ORIGINAL RESEARCH

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A Novel Clinical Predictor of Metabolic Syndrome: Vascular Risk Age

Metabolik Sendromun Yeni Bir Klinik Belirleyicisi: Vasküler Risk Yaşı

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Abstract

Objective: Metabolic syndrome (MetS) promotes the development of diabetes mellitus (DM) and atherosclerotic cardiovascular disease (ASCVD). Predicting individuals who are at high risk for developing MetS is essential. Vascular risk age (VRA) is a clinical substitute for cardiovascular risk. In this study, we ascertained whether VRA is an indicator of MetS.

Method: This study involved 169 subjects (96 females, 73 males, aged 40-83 year) without any previous diagnosis of ASCVD or DM. MetS was diagnosed as stated by ATP III-2005 and IDF-2009. The SCORE2/SCORE2-OP 10-year fatal CVD risk and VRA were computed for all participants.

Results: The frequency of MetS based on the ATP III-2005 criteria was 40.2% overall, 39.6% in females, and 41.1% in males, while it was 47.9% in total, 43.8% in females, and 53.4% in males based on IDF-2009 criteria. VRA was significantly higher in cases with MetS in comparison to the cases without MetS (p<0.001), and it was associated with all components of MetS (WC, r=0.194, p=0.011; SBP, r=0.434, p<0.001; BDP, r=0.262, p=0.001; total-C, r=0.223, p=0.003; high-density lipoprotein-C, r=-0.307, p<0.001; TG, r=0.324, p<0.001; and FG, r=0.196, p=0.011). VRA was appeared to be a power-full predictor of MetS in area under the curve (AUC)-ROC curve analysis [AUC=0.658, 95% confidence interval (CI)= 0.576-0.740; for a cut-off of 54.0 years, Youden index=0.19, sensitivity=75.0%, and specificity of 45.0%], and logistic regression (odds ratio: 1.086, p=0.041, 95% CI=1.003-1.175).

Conclusion: VRA is an important and independent predictor of MetS and can be considered for clinical purposes.

Keywords: Atherosclerosis, atherosclerotic cardiovascular disease, diabetes mellitus, metabolic syndrome, vascular risk age

Öz

Amaç: Metabolik sendrom (MetS) varlığı diabetes mellitus (DM) ve aterosklerotik kardiyovasküler hastalık (ASKVH) oluşumunu tetikler. MetS gelişimi açısından yüksek risk altında olan bireylerin öngörülmesi önemlidir. Vasküler risk yaşı (VRA) kardiyovasküler riskin klinik bir göstergesidir. Bu çalışmada, VRA'nın MetS'nin bir göstergesi olup olmadığını tespit etmeyi amaçladık.

Yöntem: Çalışmaya daha önce ASKVH ve DM tanısı olmayan 169 kişi (96 kadın, 73 erkek, yaşları 40-83) dahil edildi. ATP III-2005 ve IDF-2009 kriterleri aracılığıyla MetS tanısı koyuldu. SCORE2/SCORE2-OP 10 yıllık ölümcül KVH riski ve VRA tüm katılımcılar için hesaplandı.

Bulgular: ATP III kriterlerine göre MetS sıklığı tüm popülasyonda %40,2, kadınlarda %39,6 ve erkeklerde %41,1 olarak saptanırken, IDF-2009 kriterlerine göre tüm popülasyonda %47,9, kadınlarda %43,8 ve erkeklerde 53,4 olarak saptandı. VRA MetS saptanan bireylerde MetS saptanmayan bireylere göre anlamlı olarak yüksek saptandı (p<0,001). Ayrıca VRA ile tüm MetS komponentleri arasında ilişki saptandı (WC, r=0,194, p=0,011; SBP, r=0,434, p<0,001; BDP, r=0,262, p=0,001; total-C, r=0,223, p=0,003; yüksek yoğunluklu lipoprotein-C, r=-0,307, p<0,001; TG, r=0,324, p<0,001; ve FPG, r=0,196, p=0,011). Eğri altında kalan (AUC)-ROC analizinde VRA'nın MetS'nin güçlü bir öngörücüsü olduğu görüldü [AUC=0,658, %95 güven aralığı (CI)=0,576-0,740; for a cut-off of 54,0 yaş, Youden indeks=0,19, sensitivite=%75,0, and spesifik %45,0], and logistic regresyon (olasılık oranı: 1,086, p=0,041, %95, CI=1,003-1,175).

