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Correlation of subclinic atherosclerosis, proinflammatory status, and insulin resistance with anthropometric measurements in polycystic ovary syndrome

Polikistik over sendromu hastalarında subklinik ateroskleroz, proinflamatuvar durum ve insülin direncinin antropometrik ölçümlerle korelasyonu

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is the most frequently encountered endocrinopathy in women of reproductive age. Visceral obesity, cardiovascular complications, insulin resistance, and proinflammatory status are frequently seen in PCOS patients. Many anthropometric measurements are used to evaluate visceral obesity. The aim of this study was to evaluate the correlations of anthropometric measurements with cardiovascular risk, insulin resistance and proinflammatory status in PCOS patients.

Material and Method: This retrospective study included 68 PCOS patients and 83 healthy females. Anthropometric measurements were evaluated of waist circumference, hip circumference, waist/hip ratio, body mass index (BMI), visceral adiposity index (VAI), lipid accumulation product (LAP), body adiposity index (BAI), abdominal volume index (AVI), body roundness index (BRI), and a body shape index (ABSI) of all the participants. Carotid intima media thickness (CIMT) for subclinical atherosclerosis cardiovascular risk evaluation, HOMA for insulin resistance assessment, and hsCRP levels for proinflammatory status assessment were determined as the main outcome measure. Correlations of anthropometric measurements with each other and with the main outcome measures were evaluated.

Results: HOMA and CIMT were significantly higher in PCOS patients. Abdominal obesity indicators such as waist circumference, hip circumference, waist-to-hip ratio, BMI, LAP, BAI, BRI, AVI, VAI and ABSI were significantly higher in the PCOS group. There was no significant difference between the groups in respect of hsCRP levels (p=0.317). When the correlations of anthropometric measurements with PCOS status were evaluated, it was seen that all measurements were correlated. The highest correlation with CIMT was obtained in BMI measurement, and the highest correlation with HOMA was obtained in BRI measurement. The anthropometric measurements were not found to be correlated with proinflammatory status in PCOS patients.

Conclusion: It was observed that anthropometric measurements may be functional in predicting PCOS-related subclinical atherosclerosis and insulin resistance. Visceral adiposity was found to be predictive for insulin resistance and subclinical atherosclerosis in PCOS patients.

Keywords: Adiposity, insulin resistance, carotid intima media thickness, CIMT

ÖZ

Amaç: Polikistik over sendromu (PKOS) doğurganlık çağındaki kadınlarda sık görülen bir endokrinopatidir. PKOS hastalarında visseral obezite, kardiyovasküler bozukluklar, insülin direnci, proinflamatuvar durum sıklıkla görülebilmektedir. Visseral obezitenin değerlendirilmesi amacıyla bir çok antropometrik ölçüm kullanılmaktadır. Amacımız antropometrik ölçümlerinin kardiyovasküler risk, insülin direnci ve proinflamatuvar durum ile korelasyonlarını değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif çalışmaya 68 PKOS ve 83 kontrol katılımcı alındı. Tüm katılımcıların bel çevresi, kalça çevresi, bel/kalça oranı, vücut kitle indeksi (VKI), visseral yağlanma indeksi (VAI), lipid birikim ürünü (LAP), vücut yağlanma indeksi (BAI), abdominal hacim indeksi (AVI), vücut yuvarlaklık indeksi (BRI) ve vücut şekli indeksi (ABSI) gibi antropometrik ölçümleri yapıldı. Ana sonuç ölçütü olarak kardiyovasküler risk ve subklinik ateroskleroz değerlendirmesi için karotis intima media kalınlığı (KIMK), insülin direnci değerlendirmesi için HOMA-IR, proinflamatuvar durum değerlendirmesi amaçlı hsCRP düzeyleri belirlendi. Antropometrik ölçümlerin birbirleri ve ana sonuç ölçütleri ile korelasyonları değerlendirildi.

Bulgular: HOMA-IR ve KIMK, PCOS hastalarında anlamlı olarak daha yüksekti. PCOS grubunda bel çevresi, kalça çevresi, bel kalça oranı, LAP, BAI, BRI, AVI, VAI ve ABSI gibi abdominal obezite göstergeleri anlamlı olarak daha yüksekti. hsCRP düzeyleri arasında anlamlı farklılık yoktu (p=0,317). Antropometrik ölçümlerin PCOS olma durumu, KIMK, hsCRP ve HOMA ile korelasyonları değerlendirildiğinde tüm ölçümlerin korele olduğu görüldü. KIMK ile en yüksek korelasyon VKI ölçümü, HOMA ile en yüksek korelasyon BRI ölçümünde elde edildi. Antropometrik ölçümlerin PKOS hastalarında CRP ile korelasyon göstermediği tespit edildi.

