitus, malignant diseases, autoimmune diseases, a history of cardiovascular disease, severe anemia, hepatic disease other than steatosis, thyroid disorders, renal disease, high-sensitivity C-reactive protein (hsCRP) >10 mg/L, and pregnant women were excluded from the study.

Participants in the control group used hypolipemics [i.e., statins (23.5%) and antihypertensives (54%)]. In addition, participants with prediabetes used hypolipemics, such as statins (26.5%) and antihypertensives (65%).

Methods

Anthropometric measurements were obtained (i.e., body weight, WC, HC, and body height), whereas BMI, WHtR, and WHR were calculated as previously described[8].

The BRI was calculated using the following formula[9]:

$$BRI = 364.2 - 365.5 \times \sqrt{1 - (WC/2\pi)^2} / (0.5 \times height)^2$$

The BAI was calculated, as follows[10]:

$$[HC\ (cm) \div height\ (m)^{1.5}] - 18$$

The LAP was calculated, as follows[11]:

LAP = [(WC - 58) × triglycerides (TG)] for females and [(WC- 65) × TG] for males, where WC is expressed in cm, and TG in mmol/L.

The VAI was calculated by the following equation[12]:

{[WC/36.58 + (1.89 × BMI)] × (TG/0.81) × (1.52/high density lipoprotein cholesterol (HDL-c)} for women, and {[WC/39.68+ (1.88 × BMI)] × (TG/1.03) × (1.31/HDL-c)} for men, where WC is expressed in centimeters, BMI in kg/m^2, and TG and HDL-c levels in mmol/L.

The CMI was calculated, as follows[13]:

CMI = TG/HDL-c × WHtR, where TG and HDL-c are expressed in mmol/L.

The venipuncture was performed in the morning after at least 8 hours of fasting. Samples of whole blood in K_2EDTA tubes were used for HbA1c measurement, whereas samples in serum clot activator tubes were collected for the determination of lipid parameters, glucose, and hsCRP.

The latter samples were left to clot and, after half an hour, were centrifuged for 10 minutes at 3,000×g at ambient temperature. Serum lipid parameters and glucose levels were determined spectrophotometrically, whereas HbA1c levels were measured immunoturbidimetrically. All analyses were performed using a Roche Cobas c501 chemistry analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Serum hsCRP levels were measured nephelometrically by using a Behring Nephelometer Analyzer (Marburg, Germany).

Statistical Analysis

Data distribution was analyzed using the Kolmogorov-Smirnov test. Normally distributed data are presented as mean ± standard deviation (SD) and were compared using Student's *t*-test. Data with skewed distribution are presented as median (interquartile range) and were compared using the Mann-Whitney U-test. Categorical data were analyzed using the Chi-square test for contingency tables and are presented as absolute frequencies. Correlations between HbA1c and other clinical data were assessed using Spearman's correlation analysis and presented as a correlation coefficient (ρ). The associations between prediabetes (categorical dichotomous variables: 0, control group; 1, prediabetes) and traditional and derived anthropometric markers (independent, continuous variables) were examined using univariate and multivariate binary logistic regression analyses. Confounders included categorical data that were significantly different between the tested groups and continuous variables that were significantly correlated with HbA1c but did not enter equations for anthropometric index calculations. Data are presented as Odds Ratios (OR) and 95% Confidence Intervals (CI). The diagnostic performance of anthropometric markers in discriminating participants with prediabetes from controls was analyzed using a Receiver Operating Characteristic (ROC) curve. Data regarding this analysis are presented as area under the curve (AUCs), 95% CI, and standard error (SE).

Principal component analysis (PCA) with varimax rotation was employed to determine the adequate number of factors, consisting of traditional anthropometric and lipid status markers and separately derived anthropometric markers. Factor extraction was performed for eigenvalues greater than 1. The criterion for inclusion of variables in distinct factors was factor loadings larger than or equal to 0.5. Scores for factors were calculated in the PCA and used as independent variables in univariate and multivariate binary regression analyses to test the statistical significance of prediabetes predictors.