Sonuç: VRA, MetS'ninn önemli ve bağımsız bir belirleyicisidir ve klinik amaçlarla düşünülebilir.

Anahtar kelimeler: Ateroskleroz, aterosklerotik kardiyovasküler hastalık, diyabet, metabolik sendrom, vasküler risk yaşı

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Introduction

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality worldwide (1,2). Hyperlipidemia, increased blood pressure, insulin resistance, visceral adiposity, and prothrombotic and proinflammatory states are risk factors for ASCVD. Conditions in which these risk factors are observed together are called metabolic syndrome (MetS) (3).

However, the frequency of MetS varies among different nations; approximately one-fourth of the community has MetS. Frequency ranges of 11.6-26.3% in Europe, 13.6-36.3% in the Middle East, and 18.8-43.0% in America have been reported (3). MetS is more prevalent in Turkey than in the United States, Korea, China, and Japan (3,4). A recent meta-analysis conducted by Abacı et al. (4) revealed that the rate of MetS in Turkey was 32.9% and 43.3%, based on IDF and ATP III criteria, respectively.

MetS is classified among the considerable risk factors for the development of type 2 diabetes mellitus and ASCVD (2,3). Thus, diagnosing MetS is an essential clinical implication in terms of these devastating diseases. MetS is diagnosed based on high blood pressure, high blood sugar, low high-density lipoprotein (HDL) level, high TG level, and waist circumference measurement. Age, race, weight, postmenopausal status, smoking, low income, sugar-based diet, and immobility are linked to MetS (5,6). Beyond these traditional risk factors, additional cardiovascular risk concepts such as metabolic age and vascular risk age (VRA) may predict the development of cardiometabolic diseases (7,8). VRA may be an alternative method of demonstrating cardiovascular risk. In other words, it is an expression of endothelial dysfunction and consequently atherosclerosis. VRA can assist individuals in shared preventive decision making.

Subjects with MetS are generally in the asymptomatic preclinical stages of atherosclerosis (1-8). In individuals with MetS, paying attention to the VRA can be essential in informing and shaping the clinician-patient discussion, detection of early atherosclerosis indicators, and primary prevention therapies. VRA in the setting of MetS is not introduced yet. In our study, we investigated whether VRA can be treated as a decisive factor of MetS.

Materials and Methods

Individuals who presented to the check-up clinics were eligible for this cross-sectional study. Subjects who were older than 18 years and who consented to participate were included in this study. Individuals with active infection, pregnancy, diabetes mellitus, renal disease with a GFR <60 mL/min/1.73 m^2, coronary heart disease, and heart failure were not included. Guidelines proposed in the Declaration of Helsinki were taken into account at all stages of the study. This study was authorized by a Clinical Research Ethics Committee of Kırklareli University (3/2022.K-42, date: 20.05.2022). Informed consent was obtained from all participants.

MetS diagnosis: The National Cholesterol Education Program Adult Treatment Panel III-2005 (ATP III) (9) and the International Diabetes Federation-2009 (IDF) (2) were used to diagnose MetS. The presence of any three of the following five criteria established the diagnosis of MetsS (1-Waist circumference ≥102 cm in men and ≥88 cm in females according to the ATP III, and ≥94 cm in men and ≥80 cm in females based of IDF-2009. 2-Triglycerides ≥150 mg/dL, 3-HDL cholesterol <40 mg/dL in males and <50 mg/dL in females, 4-Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure, 5-Fasting plasma glucose ≥100 mg/dL or drug treatment for elevated blood glucose). In the statistical analysis, we used only the ATP-III criteria as these are adjacent to the recommendations of the Turkish Society of Endocrinology and Metabolism in the context of the WC.

