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Lipid accumulation product and visceral adiposity ındex: two new indices to predict metabolic syndrome in chronic kidney disease

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Abstract. – OBJECTIVE: The aim of this study was to assess the ability of lipid accumulation product (LAP) and visceral adiposity index (VAI) to predict metabolic syndrome (MetS) in patients with chronic kidney disease (CKD). We also aimed to determine whether VAI and LAP indices are superior to traditional body indices such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR).

PATIENTS AND METHODS: This study was performed by retrospectively scanning the files of patients with stage 3-5 chronic renal failure who came for nephrology outpatient follow-up between January 2017 and December 2017. Metabolic syndrome was identified using the 2009 harmonized criteria. The receiver operating characteristic curve (ROC) was used to compare the area under the ROC curve (AUC) of each index.

RESULTS: 247 patients were included in the analyses. The prevalence of MetS was 80.9%. LAP was determined as the optimal predictor in chronic kidney disease patients, with 0.864 AUC in females and 0.908 AUC in males. Optimal cut-off values for LAP were 33.5 in females and 36.6 in males. VAI was the second most optimal predictor, with 0.856 AUC in females and 0.888 AUC in males. Optimal cut-off values for VAI were 2.24 in females and 1.56 in males.

CONCLUSIONS: LAP and VAI are effective indices for the prediction of MetS in patients with chronic kidney disease; LAP is the best index for the determination of MetS in both men and women.

Key Words:
Chronic kidney disease, Metabolic syndrome, Lipid accumulation product, Visceral adiposity index.

Introduction

Chronic renal disease and metabolic syndrome are health problems worldwide. The prevalence of metabolic syndrome is rather high at 65%[1]. Moreover, metabolic syndrome is an important risk factor in terms of the development and progression of chronic renal disease[2-5]. Also, obesity is associated with a significant increase in chronic renal disease[6]. There is increasing evidence that abdominal visceral fat has a role in the development of MetS[7,8]. Body mass index (BMI) is commonly used in the assessment of obesity[9,10]. There is strong evidence indicating that BMI is not the ideal obesity measurement, particularly when it is used for the assessment of disease risk[11]. BMI does not distinguish between muscle mass and fat mass in measurements. Therefore, an individual with increased muscle mass and normal fat mass can have increased BMI and be diagnosed erroneously as overweight or obese. BMI does not consider the distribution of body fat. Therefore, additional anthropometric indices are required in order to assess the abdominal adipose accumulation. Waist-to-height ratio (WHtR) was suggested as an effective anthropometric index for the assessment of abdominal adiposity in non-dialysis chronic kidney disease[12]. While abdominal visceral fat determined with computerized tomography was strongly correlated with waist circumference (WC), it showed lower correlation with BMI in non-dialysis patients with chronic kidney disease[13]. Visceral adiposity index (VAI) and lipid accumulation product (LAP) are two new indices that are used for the determination of MetS. The Visceral Adiposity Index (VAI) is gender-specific, based on simple anthropometric (BMI and WC) and functional (triglycerides (TG) and HDL cholesterol (HDL)) parameters, and is an indicator of fat distribution and visceral adipose functionality. VAI was shown to be indepen-

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dently related to both cardiovascular and cerebrovascular events[14]. In hemodialysis patients, VAI was assessed as the optimal method for the measurement of visceral adiposity in long-term cardiovascular outcomes and all-cause mortality assessment and was found to be superior to WC and WHtR[15]. Moreover, VAI was shown to be related to subclinical atherosclerosis[16] and MetS[17]. LAP is a parameter that is calculated based on WC and serum triglyceride levels. The LAP index is strongly related to MetS in the general population[18]. It is also related to cardiovascular disease and all-cause mortality[19]. We performed this cross-sectional study in order to evaluate the ability of anthropometric measurements (VAI and LAP index) to predict MetS in patients with chronic kidney disease. At the same time, we aimed to determine whether the VAI and LAP indices are superior to BMI, WC, WHR, and WHtR.

Patients and Methods

This retrospective study was performed by scanning the files of the patients under follow-up in the nephrology clinic. Ethics Committee approval was obtained (2018/06). Patients with stage 3-5 CKD who came for nephrology outpatient follow-up between January-December 2017 were included in the study. Creatinine clearance was calculated with the MDRD formula[20]. Patients under 18 years old, pregnant patients, hemodialysis patients, peritoneal dialysis patients, and patients who had undergone renal transplantation were excluded from the study. Also, patients with missing anthropometric measurements and patients who have not fasted for at least 12 hours prior to exam were excluded. Blood samples from the cubital vein were taken into tubes with heparin after overnight fast. Biochemical parameters were measured using an Abbott Architech C16000 (Abbott Laboratories, Chicago Abbott Park IL, USA) auto-analyzer. Age, height, weight, waist circumference, hip circumference, total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, creatinine, systolic blood pressure, diastolic blood pressure, concomitant medicines, blood sugar and, if available, HbA1c, were recorded from the patient files. Blood pressure had been measured using a Mobil-O-Graph NG (İ.E.M GmbH, Cockerillstraße, Stolberg, Germany) arteriographic device in all patients.

