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Carotis Intima-Media Thickness, Lipid Accumulation Product Index, Cardiovascular Risk Calculation Score and Their Relationship with Monocyte to HDL Ratio in Middle-Aged Women with Polycystic Ovary Syndrome

Perimenopozal Polikistik Over Sendromlu Kadınlarda Monosit/HDL Oranının, Lipid Birikim Ürünleri, Karotis İntima Media Kalınlığı ve SCORE2 Kardiyovasküler Risk Hesaplama Sistemi Skoru ile Karşılaştırılması

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Abstract

Aim: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women in the reproductive age and also associated with many comorbidities that increase the risk of cardiovascular disease in later ages. This study explores the potential correlation between the monocyte to HDL ratio (MHR) and established cardiovascular risk factors in women with PCOS.

Material and Method: This cross-sectional analysis includes PCOS-diagnosed women (n=40) in menopausal transition over 40 years old, and a control group of non-PCOS healthy women (n=40) matched for age and body-mass index (BMI). Various parameters, including demographic and anthropometric measurements, lipid profiles, carotis intima-media thickness (CIMT), free androgen index (FAI), lipid accumulation product (LAP) index, homeostasis model assessment-insulin resistance (HOMA-IR), MHR, and SCORE2 risk scores were compared between the groups.

Results: Results indicate no significant differences in age, BMI, smoking, lipid profiles, fasting glucose, insulin levels, MHR, LAP index, HOMA-IR, and SCORE2 scores. However, sex-hormone binding globulin and total testosterone were higher in the PCOS group (p<0.001). Metabolic syndrome rates, FAI, and average CIMT were notably higher in the PCOS group (p=0.045, p=0.003, p=0.022). MHR was positively correlated with LAP index, HOMA-IR, FAI, and left CIMT (r=0.235; r=0.297; r=0.28; r=0.215; respectively).

Conclusion: In conclusion, PCOS women exhibit higher metabolic syndrome rates and average CIMT measurements compared to healthy age and BMI matched counterparts. Positive correlations of the MHR with various risk factors emphasize the importance of assessing cardiovascular risk in this population and shows that MHR can be used as a much cheaper predictor of cardiovascular risk compared to other predictors in perimenopausal PCOS patients.

Keywords: Polycystic ovary syndrome, monocyte to hdl ratio, lipid accumulation product index, homa-ir, carotid intima-media thickness

Öz

Amaç: Polikistik over sendromu (PCOS), reprodüktif çağdaki kadınların en sık görülen endokrin hastalığıdır ve ilerleyen yaşlarda kardiyovasküler hastalık riskinde artış ile ilişkilendirilmiş bir çok komorbiditeye yol açmaktadır. Bu çalışma, kardiyovasküler risk faktörleri ile daha önceden ilişkilendirilmiş belirteçlerle monosit/HDL oranı (MHR) arasındaki potansiyel ilişkiyi belirlemeyi amaçlamaktadır.

Gereç ve Yöntem: Kesitsel olarak tasarlanan bu çalışma, 40 tane menopozal geçiş dönemindeki PCOS tanısı almış hasta ile yaş ve beden kitle indeksi (BMI) açısından eşleşmiş 40 PCOS olmayan hasta üzerinde yürütülmüştür. Demografik ve antropometrik ölçümler, lipid profilleri, karotis intima-media kalınlığı (CIMT), serbest androjen indeksi (FAI), lipid birikim ürünleri (LAP) indeksi, homeostasis model assessment-insulin resistance (HOMA-IR), MHR ve SCORE2 risk skorları iki grup arasında karşılaştırılmıştır.