SCORE2/SCORE2-OP and VRA estimation: For participants aged 40-69 years, the high-risk countries SCORE2 (10) and for participants >70 years, the high-risk countries SCORE2-OP risk charts (11) were used to calculate the SCORE2/SCORE2-OP and VRA. Age, gender, current smoking status, total-C, HDL-C, non-HDL-C, and systolic BP levels were considered during the calculations.

To determine the VRA, the evaluated risk score was compared with the age at which risk was similar but all other risk factors were at optimum levels. For example, a 53-year-old smoker with an SBP of 170 mmHg, HDL-C 38 mg/dL, and total-C level of 270 mg/dL has a cardiovascular risk estimate of 21% according to the SCORE2 table for high-risk countries. The VRA of this person would be 76 years. Normally, a 76-year-old man with optimum risk factors (e.g. not smoking, a systolic blood pressure of 120 mmHg, and normal cholesterol levels) has 21% risk of CVD.

Anthropometrics: The weight, height, and WC information of the subjects were obtained. BMI and waist-to-height circumference were also calculated. WC was measured horizontally around the body at the upper border of the iliac crest in the standing position with a relaxed abdomen and arms at the sides.

Biochemical analysis: Venous blood was obtained after 12 h of fasting for measurement of the HbA1c, fasting glucose, and lipid panel. LDL-C was measured directly by a colorimetric method, other blood tests were performed using standard methods, and the same blood sample was used for all analyses. Non-HDL-C was counted asfollows: total cholesterol HDL-C=non-HDL-C.

Statistical Analysis

A histogram with a bell curve and one-sample Kolmogorov-Smirnov tests were used to assess the distribution. Mean ± standard deviation or median (interquartile range) was used to present continuous variables, and numbers and percentages were used to present categorical variables. We classified the participants into two groups according to their gender. Variations in baseline clinical characteristics between groups were evaluated by Mann-Whitney U and independent-samples t-test for continuous variables and the chi-square test for categorical variables. The Wilcoxon signed-rank test was applied to compare the chronologic and VRAs of the entire study population and subgroups. We performed Pearson correlation analysis to investigate the association of age surrogates with anthropometric parameters, MetS components, and SCORE2/SOCRE2-OP. In addition, ROC analysis was used to determine the predictability of VRA for MetS. Finally, we used logistic regression and tested several models to determine which factors better explained the probability of participants exhibiting MetS. The ultimate model comprised gender, chronologic age, VRA, and body mass index (BMI). We also presented odds ratios and 95% confidence intervals (CI) to measure the change in the probability of MetS when the value of an estimator increases by one unit. The primary endpoint of this study was to determine whether VRA could act as an explanatory variable of MetS. Sample size (n) was calculated using the single proportion population formula ($n=Z^2\ p\ (1-p)/d^2$, $n=1.96^2\ 0.43\ (0.57)/0.08^2$, n=148) where p; shows the prevalence of MetS in the population, which was reported as 43.3% according to the ATP III criteria (4), dis precision (8%), and Zis the statistic for a level of confidence, which equals 1.96 for a 95% CI. Based on this information, the sample size was determined to be 148 participants. Statistical analysis was performed using the software Statistical Package for Social Sciences (SPSS) (Inc., Chicago, Illinois, USA). Differences at the 2-sided p<0.05 level were considered statistically significant.