Anthropometric Measurements

Body mass index (BMI), in kg/m², was calculated as weight divided by height squared. Waist circumference (WC) was measured along the line lying midway between the iliac crest and the costal margin on the midaxillary line. WHR was calculated as the ratio of the waist and hip circumferences. WHtR was calculated by dividing the waist circumference by height. In the following formulas, the value of WC in cm and values of triglyceride and HDL in mmol/l were used.

Visceral adiposity index was calculated as follows:

Males: $VAI = (WC/(39.68 + (1.88 \times BMI))) \times (TG/1.03) \times (1.31/HDL)$

Females: $VAI = (WC/(36.58 + (1.89 \times BMI))) \times (TG/0.81) \times (1.52/HDL)$

Lipid accumulation product was calculated as follows:

Males: $LAP = (WC-65) \times TG$

Females: $LAP = (WC-58) \times TG$

Metabolic Syndrome Definition

MetS was defined using the new Harmonized IDF criteria: abdominal obesity (WC > 94 cm for males and > 80 cm for females) has to be present and at least 2 of the following 4 parameters should be present: hypertension (SBP > 130 mm Hg and/or DBP > 85 mm Hg) or history of antihypertensive use; hypertriglyceridemia (≥ 150 mg/dl) or presence of treatment for this disorder; low HDL-C (< 40 mg/dl in males and < 50 mg/dl in females) or presence of treatment for this disorder; and high fasting plasma glucose (> 100 mg/dl) or presence of diagnosis of T2DM[21].

Statistical Analysis

The data distribution was assessed using the Kolmogorov–Smirnov test. The variables are displayed as mean ± standard deviation, median (interquartile range), or count (percentage) according to their types. Differences between two groups were determined using Student's *t*-test or Mann–Whitney U test, as appropriate. Chi-squared test was used to compare categorical data. Spearman correlation analysis was used to determine the correlation between MetS and anthropometric measures. We used the area under the receiver-operating characteristic curve (AUC) and 95% confidence intervals (CI) to assess the ability of each anthropometric measure to predict MetS. The Youden's index was calculated and used to determine the cut-offs that

gave the best combination of sensitivity and specificity. A p-value of < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA).

Results

A total of 247 patients were included in the study. The mean age of the participants was 55.9 ± 12.3 years, and 53% of the patients were male. Median eGFR (estimated glomerular filtration rate) was 28 ml/min. 80.9% of the individuals were defined as having MetS. Clinical characteristics of the study population according to MetS status are shown in Table I. Although the difference was not statistically significant, MetS prevalence was higher in women (78% in males and 84.6% in females, p = 0.198). Renal functions were similar in both groups (p = 0.087). There were no differences between the two groups in terms of systolic blood pressure, diastolic blood pressure, and hypertension prevalence (p > 0.05). When patients with MetS were compared to patients without MetS, patients with MetS were older, and their fasting blood sugar, diabetes mellitus prevalence, BMI, WC, WHR, WHtR, total cholesterol, LDL cholesterol, and VAI and LAP indices were significantly higher (Table I). HDL cholesterol was significantly lower in patients with MetS compared to patients without MetS (p < 0.001).

Anthropometric measurements (VAI, LAP, BMI, WC, WHtR, WHR) and Spearman rank test results of MetS are shown in Table II. LAP and VAI provided the highest correlation with MetS in both sexes (LAP (r = 0.586 for males, r = 0.455 for females, p < 0.001 for both) and VAI (r = 0.558 for males, r = 0.447 for females, p < 0.001 for both)). WHR showed the lowest correlation with MetS in both sexes (r = 0.340 for males, p < 0.001; r = 0.239 for females, p = 0.009).

In males, among the six anthropometric measurements, the highest AUC was for LAP (AUC = 0.908). VAI followed that (AUC = 0.888). Concordantly, LAP had the highest Youden's index of 0.68 (sensitivity: 81.8%, specificity: 86.2%), with the optimal cut-off of 36.6. VAI had a Youden's index of 0.63 (sensitivity: 84.3%, specificity: 79.3%), with the optimal cut-off of 1.56. The AUCs were similar between VAI, LAP, WC, and WHtR (p > 0.05) (Figure 1 and Table III).