Bulgular: Yapılan istatistik analizde; yaş, BMI, sigara içiciliği, lipid profilleri, açlık glukozu ve insülin seviyeleri, MHR, LAP indeksi, HOMA-IR değerleri ve SCORE2 skorları açısından anlamlı fark bulunamamıştır. Ancak, seks hormon bağlayıcı globulin ve total testosteron seviyeleri PCOS grubunda istatistiki anlamlı yüksek bulunmuştur (p<0,001). Metabolik sendrom oranları, FAI ve CIMT ölçümleri PCOS grubunda istatistiki anlamlı olacak şekilde yüksek bulunmuştur (sırasıyla p= 0,045; 0,003; 0,022). MHR; LAP indeksi, HOMA-IR, FAI değerleri ve CIMT ölçümleri ile pozitif korele bulunmuştur (sırasıyla r= 0,235; 0,297; 0,28; 0,215).

Sonuç: PCOS hastası kadınlar, BMI açısından eşleştirilmiş PCOS olmayan yaşıtlarına göre artmış metabolik sendrom ve ortalama CIMT ölçümlerine sahiptir. Kardiyovasküler riskle ilişkisi daha önceden bilinen parametrelerle MHR arasındaki pozitif korelasyon değerleri, bu popülasyondaki kardiyovasküler risk faktörlerini değerlendirme konusunda dikkat çekmektedir ve perimenopozal PCOS hastalarında MHR'nin diğer kardiyovasküler risk prediktörlerine oranla çok daha ucuz bir prediktör olarak kullanılabilirliğini göstermektedir.

Anahtar Kelimeler: Polikistik over sendromu, monosit/HDL oranı, lipid birikim ürünleri indeksi, HOMA-IR, karotis intima-media kalınlığı

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting women in reproductive ages, with reported prevalence rates ranging from 6% to 20% depending on which diagnostic criteria used.[1,2] PCOS presents as a complex interplay of neuroendocrine, metabolic and ovarian dysfunctions, contributing to its perpetuating cycle.

In reproductive years, PCOS shows up with ovulatory and cosmetic issues, such as infertility, oligomenorrheae and increased body hair. In PCOS women, prevalance and numbers of cardiovascular risk factors increases over the years.[3] However, it remains uncertain to what extent PCOS itself, or its common comorbidities, mediates the increased risk for severe adverse outcomes, like cardiovascular disease (CVD).

In women with PCOS, the prevalence of insulin resistance, a comorbidity that accompanies PCOS and increases the risk of cardiovascular disease (CVD), ranges from 60-80%, while the prevalence of type 2 diabetes mellitus is around 10%.[4] Additionally, PCOS has been associated with metabolic syndrome (MS).[5] Due to the complexity of diagnostic criteria for MS, the simpler metabolic status assessment tool, the LAP index, has been introduced.[6] It was found to predict the presence of MS with 85% sensitivity when the threshold value was set at 28.4 cm.mmol/L.[7] The SCORE, a cardiovascular risk calculation system, was revised by the European Society of Cardiology in 2021 and reintroduced as SCORE2.[8,9] Beyond predicting CVD risk, direct visualization is possible. CIMT measurement provides valuable predictive insights into asymptomatic early atherosclerosis in women with PCOS.[10,11] Instead of separately evaluating the increase in monocyte count, a source of proinflammatory cytokines, and the decrease in HDL cholesterol (HDL-C), MHR has been proposed. MHR was found to be elevated in women with PCOS, emphasizing its utility in predicting cardiovascular risk in the chronic inflammatory nature of PCOS.[12]

This study aims to assess the presence of multiple cardiovascular risk factors in PCOS and evaluate the value of MHR as a simpler marker compared to multiple cardiovascular risk factor determination systems. The findings may provide valuable insights into better risk assessment and management strategies for women with PCOS, ultimately leading to improved cardiovascular outcomes in this vulnerable population.