Results

From May 2021 to March 2022, 169 participants (females; 96, males; 73, aged; 40-83 years, with MetS: 68, without MetS: 101) were recruited for the study. In our analysis, the incidence of MetS as specified by the ATP III-2005 criteria was 40.2% overall, 39.6% in females, and 41.1% in males, whereas it was 47.9% in total, 43.8% in females, and 53.4% in males based on the IDF-2009 criteria. Table 1 shows the baseline characteristics for the entire sample and compares them with the MetS groups. The mean height, total-C, and LDL-C, along with the frequency of female gender and current smoking state, were not significantly different across the groups. Similarly, no significant difference was observed between the groups according to the median chronologic age. However, individuals with MetS were more likely to have a higher mean weight (p<0.001), MBI (p<0.001), WC (p<0.001), WHR (p<0.001), SBP (p<0.001) HDL (p<0.001), non-HDL-C (p=0.001), fasting glucose (p<0.001) and HbA1c (p<0.001). In addition, the median VRA (p<0.001), DBP (p<0.001), TG (p<0.001), and SCORE2/SCORE2-OP (p<0.001) along with the frequency of HT (p<0.001) and MetS-IDF2009 (p<0.001) were higher in participants with MetS. In contrast, the mean HDL-C (p<0.001) was higher in persons without MetS.

Our results also revealed that chronologic age was significantly correlated with VRA (p<0.001), WHR (p=0.003), height (p=0.019), SBP (p=0.006), FG (p=0.007) and SCORE2/SCORE2-OP (r=0.652, p<0.001). Contrast weight, height, BMI, WC, DBP, total-C, HDL-C, non-HDL-C, LDL-C, TG, and HbA1c were not significantly correlated with chronologic age. VRA was significantly correlated with weight (p=0.039), BMI (p=0.021), WC (p=0.011), WHR (p=0.031), SBP (p<0.001), BDP (p=0.001), total-C (p=0.003), HDL-C (p<0.001), non-HDL-C (p<0.001), LDL-C (p=0.001), TG (p<0.001), FG (p=0.011) and SCORE2/SCORE2-OP (r=0.995, p<0.001). Whereas, VRA was not correlated significantly with height and HbA1c. Our analysis showed that VRA was associated with almost all variables, including all constituents of MetS, as highlighted in Table 2.

ROC analysis was used to determine the predictability of the VRA for MetS (Table 3, Figure 1). VRA was a good predictor for MetS in the entire study population [area under the curve (AUC)=0.658, 95% CI 0.576-0.740), and a cut-off of 54.0 years was determined using a significant Youden index (Youden index=0.25, sensitivity=75.0%, and specificity of 45.0%). More significant results were determined when the data were specified to females. VRA was a better predictor for MetS in the female gender than in the entire

Table 1. General characteristics of the study subjects

	Entire sample	With MetS n=68	Without MetS n=101	p
Female n, %	96 (56.8%)	38 (55.9%)	58 (57.4%)	0.843
Male n, %	73 (43.2%)	30 (44.1%)	43 (42.6%)	0.843
Chronological age (year)	51 (40-83)*	53 (40-76)*	50 (40-83)*	0.126
Vascular risk age (year)	55 (40-80)*	56 (45-80)*	51 (40-80)*	<0.001
Weight (kg)	79.23±15.71	86.73±15.53	74.18±13.75	<0.001
Height (cm)	166.89±9.67	166.34±10.10	167.26±9.38	0.546
BMI (kg/cm^2)	28.42±5.05	31.35±4.96	26.45±4.07	<0.001
WC (cm)	95.86±12.24	102.65±9.92	91.29±11.56	<0.001
WHR	0.58±0.08	0.62±0.07	0.55±0.07	<0.001
SBP (mmHg)	126.36±14.96	133.88±15	121.29±12.69	<0.001
DBP (mmHg)	80 (60-100)*	85 (60-100)*	75 (60-92)*	<0.001
Total-C (mg/dL)	215.34±37.91	219.75±39.86	212.38±36.44	0.216
HDL-C (mg/dL)	58.05±16.94	50.12±11.87	63.39±17.79	<0.001
Non-HDL-C (mg/dL)	157.30±38.52	169.63±37.74	148.99±36.94	0.001
LDL-C (mg/dL)	139.74±30.88	144.28±30.46	136.68±30.93	0.117
TG (mg/dL)	120 (38-485)*	169 (41-485)*	102 (38-341)*	<0.001
Fasting glucose	97.41±10.08	102.01±10.64	94.31±8.40	<0.001
HbA1c	5.75±0.47	5.9±0.56	5.64±0.36	<0.001
SCORE2/SCORE2-OP %	4 (1-28)*	5 (1-26)*	3 (1-28)*	<0.001
Hypertension (%)	37 (21.9%)	28 (41.2%)	9 (9.8%)	<0.001
Current smoking n (%)	57 (33.7%)	18 (26.5%)	39 (38.6%)	0.102