Statistical analyses were performed using SPSS (version 22.0; IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$.

Results

Table I shows the demographic characteristics and laboratory markers of the study groups. There were more male and younger examinees in the control group than in the prediabetic group. Prediabetic examinees had higher WC, TG, glucose, and HbA1c levels than controls. However, the control group had higher HDL-c levels than the prediabetic group. Prediabetics consumed more antihypertensives than the controls.

All derived anthropometric markers were significantly higher in the prediabetic group than in the control group, except for BAI (Table II).

In Table III, we present the correlation coefficients between HbA1c and all tested markers. HbA1c was positively correlated with age, weight, height, WC, HC, BMI, WHtR, WHipR, BRI, CMI, VAI, LAP, SBP, DBP, TC, LDL-c, TG, glucose, and HbA1c, and negatively correlated with HDL-c.

Furthermore, we investigated whether the traditional and derived anthropometric mark-

Table I. Clinical markers of tested population.

	Control group	Prediabetic group	*p*
N (male/female)	609 (162/447)	177 (72/105)	< 0.001
Age, years	59 (51-67)	64 (58-71)	< 0.001
Weight, kg	79 (69-89)	81 (73-90)	0.030
Height, m	168 (162-174)	168 (162-176)	0.676
WC, cm	95 (87-101)	97 (91-104)	0.001
HC, cm	105 (100-110)	106 (102-111)	0.140
SBP, mmHg	130 (120-139)	135 (128-140)	< 0.001
DBP, mmHg	79 (70-85)	80 (75-88)	0.001
Smoking habits, (Smoker/Non-smoker)	137/472	49/128	0.153
Hypolipemics (Yes/No)	143/466	47/130	0.401
Antihypertensives (Yes/No)	329/280	115/62	0.010
TC, mmol/L	5.7 (4.9-6.5)	5.8 (4.9-6.6)	0.216
HDL-c, mmol/L	1.5 (1.2-1.8)	1.3 (1.1-1.6)	< 0.001
LDL-c, mmol/L	3.4 (2.7-4.0)	3.6 (2.7-4.3)	0.082
TG, mmol/L	1.4 (1.1-1.9)	1.7 (1.2-2.5)	< 0.001
Glucose, mmol/L	5.6 (5.3-5.9)	6.5 (6.1-6.8)	< 0.001
HbA1c, %	5.1 (4.9-5.3)	5.8 (5.7-6.0)	< 0.001
HsCRP, mg/L	1.1 (0.6-2.0)	1.3 (0.6-2.6)	0.054

Data are presented as median (interquartile range) and were compared using the Mann-Whitney test. WC-Waist circumference; HC-Hip circumference; SBP-Systolic blood pressure; DBP-Diastolic blood pressure; TC-Total cholesterol; HDL-c-High-density lipoprotein cholesterol; LDL-c-Low-density lipoprotein cholesterol; TG-Triglycerides; HbA1c-Glycated hemoglobin; hsCRP-High sensitivity C-reactive protein.

ers were associated with prediabetes (Table IV). Univariate binary regression analysis revealed positive associations between prediabetes and WC, WHtR, WHipR, BRI, CMI, VAI, and LAP, as demonstrated by the following OR: 1.026, 46.282, 23.281, 1.160, 1.620, 1.145, and 1.007, respectively. Due to the high upper limit of the 95% CI, WHtR and WHipR were not assessed in the multivariate binary regression analysis. Except for BRI, the other indices (WC, CMI, VAI, and LAP) maintained independent predictions of prediabetes.

The discriminatory abilities of the anthropometric markers for prediabetes were examined using ROC analysis. All calculated AUCs for anthropometric markers were lower than 0.75, indicating their low discrimination potential towards prediabetes[18] (Table V).