MATERIAL AND METHOD

Women aged ≥40 years who were previously diagnosed with PCOS and 40 non-PCOS healthy women, who were in similar age and body mass index (BMI) range and applied to Evliya Çelebi Education and Research Hospital between June 2021-April 2022 were included in this study. Approval of Kütahya Health Science University Ethics Committee was provided in 10.06.2021 with decision number: 2021/10-23. Informed consent was obtained from all patients participating in the study. The study was conducted in accordance with the ethical rules of the WMA Declaration of Helsinki. Inclusion criterias for the study were:

For the PCOS Group:

- Women aged 40 years and older with menstrual bleeding.
- Women in menopausal transition without vasomotor symptoms
- Women with history of PCOS based on Rotterdam ESHRE/ASRM criteria and under follow-up.

For the Control Group:

- Similar age and BMI
- No history of oligomenorrhea/amenorrhea, hirsutism complaints, and/or infertility.

Exclusion Criterias for the study were:

- Menstrual period absence for at least one year.
- For the women with history of oligomenorrhea/secondary amenorrhea; FSH levels >45 IU/L.
- Presence of vasomotor symptoms, pregnancy, lactation, cardiovascular disease (CVD) history, family CVD history, thyroid, adrenal, pituitary diseases, diabetes (fasting blood glucose >126 mg/dl), chronic kidney or lung disease.
- Use of non-steroidal anti-inflammatory drugs in the last ten days, hormonal contraception, antihypertensive drugs, steroids, oral antidiabetic drugs, anticoagulant drugs in the last three months.
- Immun-suppressive therapy use for any diagnosis.
- Heavy smoking (>20 cigarettes per day).

In the statistical analysis, the sample size of the study with 0.05 α-error probability, 0.5 effect size and 85% power were calculated 40 for the PCOS group and 40 for the control group.

Age, BMI, arterial blood pressure in a resting position, waist circumference (WC) measurement, menstrual cycle features, smoking habit, presence of clinic features for hyperandrogenism (modified Ferriman- Gallwey score were higher than 8) and detailed medical/ obstetric/ gynecologic histories were recorded.

The ovaries of all women were evaluated by transvaginal ultrasonography using a Voluson 730 Professional Edition (General Electric Company, USA) device with an endovaginal 5 MHz probe; polycystic ovarian morphology in the ovaries was recorded for phenotypic evaluation.

Following an overnight fasting; complete blood count, fasting glucose, fasting insulin, total cholesterol, HDL-C, LDL-C, triglyceride, total testosterone and SHBG values were evaluated and the results were recorded. Menopause status was excluded by evaluating the FSH levels of women in the PCOS group who described amenorrhea or oligomenorrhea. Biochemical and hormonal parameters were acquired by enzyme-linked immuno assays in UniCel DxI 600 Access Immunoassay System biochemistry device (Beckman Coulter Life Sciences Headquarters, Indianapolis, IN).

BMI of the cases were calculated by dividing body weight by the square of their heights in meters (kg/m^2). WHR were calculated by dividing waist circumference by hip circumference in centimeters. The normal value for WHR was accepted as less than 0,83.[13] Free androgen index (FAI) was calculated by dividing the total testosterone value (nmol/L) by the SHBG value (nmol/L) and multiplying the obtained value by 100. Values greater than 5% were considered abnormal.[14] The HOMA-IR value was calculated by multiplying the fasting glucose values (mg/dL) with the simultaneous fasting insulin values (IU/L) and dividing the obtained value by 405. IR values of 2.5 and above were considered abnormal.[15] LAP index was calculated with the formula "[Waist circumference(cm)-58] x Triglyceride(mg/dL) x 0.0113". Values of 39.82 cm.mmol/L and above were considered abnormal.[16]

SCORE cardiovascular risk scores were calculated by entering age, gender, systolic blood pressure, total cholesterol, HDL-cholesterol, LDL-cholesterol and smoking information of the cases on the calculator of the website "https:// heartscore.escardio.org/Calculate/quickcalculator.aspx?". The obtained values were compared with the SCORE2 European High-Risk Region cards. For cases under 50 years of age, <2.5% was considered low risk, 2.5-7.5% moderate risk and ≥7.5% high risk.