* Data are presented as median and minimum-maximum;±, standard deviation, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WC: Waist circumference, WHR: Waist-to-height ratio, HDL: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, Total-C: Total cholesterol, HbA1c: Hemoglobin A1c, MetS: Metabolic syndrome, SCORE2/SCORE2-OP: Systemic coronary risk evaluation2-older person, TG: Triglyceride

Table 2. Association of vascular risk age with anthropometric parameters, components of metabolic syndrome, and SCORE2/SCORE2-OP

	Chronological age (year)	p	Vascular risk age (year)	p
Chronological age (year)	1		0.683	<0.001
Vascular risk age (year)	0.683	<0.001	1	
Weight (kg)	-0.003	0.973	0.159	0.039
Height (cm)	-0.180	0.019	0.047	0.540
Body mass index (kg/cm^2)	0.143	0.063	0.178	0.021
Waist circumference (cm)	0.132	0.086	0.194	0.011
Waist-to-height ratio	0.225	0.003	0.166	0.031
Systolic blood pressure (mmHg)	0.210	0.006	0.434	<0.001
Diastolic blood pressure (mmHg)	0.108	0.163	0.262	0.001
Total-C (mg/dL)	0.081	0.293	0.223	0.003
HDL-C (mg/dL)	0.047	0.547	-0.30	<0.001
Non-HDL-C (mg/dL)	0.028	0.715	0.343	<0.001
LDL-C (mg/dL)	0.047	0.546	0.259	0.001
Triglyceride (mg/dL)	0.025	0.746	0.324	<0.001
Fasting glucose	0.207	0.007	0.196	0.011
HbA1c	0.116	0.133	0.046	0.551
SCORE2/SCORE2-OP %	0.652	<0.001	0.995	<0.001

HDL: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, Total-C: Total cholesterol, HbA1c: Hemoglobin A1c, SCORE2/SCORE2-OP: Systemic coronary risk evaluation2-older person