Principal component analysis (PCA) was applied separately to classify traditional anthropometric and lipid status markers on one side and derived anthropometric markers on the other and to determine their relationship with prediabetes. In the first PCA performed on traditional anthro-

Table II. Derived anthropometric markers in the tested population.

	Control group	Prediabetic group	*p*
BMI, kg/m^2	27.7 (25.1-30.9)	28.6 (26.1-31.6)	0.024
WHtR	0.56 (0.52-0.60)	0.57 (0.53-0.62)	0.002
WHipR†	0.89 ± 0.08	0.89 ± 0.07	0.004
BAI	30.3 (27.0-33.4)	30.2 (26.7-34.9)	0.407
BRI	4.53 (3.71-5.48)	4.80 (3.98-5.80)	0.002
CMI	0.51 (0.33-0.86)	0.76 (0.46-1.25)	< 0.001
VAI	1.65 (1.09-2.54)	2.28 (1.37-3.65)	< 0.001
LAP	48.26 (31.04-71.71)	61.05 (41.40-94.55)	< 0.001

Data are presented as median (interquartile range) and were compared using the Mann-Whitney test. †Data are presented as arithmetic mean ± standard deviation and were compared using Student's *t*-test. BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index.

Table III. Spearman's correlation analysis of HbA1c and other clinical markers.

	ρ	*p*
Age, years	0.200	< 0.001
Weight, kg	0.191	< 0.001
Height, m	0.086	0.016
WC, cm	0.232	< 0.001
HC, cm	0.140	<0.001
BMI, kg/m^2	0.173	<0.001
WHtR	0.205	< 0.001
WHipR	0.193	< 0.001
BAI	0.033	0.356
BRI	0.205	< 0.001
CMI	0.233	< 0.001
VAI	0.179	< 0.001
LAP	0.234	< 0.001
SBP, mmHg	0.147	< 0.001
DBP, mmHg	0.171	< 0.001
TC, mmol/L	0.081	0.023
HDL-c, mmol/L	-0.191	< 0.001
LDL-c, mmol/L	0.102	0.004
TG, mmol/L	0.174	< 0.001
Glucose, mmol/L	0.734	< 0.001
HsCRP, mg/L	0.095	< 0.001

Data are presented as correlation coefficient Rho (ρ). WC-Waist circumference; HC-Hip circumference; BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index; SBP-Systolic blood pressure; DBP-Diastolic blood pressure; TC-Total cholesterol; HDL-c-High-density lipoprotein cholesterol; LDL-c-Low-density lipoprotein cholesterol; TG-Triglycerides; HbA1c-Glycated hemoglobin; hsCRP-High sensitivity C-reactive protein.

pometric and lipid status markers, the sample adequacy given by the Keiser-Meier-Olkin measure was not sufficient (KMO index = 0.338). However, the Bartlett's test of sphericity was significant (p<0.001). These factors are listed in Table VI.

Considering that the KMO index was inadequate, further statistical analyses of the factors listed in Table VI were not conducted.

In the second PCA performed on the derived anthropometric markers, sample adequacy was confirmed using the Keiser-Meier-Olkin measure (KMO index = 0.666). The Bartlett's test for sphericity was significant (p<0.001).

This PCA extracted three significant factors, with 96% of the explainable variation in the investigated markers (Table VII). The first factor (Traditional and Non-traditional/non-lipid anthropometric-related factors) explained 42% of the total variance and was associated with positive loadings of BMI, BRI, BAI, and WHtR. The second factor (non-traditional anthropometric/lipid-related factor) explained 35% of the variance and was associated with positive loadings of VAI, CMI, and LAP. The third factor (WHipR-related factor) explained 19% of the variance and was associated with a positive loading of WHipR.