CIMT measurements were performed on the Acuson S3000 ultrasonography device (Siemens Medical Solutions, Mountain View, CA) by the same trained ultrasonographer, following the methods specified in the literature.[10] The recorded values included left CIMT, right CIMT and their mean CIMT. Abnormal values were defined as those exceeding the 75th percentile or 0.634 mm in population-based studies.[17]

MHR was calculated by dividing monocyte counts per mililiter by HDL-C levels in mg/dl. A cut-off value of 9,9 and above was considered abnormal.[18]

Patients meeting three or more of the ATP-III criteria (waist circumference >88 cm; triglyceride ≥150 mg/dL; HDL-C <50 mg/dL; blood pressure ≥130/85 mmHg; fasting glucose ≥110 mg/dL) was diagnosed and recorded as present or no metabolic syndrome.

Coding and analysing of datas were made with The Statistical Package for the Social Sciences version 26.0 (SPSS Inc. Chicago, IL). Normality tests of the variables were obtained by Kolmogorov-Smirnov and Shapiro-Wilk tests. Continous variables were compared with Student's t test or Mann-Whitney U test, depending on normal distribution. The results were presented as "mean- standart deviation" or "median-interquartile range". Categorical variables were evaluated with Chi-Square test and the results were reported as "number-percentage". The relationship between MHR, LAP index, WHR, CIMT measurements (left, right and mean), FAI and HOMA-IR were evaluated with Spearman correlation analysis. Parameters with p value of <0.05 were considered statistically significant.

RESULTS

Mean age of 80 women included in the study was 42.69±2.72. Mean BMI was 27.89± 4.91 kg/m^2. Two groups were similar in terms of age and BMI. Due to cluster in phenotype C and D (35 cases) and only five cases were in phenotype A, phenotype based subgroup analysis couldn't be done in PCOS group. Among PCOS cases, modified Ferriman-Gallwey score was calculated 8 and above for 11 cases. Free androgen index was calculated above 5 for only one case.

In comparison analysis, total testosterone levelwas significantly higher in PCOS group (p<0.001) but other biochemical and anthropometric values were similar. Demographic features, lipid profiles, laboratory values and metabolic parameters was shown in **Table 1**.

Table 1. Comparison of demographic features, lipid profiles, laboratory values and methabolic parameters between PCOS and control groups

Variable	PCOS(n=40)	Control (n=40)	p-value
Age	41.00 (40.75-44.00)	42.00 (41.00-43.00)	0.182[a]
BMI	28.42±5.48	27.38±4.27	0.352[b]
WC (cm)	92.58±13.46	95.35±9.03	0.283[b]
WHR	0.87±0.07	0.89±0.05	0.219[b]
Smoking Status			
Yes	25 (62.5 %)	21 (52.5 %)	0.497[c]
No	15 (37.5 %)	19 (47.5 %)	
Fasting Glucose (mg/dL)	98.00 (88.75-105.25)	95.00 (87.00-101.25)	0.326[a]
Fasting Insulin (IU/L)	7.21 (5.44-11.22)	6.10 (3.88-8.27)	0.082[a]
T.testosteron (nmol/L)	0.44 (0.31-0.66)	0.25 (0.15-0.40)	<0.001[a]
SHBG (nmol/L)	43.65 (30.08-60.12)	45.55 (38.60-56.73)	0.548[a]
T.Cholesterol (mg/dL)	200.50 (179.00-230.00)	186.50 (170.00-212.25)	0.133[a]
HDL-C (mg/dL)	46.00 (43.75-58.50)	50.50 (45.00-57.00)	0.512[a]
LDL-C (mg/dL)	125.53±36.96	117.33±25.58	0.253[b]
Triglyceride (mg/dL)	120.00 (88.00-185.00)	108.50 (89.25-152.00)	0.430[a]
Monocyte (count/mL)	0.48 (0.36-0.51)	0.42 (0.35-0.52)	0.438[a]
SBP (mmHg)	125.00 (120.00-130.00)	120.00 (120.00-130.00)	0.247[b]

BMI: Body Mass Index; WHR: Waist-to Hip Ratio; SHBG:Sex Hormone Binding Globulin; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein SPB: Systolic Blood Pressure
a: Mann-Whitney U test; datas are shown as median (interquartile range).
b: Student's t test; datas are shown as mean±standart deviation.