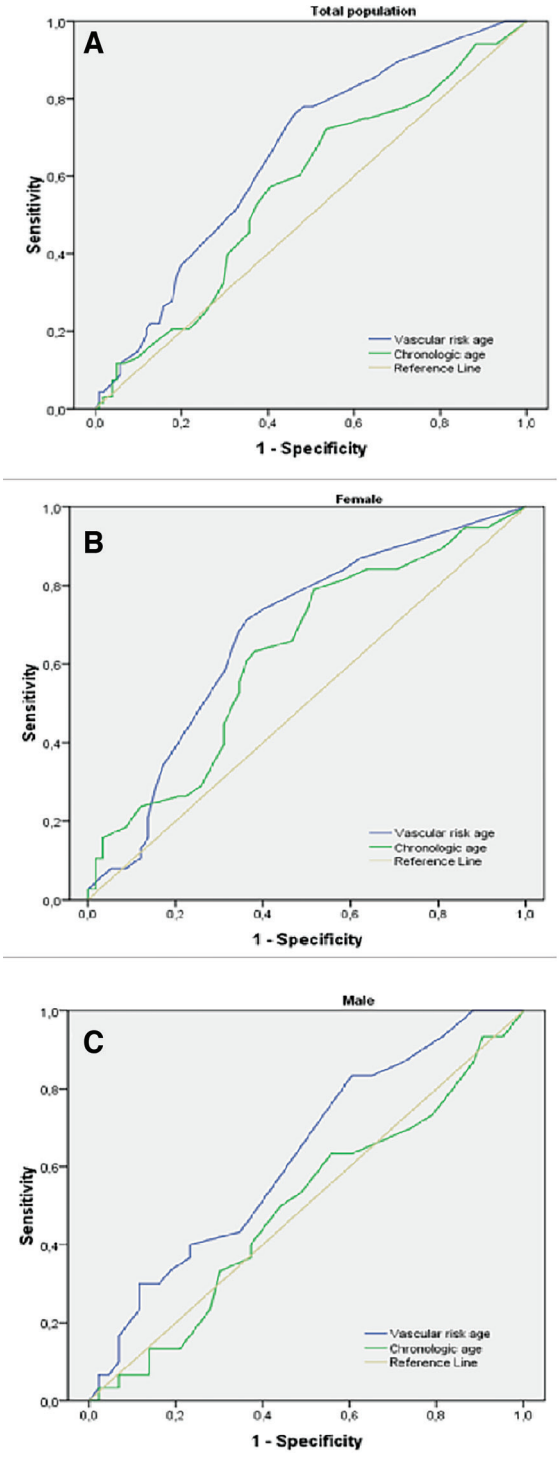

Figure 1. "Subjects with MetS are more accurately predicted by vascular risk age than chronologic age. (A) ROC curve was produced and AUC was computed to establish vascular risk-age (blue line) and chronological age (green line) predictability for metabolic syndrome. Subsequently, the cohort was re-analyzed as was ranked by sex into females (B) and males (C). The reference line (yellow line) matches no predictability (AUC=0.500).''

AUC: Area under the curve, MetS: Metabolic syndrome

study population (AUC=0.677, 95% CI 0.568-0.786), and a cut-off of 55.5 years was determined using a significant Youden index (Youden index=0.31, sensitivity=68.4%, and specificity of 65.0%). In comparison with the chronologic age, VRA was a significantly better predictor of MetS, particularly in the female gender.

In addition, we performed logistic regression analysis to evaluate the role of gender, chronologic age, VRA, BMI, WC, fasting glucose, and non-HDL-C levels in terms of the probability of MetS. The full model including all seven predictors was statistically significant [X^2 (7, n=169 = 73,318, p<0.001)], indicating that the model was able to discriminate between the presence and absence of MetS. In general, 35.2% (Cox and Snell R square) to 47.6% (Nagelkerke R square) variance in MetS status was explained by the entire model, and 81.1% of the cases were correctly classified. As demonstrated in Table 4, VRA was an important predictor of MetS in this sample, with an odds ratio of (OR: 1.086, p=0.041). This suggests that for each one-year increase in VRA the odds of presenting MetS increases by a factor of 1.086. In addition, fasting glucose was a significant predictor of MetS (OR: 1.082, p=0.001). This indicates that for each 1 mg/dL increase in fasting glucose, the odds of having MetS increases by a factor of 1.082.

Discussion

In this study, we found that individuals with MetS had an increased BMI, WC, WHR, SBP, DBP, non-HDL-C, TG, FG, HbA1c, and decreased HDL-C compared with individuals without MetS. Previous studies have revealed that increased body weight, insulin resistance, increased blood pressure, and atherogenic dyslipidemia participate in the development of MetS (1-5). In this context, our results are consistent with previously published data. Differing from previous reports, in this work we mainly investigated whether VRA might significantly predict MetS. Therefore, individuals with MetS were divided into two groups on the basis of the sensitivity and specificity values of the chronologic age and the VRA, with a cut-off age of 54.0 years. This study mainly found that individuals with MetS had increased VRA and SCORE2/SCORE2-OP %. Furthermore, it was evident that VRA can significantly predict MetS in general and particularly in the female gender. Our analysis showed that the ROC-AUC of MetS in the entire study population increased from 0.569 in a model with chronological age to 0.658 in a model with SCORE2-based calculated VRA. Furthermore, AUC was even more

pronounced when the model was adjusted only for females (up to 0.677). In addition, our logistic regression model also supported us and showed an OR of 1.086 (p=0.041, 95% CI=1.003-1.175) for VRA in the prediction of MetS. As we all know, this is the first study showing the prediction of MetS by VRA.