Sonuç: Antropometrik ölçümlerin PKOS ilişkili subklinik ateroskleroz ve insülin direncini öngörmede işlevsel olabileceği görülmüştür. PCOS hastalarında visseral adipozitenin subklinik ateroskleroz ve insülin direncini için prediktif olduğu görülmüştür.

Anahtar Kelimeler: Adipozite, insülin direnci, karotis intima media kalınlığı, KIMK

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinopathy in women of childbearing age. PCOS is characterized by hyperandrogenism, oligo-anovulation, menstrual dysfunction and polycystic ovaries (1). It was first described in 1935 by American gynecologists, Irving F. Stein and Michael L. Leventhal (2). A high cardiovascular risk profile has been demonstrated in PCOS with an increased incidence of type 2 diabetes, insulin resistance, dyslipidemia, hypertension, and obesity (1,3,4). In addition, some studies have found that subclinical inflammation is increased in patients with PCOS and insulin resistance (5).

Obesity is present in 30-75% of women with PCOS and is a factor that exacerbates the clinical entitie metabolic syndrome (6). In particular, visceral adiposity aggravates hirsutism and menstrual abnormalities and exacerbates the clinical presentation of PCOS. In addition, the benefit seen in infertility treatments decreases in the case of obesity (7).

PCOS is often accompanied by abnormal fat distribution beyond obesity. This condition is referred to as visceral adiposity, and is associated with abnormal lipid-metabolic profile, proinflammatory activity, insulin resistance, and subclinical atherosclerosis. Visceral adiposity increases the risk of metabolic syndrome, type 2 diabetes, and cardiovascular events in PCOS patients. Visceral adiposity also exacerbates ovulatory dysfunction and hyperandrogenism (8–10).

Different methods such as bioelectrical impedance, ultrasonography, dual x-ray absorptiometry and magnetic resonance imaging can be used to demonstrate visceral adiposity (11). However, further methods are needed to assess visceral adiposity because of the difficulty and cost of accessing these devices. Body mass index (BMI) is insufficient to predict body fat distribution. Therefore, in addition to conventional methods such as waist circumference, hip circumference, and waist / hip ratio, new anthropometric measurements such as visceral adiposity index (VAI), lipid accumulation product (LAP), body adiposity index (BAI), abdominal volume index (AVI), body roundness index (BRI) and a body shape index (ABSI) have been investigated in some studies recently.(12–19).

The aim of this study was to evaluate the relationship of subclinical atherosclerosis, insulin resistance and proinflammatory activity with obesity and abdominal adiposity in PCOS patients through anthropometric measurements.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Researches Ethics Committee (Date: 18.10.2021, Decision No: 122/4). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Sixty eight PCOS patients and 85 healthy control subjects referred to the endocrinology and metabolism department of our clinic is included in this retrospective study.

Diagnosis of PCOS is established according the 2003 Rotterdam criteria. Patients with any two of the criteria for menstrual disturbances, clinical and/or biochemical androgen excess, and multiple cystic ovarian morphology were accepted as PCOS (20). Patients with diabetes mellitus, acute infection, cardiovascular disease, renal failure, history of immuno-rheumatic disease, or gynecological neoplasms, were excluded from the study. The control group was formed of patients who presented with non-specific complaints and no pathology was found in the examinations. The anthropometric, clinical, and laboratory findings were recorded.

BMI was calculated by dividing body weight (kg) by height squared(m2). Waist circumference was measured at the midpoint of the the iliac crests and the twelfth rib while standing. Afterward hip circumference was measured at the widest part of the hips (21). The waist-hip ratio was obtained by dividing these two values. Abdominal obesity was assessed using the formulas of ABSI, AVI, BAI, BRI, LAP, and VAI (22–24) (**Table 1**).

Table 1. Formulas of anthropometric measurements

ABSI=	Waist circumference / (BMI 2/3 x Height (meter) 1/2)
AVI =	[2 x (Waist circumference (cm))2 + 0.7 x (Waist circumference (cm) – Hip circumference (cm))2] / 1.000
BAI=	[Hip circumference (cm) / Height (m)3/2]-18
BRI=	364.2-365,5x [1 – ((Waist circumference (m)/ (2π)2) / (0,5x Height (m))2]1/2
LAP (Female)=	(Waist circumference (cm)-58) x Triglyceride (mmol/L)
VAI (Female)=	[Waist circumference (cm)/ (36.58+ (1.88 × VKI)] × (Triglyceride (mmol/L) /0.81) × (1.52/HDL-C (mmol/l))

VAI: visceral adiposity index, LAP: lipid accumulation product, BAI: body adiposity index, AVI: abdominal volume index, BRI: body roundness index, ABSI: body shape index, HDL-C: high density lipoprotein cholesterol

Carotid intima media thickness (CIMT) was measured in term of the evaluation of subclinical atherosclerosis during the first examination of all participants. Measurements were made with a 13 MHz high resolution B-mode ultrasound (EUB 7000 HV; Hitachi, Tokyo, Japan) and linear probe. Three measurements were taken near 1 cm proximal of both right and left common carotid artery bifurcations. The distance between posterior wall lumen echogenicity and media-adventitia echogenicity was measured only from the posterior part of the carotis artery. CIMT was computed as the mean of the three measurements in both arteries.