HOMA-IR values, FAI values, LAP indices and MHR were similar between two groups. Mean CIMT and left CIMT measurements were significantly higher in PCOS group (p=0.022; p=0.01; respectively) (**Table 2**).

In Chi-Square analysis, presence of metabolic syndrome was statistically significantly higher in PCOS group (p=0,045). The distribution of cases between PCOS and control group depending on SCORE2 risk group was similar (**Table 2**).

Table 2. Comparison of cardiovascular risk parameters between PCOS and control groups

Variable	PCOS(n=40)	Control(n=40)	p-value
Right CIMT(mm)	0.70 (0.60-0.90)	0.70 (0.60-0.80)	0.086[a]
Left CIMT(mm)	0.70 (0.60-0.90)	0.60 (0.60-0.72)	0.010[a]
Mean CIMT(mm)	0.70 (0.64-0.88)	0.65 (0.60-0.76)	0.022[a]
HOMA-IR	1.64 (1.17-2.89)	1.36 (0.88-2.09)	0.156[a]
FAI	0.85 (0.57-2.02)	0.52 (0.31-0.90)	0.003[a]
LAP index(cm.mmol/L)	42.10 (28.10-86.04)	50.18 (30.79-67.00)	0.942[a]
MHR	9.29±3.47	8.90±3.12	0.595[b]
Metabolic syndrome			
Present	19 (47.5%)	11 (27.5%)	0.045[c]
No	21 (52.5%)	29 (72.5%)	
SCORE2 risk category			
Low risk	24 (60%)	21 (52.5%)	0.499
Moderate risk	16 (40%)	19(47.5%)	

CIMT: Carotid Intima-Media Thickness; HOMA-IR:Homeostasis Model Assessment-Insulin Resistance; FAI:Free Androgen Index; LAP: Lipid Accumulation Product; MHR: Monocyte to HDL Ratio.
a: Mann-Whitney U test; datas are shown as median (interquartile range).
b: Student's t test; datas are shown as mean±standart deviation.
c:Pearson Chi-Square test, datas are shown as count (column- percent)
p<0,05 is considered statistically significant.

In Spearman correlation analysis, MHR was found correlated with HOMA-IR (r=0.297; p=0.007), LAP index (r=0.235; p=0.035), left CIMT measurement (r=0.215; p=0.049) and FAI (r=0.280; p=0.012). MHR was also positively correlated with WHR, right CIMT and mean CIMT measurements but no significance was found. Correlation table is presented in **Table 3**.

Table 3. Correlation table of cardiovascular risk parameters

n=80	MHR correlation r value	p-value
HOMA-IR	0.297	0.007
LAP Index	0.235	0.035
WHR	0.108	0.341
Right CIMT	0.081	0.477
Left CIMT	0.215	0.049
Mean CIMT	0.143	0.205
FAI	0.280	0.012
SCORE risk point	-0.044	0.697
HOMA-IR correlation r value		
LAP Index	0.301	0.007
FAI	0.238	0.033

MHR: Monosit/ HDL Ratio; LAP: LipidAccumulation Product); WHR: WaisttoHipRatio; CIMT: CarotisIntima- Media Thickness;
FAI: FreeAndrogen Index; SCORE: SystemicCoronor Risk Evalution; HOMA-IR: Homeostasis Model Assessment-InsulinResistance
p<0,05 is considered statistically significant.
Spearman correlation analysis is used for all correlation analyzes.