VRA is a surrogate of an individual's excess cardiovascular risk, which is calculated using a risk prediction model such as Framingham or SCORE2/SOCRE2-OP (1,10,11). Furthermore, VRA can be investigated by additional methods, such as measurement of carotid intima-media thickness and plaque detection, coronary artery calcification, pulse wave velocity, and pulse wave analysis that reflect arterial stiffness (1,12,13). In the recently mentioned methods, VRA is the age at which the result of an imaging test would equal the population reference values. In all terms, VRA is considered to improve cardiovascular risk prediction models and may help in a better understanding of cardiovascular risk at the preclinical stages, particularly in young patients, as the long-term effects of high-risk factors can be disguised (1). In all respects, VRA is considered to improve cardiovascular risk prediction models and may aid a better understanding of cardiovascular risk, particularly in the preclinical stages in younger patients, as the long-term effects of high-risk factors may be obscured (1). Here, we used the recently recommended SCORE2/SCORE2-OP risk chart calibrated to the high-risk countries (including Turkey) for calculating fatal and non-fatal CVD events as well as VRA with regard to recognizing MetS. In almost all previous reports (1), the mean VRA is usually higher than chronological age, with the differences ranging from 1 to 26.5 years. Our findings were in agreement with these observations, as we found VRA to be significantly higher than chronologic age in the overall sample (p<0.001), subjects with MetS (p<0.001), and those without MetS (p=0.008).

Many reports have demonstrated older chronologic age as a predictor of MetS (14,15). However, using chronological age alone could cause misunderstanding of cardiometabolic risk because it excludes the subject's lifestyle, distribution of the adipose tissue, and accompanying diseases (16). Thus, risk scales, including chronologic age analysis, may cause underestimation of subjects in whom aggressive management of CV disease risk factors should be applied (17,18). In our sample, subjects diagnosed with MetS were not significantly older than subjects without MetS (p=0.126). In contrast, we showed that VRA was significantly higher in individuals with MetS

Table 3. Receiver operating characteristic analysis of the entire study population and gender-specific values

Variables	AUC	Std. error	p	95% CI	Cut-off	sensitivity	Specificity	J-index
Entire population vascular risk age	0.658	0.042	<0.001	0.576-0.740	54.0	75.0	45.0	0.19
Chronologic age	0.569	0.045	0.126	0.481-0.657	54.0	46.0	65.0	0.09
Females								
Vascular risk age	0.677	0.056	0.004	0.568-0.786	54.0	68.4	65.0	0.27
Chronologic age	0.629	0.058	0.034	0.515-0.742	54.0	52.0	65.0	0.13
Males								
Vascular risk age	0.627	0.066	0.067	0.498-0.755	54.0	83.0	0.43	0.00
Chronologic age	0.495	0.069	0.942	0.359-0.631	54.0	43.0	0.60	-0.035

AUC: Area under the curve, CI: Confidence interval, J-index: Youden index

Table 4. Predictors of metabolic syndrome based on the logistic regression model

Predictors	B	S.E.	Wald	df	P	Odds ratio	95% CI for EXP (B)	
							Lower	Upper
Gender (F=1, M=0)	0.812	0.481	2.851	1	0.091	2.252	0.878	5.777
Age (year)	-0.061	0.039	2.433	1	0.119	0.941	0.871	1.016
Vascular risk age (year)	0.082	0.040	4.187	1	0.041	1.086	1.003	1.175
BMI (kg/m^2)	0.120	0.081	2.199	1	0.138	1.128	0.962	1.323
WC	0.054	0.034	2.465	1	0.116	1.056	0.987	1.129
Fasting glucose	0.079	0.023	11.460	1	0.001	1.082	1.034	1.133
Non-HDL-C	0.011	0.006	3.284	1	0.070	1.011	0.999	1.022
Constant	-20.332	3.445	34.841	1	<0.001	<0.001		