Afterward, we applied binary logistic regression analysis to determine the factors associated with prediabetes by using scores derived from PCA. Significant predictive capability was demonstrated for non-traditional anthropometric/lipid-related factors and WHipR-related factors for prediabetes severity (OR=1.334 and OR=1.202, respectively). Increased non-traditional anthropometric/lipid-related factors were associated with a 1.334 times greater probability, and WHipR-related factors were associated with a 1.202 times greater probability of prediabetes onset. However, only non-traditional anthropometric/lipid-related factors (i.e., VAI, CMI, and LAP) demonstrated an independent significant posi-

Table IV. Odds ratios (OR) after univariate and multivariate binary logistic regression analysis for anthropometric markers predicting abilities towards HbA1c

Predictors	Unadjusted OR (95% CI)	*p*
Weight	1.010 (0.999-1.021)	0.065
Height	1.003 (0.986-1.021)	0.690
WC	1.026 (1.011-1.042)	0.001
HC	1.018 (0.998-1.038)	0.074
BMI	1.016 (0.990-1.043)	0.236
WHtR	46.282 (3.842-557.527)	0.003
WHipR	23.281 (2.558-211.864)	0.005
BAI	1.007 (0.985-1.030)	0.524
BRI	1.160 (1.041-1.294)	0.007
CMI	1.620 (1.274-2.058)	< 0.001
VAI	1.145 (1.056-1.242)	0.001
LAP	1.007 (1.003-1.011)	< 0.001
Models	**Adjusted OR (95% CI)**	***p***
WC	1.028 (1.008-1.048)	0.005
BRI	1.061 (0.947-1.189)	0.305
CMI	1.619 (1.273-2.060)	< 0.001
VAI	1.148 (1.059-1.245)	0.001
LAP	1.006 (1.002-1.010)	0.001

Model confounders: age, antihypertensives, and hsCRP.WC-Waist circumference; HC-Hip circumference; BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index.

Table V. ROC analysis for anthropometric markers discriminatory abilities regarding prediabetes.

Predictors	AUC (95% CI)	SE	p
BMI, kg/m^2	0.556 (0.508-0.603)	0.024	0.024
WC, cm	0.581 (0.534-0.627)	0.024	0.001
WHtR	0.578 (0.532-0.625)	0.024	0.002
WHipR	0.571 (0.524-0.618)	0.024	0.004
BAI	0.521 (0.471-0.570)	0.025	0.407
BRI	0.578 (0.532-0.625)	0.024	0.002
CMI	0.641 (0.594-0.687)	0.024	< 0.001
VAI	0.623 (0.575-0.671)	0.025	< 0.001
LAP	0.614 (0.567-0.661)	0.024	< 0.001

WC-Waist circumference; BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index.

Table VI. Traditional anthropometric and lipid status related factors extracted by principal component analysis with variables' loadings and percent of variability.

Factors	Variables (loadings)	Factor variability
Traditional anthropometric related factor	Weight (0.914) WC (0.893) HC (0.8374)	35%
Total cholesterol/LDL-c related factor	TC (0.996) LDL-c (0.961)	30%
Triglycerides/HDL-c related factor	TG (0.802) HDL-c (-0.897)	22%

WC-Waist circumference; HC-Hip circumference; TC-Total cholesterol; HDL-c-High-density lipoprotein cholesterol; LDL-c-Low-density lipoprotein cholesterol; TG-Triglycerides

Table VII. Derived anthropometric-related factors extracted by principal component analysis with variables' loadings and percent of variability.

Factors	Variables (loadings)	Factor variability
Traditional and Non-traditional/non-lipid anthropometric related factor	BMI (0.939) BRI (0.888) BAI (0.837) WHtR (0.864)	42%
Non-traditional anthropometric/lipid related factor	VAI (0.981) CMI (0.977) LAP (0.908)	35%
WHipR related factor	WHipR (0.967)	19%

BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index.

tive relationship with prediabetes in multivariate binary regression analysis. Increased non-traditional anthropometric/lipid-related factor was associated with a 1.349 times greater probability of prediabetes onset when confounders were age, hsCRP, and antihypertensive drugs. The results of these analyses are presented in Table VIII.