Among smoker cases, median values for MHR were 11.36 for PCOS group (9.35-11.90; interquartile range) and 8.0 for control group (6.36-9.60; interquartile range) and the difference was statistically significant (p=0.001). Also, among SCORE2 moderate risk cases, median values for MHR were 10.69 for PCOS group (8.20-13.10; interquartile range) and 7.81 for control group (5.71- 9.60; interquartile range) and the difference was statistically significant (p=0.017)

DISCUSSION

It's known that cardiovascular risk count and severity was increased with advancing age in PCOS women.[19-21] In this study, metabolic parameters and scoring systems which may present cardiovascular risk such as MHR, SCORE2 risk point, LAP index, HOMA-IR, WHR, CIMT measurements and FAI were compared and correlation was investigated between MHR and the other parameters among 40 middle-aged PCOS women and 40 non-PCOS healthy women, matched in terms of age and BMI. In results, we found that MHR was positively correlated with LAP index, HOMA-IR, left CIMT measurement and FAI (r=0.235; r=0.297; r=0.215; r=0.280; respectively). In comparison analysis, metabolic syndrome presence was more frequent in PCOS group than control group.

In a large-sampled study, rates of diabetes mellitus, hypertension and dyslipidemia were found higher in PCOS group than non-PCOS group; however coronary heart disease, cerebrovascular disease and peripheral vascular disease frequencies were found similar.[22] In another long-term follow up study, PCOS women's prevalance of DM, hypertension, hypercholesterolemia, hypertriglyceridemia and WHR values were found higher than non-PCOS group. However coronary heart disease dependent morbidity and mortality were similar between two groups.[21] Many studies on perimenopasual and postmenopausal PCOS women's cardiovascular risk were retrospective and the results were controversial. Our study is a rare prospective study that evaluating many cardiovascular parameters together in middle-aged PCOS women.

MHR was correlated with mortality rate among patients who underwent percutan coronary intervention in follow-up.[23] In a study, higher MHR values were found in cases of young PCOS women compared to age matched non-PCOS women.[12] All studies in literature that investigating MHR and PCOS correlation were conducted among reproductive ages.[12,18,24-28] Our study has the feature to be the first study to evaluate cardiovascular risk in perimenopausal PCOS women via MHR. The studies that resulted with remarkably higher MHR values had also lower HDL-C levels in PCOS group while our study was conducted between two groups matched in terms of WC, WHR, smoking status, BMI, age and blood lipid profiles. Although, in our study, analysis conducted among only smoker cases showed that MHR values were significantly higher in PCOS group than control group. It can be concluded that in PCOS women, smoking habit was triggering inflammatory processes more than non-PCOS women.

Soysal et al. have reported that phenotype A PCOS women had higher MHR values than other phenotypes.[27] In our study, there was a cluster on phenotype D due to improved hyperandrogenic and menstrual cycle features of PCOS in menopausal transition age, so phenotype based statistical analysis could not be done. MHR values could differ in a study with a larger sample size and including also phenotype A cases.

In a meta-analysis evaluating 19 studies, it was stated that measurement of the carotid intima media thickness was higher in PCOS group than in the control group.[29] It was reported that thickening in the left carotid begins approximately 10 years earlier than right carotid and while right CIMT measurements were more affected by hemodynamic parameters, left CIMT measurements were more related to inflammatory processes.[30] Since the right carotid originates from the brachiocephalic trunk and the left carotid exits directly from the thoracic aorta, left carotid does not have to share inflammatory substances with the subclavian artery unlike right carotid so that may be more affected more by inflammatory accumulations than right carotid artery.[31] While in our study, left and mean CIMT measurements were found to be significantly higher in the PCOS group, and a positive correlation was reported between left CIMT measurements and MHR; we can conclude that MHR could be used instead of CIMT measurement which was requiring special equipment and specialized health worker.