BMI: Body mass index, B: Unstandardized regression weight Wald, Wald statistic test, df: Degrees of freedom, 95% CI for EXP(B): 95% Confidence interval for the odds ratio, WC: Waist circumference, Non-HDL-C: Non-HDL-C

than in those without MetS (p<0.001). In addition, rather than chronologic age, VRA was an independent predictor of MetS. The increase in the prevalence of MS based on age is significantly influenced by the high frequency of metabolic risk factors developed at the oldest age, in particular, >65 years (19). Our sample was free of high-risk features such as CVD and DM along with a higher number of young individuals (overall median age=51 years), which may explain the equivalence of age in subjects with and without MetS.

Previous papers have reported that the female gender was more likely to develop MetS (16). Contrary to the latter study, which enrolled only Brazilian patientswas assessed a cross-section of the Turkish population (Caucasian ethnicity) and demonstrated no significant difference in the frequency of MetS regarding gender. In this context, our findings were consistent with recent domestic population reports (4).

Hyperlipidemia is one of the main triggers of atherosclerosis, which manifests in its early form as coronary artery calcification or increased carotid IMT, which have been proposed as surrogates of VRA (20). In this regard, our results indicate that VRA is in excellent correlation with all components of the lipid panel, as previously published works experienced (1,2,9). This association may explain the higher atherosclerotic features of VRA in subjects with MetS. However, chronologic age was not associated with any lipid parameter.

Increased BMI and WC and cigaret smoking are other potential factors contributing to both a high VRA and MetS development (1,16). Our findings also complement this idea, with the exception of cigaret smoking. Our results revealed that VRA is significantly associated with BMI and WC. This interrelationship may account for the hazardous characterization of both MetS and increased VRA.

High fasting glucose and insulin resistance are the main features of MS (2). Consistent with general acceptance, our logistic regression results showed that fasting blood glucose was an independent predictor of MS (2,4,5).

This is the first study to investigate VRA age in the context of MetS. Our results demonstrated that VRA is a novel clinical marker of risk for MetS. In this analysis, we used complete data on SCORE2/SCORE2-OP charts and MetS criteria. In addition, we tested vascular risk of prediction of MetS through several statistical analyses (logistic regression and AUC-ROC curve analysis). The present study has some limitations as well; it was a cross-sectional work, done in a single center, included only a Turkish sample (Caucasian ethnicity), the sample was entirely above 40 years of age, and individuals with DM and ASCVD were not included in the study, which could cause a miscalculation of the incidence of MetS.

Conclusion

Our analysis showed that VRA is a significant clinical predictor of MetS. In clinical evaluation, paying attention to the VRA may help in the early detection of MetS, the precursor of ASCVD and DM. Thus, it contributes to an effective clinician-patient discussion regarding primary prevention treatments. However, to evaluate the diagnostic and prognostic value of VRA in the context of MetS, prospective studies are needed.

Ethics

Ethics Committee Approval: This study was authorized by a Clinical Research Ethics Committee of Kırklareli University (3/2022.K-42, date: 20.05.2022).

Informed Consent: Informed consent was obtained from all participants

Authorship Contributions

Surgical and Medical Practices: A.N., R.Ç.G., S.S., Ö.Ş., Concept: A.N., D.E.A., S.S., Design: A.N., D.E.A., R.Ç.G., Ö.Ş., Data Collection or Processing: A.N., D.E.A., R.Ç.G., S.S., Analysis or Interpretation: A.N., S.S., Ö.Ş., Literature Search: D.E.A., R.Ç.G., S.S., Ö.Ş., Writing: A.N., D.E.A., R.Ç.G., S.S., Ö.Ş.

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