In females, among the six anthropometric measurements, the highest AUC was for LAP (AUC = 0.864). VAI followed that (AUC = 0.856). VAI had the highest Youden's index of 0.61 (sensitivity: 72.4%, specificity: 88.9%), with the optimal cut-off of 2.24. LAP had a Youden's index of 0.55 (sensitivity: 93.9%, specificity: 61.1%), with the optimal cut-off of 33.5. The AUCs were similar

Table I. Clinical characteristics of study population.

Variables	Non-MetS group (n=47)	MetS Group (n=200)	p
Age (years)	49.6±13.7	57.5±11.4	0.000
Men/Women	28/19	102/98	0.198
eGFR (ml/dk)	29 (18)	27 (17)	0.087
Systolic blood pressure (mmHg)	133.7 ±14.7	139.9±21.0	0.09
Diastolic blood pressure (mmHg)	90.4±11.4	88.6±13.5	0.396
Fasting blood glucose (mg/dL)	91 (11)	103 (31)	0.000
Diabetes mellitus (%)	4 (8.5)	66 (33)	0.001
Hypertension (%)	38 (81)	185 (92.5)	0.059
BMI (kg/m²)	25.7 (7.5)	30.0 (7.5)	0.000
WC (cm)	86.1±13.6	100.7±13.3	0.000
WHR	0.93±0.12	0.98±0.14	0.035
WHtR	0.52±0.08	0.62±0.09	0.000
Total cholesterol (mg/dL)	193.2±38.4	214.8±53.8	0.010
LDL cholesterol (mg/dL)	123.6±33.6	136.7±41.8	0.046
Triglyceride (mg/dL)	101.0 (41)	180.5 (121.2)	0.000
HDL cholesterol (mg/dL)	48.0 (17)	38.0 (12)	0.000
Visceral adiposity index	1.24 (0.87)	3.27 (2.8)	0.000
Lipid accumulation product index	27.5 (23.9)	74.6 (68.1)	0.000

Abbreviations: MetS: metabolic syndrome; eGFR: estimated glomerular filtration rate; BMI: body mass index; WC: waist circumference; WHR: waist hip ratio; WHtR: waist to height ratio.

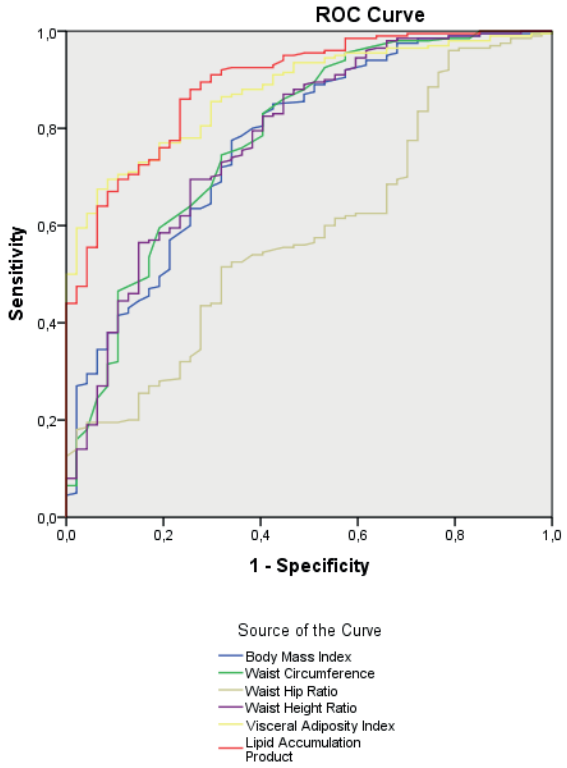

Figure 1. ROC curves for each variable for the screening of metabolic syndrome in women and men

between VAI, LAP, WC, and WHtR ($p > 0.05$) (Figure 1 and Table III).

Discussion

MetS was detected in 80.9% of the patients with stage 3-5 chronic kidney diseases in this study. The prevalence of MetS was reported to be 65% in the Chronic Renal Insufficiency Cohort (CRIC) study[1], while the prevalence of MetS was found to be 75.3% in hemodialysis patients according to Harmonizing the Metabolic Syndrome Criteria[22]. Although the reported prevalence of MetS differs according to various definitions of MetS, exclusion criteria, and ethnicity, MetS is common in patients with chronic kidney disease. As far as we know, there is no study examining the relationship of MetS with new anthropometric indices in chronic kidney disease, despite the fact that MetS is common in this patient group. We determined that the LAP index is the optimal index for prediction of MetS in this patient group. The LAP index had the highest AUC value both in females and males (0.864 and 0.908, respectively). Moreover, when the correlation of anthropometric indices with MetS was considered, the highest correlation was the LAP index in both females and males (r = 0.45 and r = 0.58, respectively). These findings support that the LAP index is a good indicator for the prediction of MetS. LAP demonstrated a strong predictive accuracy for MetS in previous studies[23,24]. In a study conducted on 3752 Kazakh adults, 6 anthropometric and 6 atherogenic indices were compared using different MetS criteria, and LAP was found to be superior to the other indices for the prediction of MetS as defined according to the ATP III and harmonized criteria[25]. In MetS screening in Kenya, LAP had the maximal ability with the highest AUC level 0.88 for predicting MetS among the four indices (LAP, VAI, BMI, WC)[26]. In a community-based study performed with 10029 participants, when VAI, WHtR, and body adiposity index were compared, LAP was the most accurate index for defining MetS in both sexes. Moreover, in this study, the optimal cut-off values were reported as 34.7 in males and 27.4 in females for MetS screening according to the harmonized criteria[27]. This cut-off value was found as 39.9 in males and 49.7 in females in an Iranian population[23]. The cut-off value