The positive correlation between HOMA-IR and FAI in our study draws attention to the activator role of insulin in IGF-1 and IGF-2 mediated androgen biosynthesis in ovarian tissue. Considering the studies in which HOMA-IR values were higher in women with PCOS than in the control group,[32] the importance of the hyperandrogenic pathophysiology of PCOS in insulin resistance can be emphasized.

In a study conducted in the age group similar to our study, it was shown that women with oligomenorrhea and hyperandrogenism were diagnosed with metabolic syndrome more than other groups, and the prevalence was 41%.[33] In our study, the frequency of metabolic syndrome in the PCOS group was 47.5%, similar to aforementioned study.

The LAP index's relation with cardiovascular risk, metabolic syndrome and insulin resistance in PCOS has been found in various studies.[16,34,35] In a study investigating 1720 genes focusing on the transcriptional and epigenetic changes of adipose tissue, PCOS women have multiple transcriptional and epigenetic changes in the adipose tissue associated with the development of the disease.[36] In an animal experiment conducted on rats, it was found that mesenteric fat tissues of mice fed with a high-fat diet exhibited a greater chemotactic response to MCP-1 in cell cultures compared to those obtained from mice fed a normal diet. Additionally, higher levels of nitric oxide and TNF-alpha were detected in mice fed with a high-fat diet.[37] This highlights the importance of inflammatory processes in adipose tissue. This study can be seen as the first study to reveal a positive correlation between MHR and LAP index, emphasizing the importance of lipid accumulation and its inflammatory activity.

There are many scoring systems to prevent mortality and morbidity by revealing the existing risks before CVD occurs. Framingham and SCORE2 are well-known and widely used CVD risk calculator systems.[9,38] In a multicenter study, comparing patients' SYNTAX scores with Framingham and SCORE values, it was reported that SCORE risk scores matched moderately better with SYNTAX scores.[39] Therefore, we preferred the SCORE2 calculation system, since the risk regions including our country are defined in the SCORE2 calculation system and it provides gender-specific assessment. In our study, there was no significant difference in SCORE2 risk between the groups and it may be attributed to the similarity between the SCORE2 variables of the groups.

The weakness of this study is the lack of assessment of lifestyles (exercise, alcohol use, eating habits, etc.) that have been habituated over the years and may affect the parameters studied. In addition, women who were diagnosed and followed up with PCOS during the reproductive period were included in our study. The fact that hyperandrogenic and reproductive problems can improve with age, and metabolic problems increase with age may be a factor may be the cause of cluster on phenotype D. For this reason, the change in CVD risk according to PCOS phenotypes was not mentioned in our study.

The strengths of this study are that it is the first study to investigate the relationship with PCOS and CVD with parameters that have been shown to be associated with CVD risk in different population and to evaluate the correlation of these parameters with the simple and inexpensive MHR test, especially in women approaching or in the menopausal transition period. Our study is also the first to evaluate MHR in PCOS patients over the age of 40. The similarity of anthropometric measurements and laboratory values between PCOS and control groups emphasizes the importance of increased cardiovascular risk markers in the PCOS group, as revealed by the study.

CONCLUSION

In summary, it was shown that cardiovascular risk factors in PCOS women worsens over years in our study. MHR was found correlated with HOMA-IR, LAP index and CIMT measurement. These findings offer that MHR could be a substitute for multiple cardiovascular risk predictor systems such as CIMT, LAP index, HOMA-IR, metabolic syndrome and SCORE2 risk points to reveal the cardiovascular risk in perimenopausal PCOS women. MHR can be used as a cardiovascular risk screening test, especially in women in the menopausal transition who smoke and have a moderate risk SCORE2 risk, compared to other expensive and specialized tests.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was obtained from Kutahya Health Science University Ethics Committee (Date: 10.06.2021, Decision No: 2021/10-23).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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