Discussion

To the best of our knowledge, the present study is the first to include a more thorough statistical approach (i.e., PCA) to identify the potential relationships between traditional and non-traditional anthropometric parameters and prediabetes. PCA

Table VIII. Univariate and multivariate binary regression analysis of PCA factors in prediction of prediabetes.

Predictors	Unadjusted OR (95% CI)	p
Traditional and Non-traditional/non-lipid anthropometric related factor (i.e. BMI, BRI, BAI and WHtR)	1.111 (0.949-1.302)	0.190
Non-traditional anthropometric/lipid related factor (i.e. VAI, CMI and LAP)	1.334 (1.130-1.576)	0.001
WHipR related factor	1.202 (1.010-1.431)	0.038
Models	**Adjusted OR (95% CI)**	**p**
Non-traditional anthropometric/lipid related factor (i.e., VAI, CMI and LAP)	1.349 (1.141-1.596)	< 0.001
WHipR related factor	1.107 (0.923-1.235)	0.272

Model confounders: age, antihypertensives, and hsCRP. BMI-Body mass index; WHtR-Waist-to-Height ratio; WHR-Waist-to-Hip ratio; BAI-Body adiposity index; BRI-Body roundness index; CMI-Cardiometabolic index; VAI-Visceral adiposity index; LAP-Lipid accumulation product index.

was used to identify groups with a smaller number of factors that were significantly correlated with prediabetes. We have demonstrated that some derived anthropometric indices, such as VAI, CMI, and LAP, are advantageous over the other examined non-traditional indices (i.e., BAI and BRI) for prediabetes discrimination, suggesting that a combination of anthropometric and lipid parameters can provide more information on cardiometabolic risk than if only anthropometric indices are combined. Moreover, the former (i.e., VAI, CMI, and LAP) were shown to be superior to all examined traditional anthropometric measurements (i.e., WC, BMI, WHtR, and WHipR) in the discrimination of patients with prediabetes. To further confirm this relationship, among several PCA-extracted significant factors, only non-traditional anthropometric/lipid-related factors (i.e., VAI, CMI, and LAP) showed an independent significant positive relationship with prediabetes in multivariate binary regression analysis. Increased non-traditional anthropometric/lipid-related factor (i.e., VAI, CMI, and LAP) was associated with a 1.349 times higher probability of prediabetes onset (after adjustment for confounders, such as age, hsCRP, and antihypertensive drugs).

Previous studies[14,16-18] have examined the association between derived/non-traditional anthropometric indices and cardiometabolic risk, but studies dealing with the relationship between the former and prediabetes are scarce, as the majority of them have been investigated in individuals with T2D. In addition, previous studies[14-16,19,20] included a smaller number of non-traditional parameters than the current study. Since discrepant results were presented in previous reports[21], it is assumed that besides sample size and different duration of obesity, some ethnic differences might be the reason for such inconsistencies[19]. This is the first study conducted in the Montenegrin population (i.e., Caucasians) free of T2D. Indeed, a study[15] in the Chinese population showed that WC was superior to VAI in predicting both prediabetes and diabetes. In another Chinese study[16], during a 15-year follow-up (n=687 participants), VAI did not show a stronger power of discrimination for T2D than WC and BMI. A study[22] conducted among Canadians demonstrated that VAI had similar power of prediction VAI for T2D, as BMI and WC.

In contrast, a recent study[17] conducted in the Qatari population demonstrated a superior prediction ability of VAI over BMI and BAI. Additionally, BAI was found not to be predictive of T2D risk, which is in line with our results. Similarly, another study[23] showed that neither BRI nor BAI showed superiority over the other anthropometric indices (i.e., VAI, WC, BMI, and WHtR) for insulin resistance prediction in Chinese diabetes-free participants (n=570).