Table II. Spearman rank test of anthropomethric measures (VAI, LAP, BMI, WC, WHtR, WHR) and metabolic syndrome.

	VAI	LAP	BMI	WC	WHtR	WHR
Men (n=131)						
r	0.558	0.586	0.407	0.455	0.435	0.340
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Women (n=117)						
r	0.447	0.455	0.315	0.304	0.311	0.239
p-value	<0.001	<0.001	0.001	0.001	0.001	0.009

VAI: Visceral Adiposity Index; LAP: Lipid Accumulation Product; BMI: body mass index; WC: waist circumference; WHtR: waist to height ratio; WHR: waist hip ratio.

Table III. The cut-off, sensitivities, specificities, Youden's index and area under curve of each variable for the screening of metabolic syndrome in men and women.

Variables	Cut-off	Sensitivity	Specificity	Youden's index	AUC (95%CI)	p
Men						
WC	92.0	76.7	72.4	0.49	0.817 (0.740~0.879)	0.000
WHtR	0.52	83.3	65.5	0.48	0.803 (0.724~0.867)	0.000
WHR	0.96	92.2	51.7	0.49	0.737 (0.654-0.810)	0.000
BMI	26.2	76.5	68.9	0.45	0.783 (0.703-0.850)	0.000
VAI	1.56	84.3	79.3	0.63	0.888 (0.821~0.936)	0.000
LAP	36.6	81.5	86.2	0.68	0.908 (0.846~0.952)	0.000
Women						
WC	87.0	82.8	61.1	0.44	0.743 (0.654~0.820)	0.000
WHtR	0.59	71.7	72.2	0.44	0.749 (0.660~0.824)	0.000
WHR	0.77	91.9	50.0	0.42	0.691 (0.599-0.773)	0.02
BMI	26.6	88.7	50.0	0.38	0.751 (0.663-0.827)	0.000
VAI	2.24	72.4	88.9	0.61	0.856 (0.779-0.914)	0.000
LAP	33.5	93.9	61.1	0.55	0.864 (0.789-0.921)	0.000

AUC: area under curve; CI: confidence interval; WC: waist circumference; WHtR: waist to height ratio; VAI: visceral adiposity index; LAP: lipid accumulation product; WTI: waist circumference-triglyceride index.

for the prediction of MetS in individuals over 50 years was reported as 31.6 in both[28]. These divergent cut-off values could be the result of racial differences. Though there is no specified cut-off value in chronic kidney disease, we found the cut-off value as 33.5 in females and 36.6 in males. VAI had the second highest AUC value for MetS in both females and males. VAI is a more complex parameter than triglyceride, which is used in the LAP index. To calculate VAI, waist circumference is used together with BMI and HDL. In concordance with previous studies, VAI was not superior to the LAP index for MetS screening in either females or males[27,29]. More attention has been drawn to visceral obesity in recent years[30], and abdominal obesity is central to the definition of MetS. It has been suggested that the abdominal visceral fat area, which is measured with MR, is the best indicator for the assessment of abdominal obesity[31]. Nevertheless, this method is not appropriate for routine use, as it is expensive and has serious risks for patients with chronic kidney disease. LAP and VAI are effective indices for the prediction of metabolic obesity[32], as they were found to be correlated with MetS[25]. It is rather important to reduce the incidence of MetS in this patient group due to existing high cardiovascular risk. Early screening together with diet and lifestyle changes for MetS will be effective for this. Our study has some limitations. First, our study population was relatively small. Second, it was a retrospective study.

Conclusions

We found that MetS prevalence is high in patients with chronic kidney disease. LAP and VAI are effective indices for screening for MetS in patients with chronic kidney disease; LAP is the superior index for the determination of MetS in both females and males. Data from larger samples are needed to confirm these findings.

Conflict of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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