VAI and LAP were superior for prediabetes risk prediction compared to WC, WHipR, and BMI in the Asian Indian population in both, males and females[24]. Although the latter study included a smaller sample size than ours (n=83 participants with prediabetes and 84 age- and sex-matched healthy counterparts), they also suggested a better accuracy of parameters that include a combination of lipids and anthropometric indices as better discriminators of prediabetes than traditional anthropometric indices alone[24].

In a large nationwide study[20] of 7,347 Chinese

participants, those with a higher CMI at baseline exhibited a significantly higher risk of T2D onset. This relationship was also confirmed in a longitudinal study[20] during a 7-year follow-up. The association between CMI and hyperglycemia and T2D in both genders has also been confirmed in a large Japanese population study[13] (n=10,196).

The advantage of a combination of anthropometric and lipid parameters over traditional anthropometric parameters was also confirmed for metabolic dysfunction-associated fatty liver disease prediction[25,26], as well as for metabolic syndrome[27] discrimination.

Given the fact that visceral obesity is more related to cardiometabolic disturbances, traditional/conventional anthropometric indices (i.e., BMI, WC, WHtR, and WHipR) may not be sufficient to discriminate patients with increased cardiometabolic risk, such as prediabetes, because of their inability to differentiate fat mass from lean mass[8,28].

The dysfunctional relationship between obesity, dyslipidemia, insulin resistance, and hyperglycemia can be attributed to several mechanisms. Visceral adipose tissue is more active in hormonal and metabolic processes than is subcutaneous adipose tissue. The adipose tissue of the visceral region secretes a large number of adipokines and cytokines that play a key role in the disruption of insulin signaling pathways, leading to the progression of insulin resistance, glucose intolerance, T2D, and cardiovascular diseases[28].

Insulin resistance favors atherogenic dyslipidemia in patients with diabetes due to higher synthesis of free fatty acids[29]. Moreover, increased lipolysis and free fatty acid flux in the liver leads to *de novo* hepatic lipogenesis, hepatic TG accumulation, and hepatic insulin resistance, which is characterized by enhanced gluconeogenesis and glycogenolysis, with increased endogenous glucose synthesis and progression to non-alcoholic fatty liver disease[30,31]. Insulin resistance also affects skeletal muscles with decreased glucose uptake due to diminished GLUT4 translocation and higher glucose levels in circulation[28].

Strengths and Limitations

The strength of the present study lies in the fact that it is the first study to apply PCA to further examine the relationship between traditional and non-traditional anthropometric indices and prediabetes, and the first such study that was conducted among Montenegrin adults. In addition, a relatively large sample size of examinees was included. A limitation of this study is its cross-sectional nature; thus, causality could not be confirmed. In addition, participants with prediabetes were older than the control group, and among the examined population, some participants used medications that might have affected the results. However, adjustments were made for all confounders. Since only the Montenegrin population (i.e., Caucasians) was examined in the present study, these results cannot be applied to other ethnic groups.

Conclusions

The derived anthropometric indices, CMI, VAI, and LAP, could be superior to BAI and BRI, and conventional anthropometric parameters to discriminate patients with prediabetes in the adult population. Prospective trials are needed to confirm our results. Screening for visceral obesity (determined by higher CMI, VAI, and LAP) should be included in primary care settings to prevent undesirable consequences such as diabetes, since these parameters are low-cost and easily obtainable.

Conflict of Interest

The authors declare that they have no conflict of interests.

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Ethics Approval

The Ethical Committee of the Primary Health Care Center where the study was conducted gave the approval (05/01-E.K.-4692/1).

Informed Consent

An informed consent was signed by each participant.

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Authors' Contributions

All authors contributed to the conception and design of this study. Material preparation, data collection, and laboratory analyses were performed by AK. Statistical analyses were performed by AN. The first draft of the manuscript was written by AK, and all the authors commented on the previous versions of the manuscript. All authors have read and approved the final version of the manuscript.

Data Availability

The data will be available upon reasonable request (contact person: aleksandranklisic@gmail.com).

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