Blood samples were taken from all the subjects between 08:00 and 10:00 in the morning after an overnight fast in the follicular phase of the menstrual cycle. Fasting blood was drawn to measure serum glucose, insulin and lipid profile. Insulin resistance was calculated using the homeostasis model assessment formula (HOMA) [Fasting insulin (μU/mL) × Fasting glucose (mg/dl)/405)]. To assess the proinflammatory state, hsCRP levels were evaluated.

Statistical Analysis

The parametric distribution of numerical data was defined using the Shapiro-Wilk test. Mean±standard deviation values were used for parametric distributed variables, and median and range values for non-parametric distributed variables. The Student's t test was used to compare normally distributed variables between the groups. The Mann-Whitney U test was used to compare variables with non-normal distribution in independent groups. Categorical variables of the groups were compared with the Chi-square ($\chi 2$) test. Spearman correlation analysis was applied to non-normally distributed data. Correlation analyses were evaluated both in the whole sample and in patients with PCOS only. A value of $p < 0.05$ was considered statistically significant.

RESULTS

The median age was 25 years (range, 18-47 years) in the control group and 23 years (range, 18-36 years) in the PCOS group. In terms of age statistically significant difference did not determined between the groups (p=0.179). PCOS patients had higher triglyceride, LDL, and total cholesterol levels when compared to the control group (**Table 2**). No significant difference was determined between the groups in respect of HDL levels (p=0.056). CIMT and HOMA-IR were meaningfully elevated in PCOS patients. In the PCOS group, visceral obesity indicators such as waist circumference, hip circumference, waist-hip ratio, LAP, BAI, BRI, AVI, VAI and ABSI were significantly higher (p<0.05). There was no significant difference between the groups in respect of hsCRP levels (p=0.317). The demographic data, laboratory findings, and anthropometric measurements are given in **Table 2**.

When the anthropometric measurement correlations were evaluated in all participants, with the exception of ABSI, all anthropometric measurements were found to be correlated with each other. The ABSI value was not correlated with BAI and BMI (r:0.102; p:0.278 and r:0.005; p:0.954, respectively). When the anthropometric measurement correlations were evaluated only in the 68 PCOS patients, the ABSI value showed no significant correlation with VAI (r:0.168; p:0.192), BAI (r:0.023; p:0.860), or BMI (r:0.166; p:0.196). When all the patients were evaluated, a significant correlation was determined between BAI and waist-hip ratio (r:0.321; p<0.001). The correlation between BAI and waist-hip ratio was lost when only PCOS patients were evaluated (r:-0.041; p:753). All other anthropometric measurements were found to be correlated with each other in the PCOS group.

Table 2. Demographic data, laboratory findings, and anthropometric measurements of the PCOS and control groups

	Control	PCOS	p
n	83	68	
Age (years)	25 (18-47)	23 (18-36)	0.179
Height (cm)	161.4 ± 5.8	161.5 ± 6.1	0.774
Weight (kg)	55 (43-94)	69 (35-115)	<0.001
Waist circumference (cm)	71 (61-102)	87 (65-121)	<0.001
Hip circumference (cm)	95.5 (85-123)	103 (77-141)	0.001
Waist/hip ratio	0.72 (0.66-0.81)	0.85 (0.72-0.98)	<0.001
Total cholesterol (mg/dl)	159 (127-251)	168 (126-243)	0.027
Triglyceride (mg/dl)	75 (21-273)	98 (32-382)	0.001
HDL (mg/dl)	56.95 ± 14.45	52.82 ± 12.82	0.056
LDL (mg/dl)	82 (38-176)	94 (69-175)	<0.001
Glucose (mg/dl)	82 (65-104)	81 (75-106)	0.039
Insulin (μU/mL)	8.7 (4.2-13.9)	16.2 (3.73-43.07)	<0.001
HOMA-IR	1.63 (0.79 – 3.0)	3.73 (0.78 – 9.25)	<0.001
CRP	1.0 (0.1-7.0)	1.0 (0.1-8.0)	0.317
CIMT (mm)	0.47 (0.25 -0.85)	0.50 (0.30 -0.80)	0.002
ABSI	0.073 (0.07-0.09)	0.0751 (0.07-0.09)	0.044
LAP	9.21 (1.45–74.52)	29.27 (6.95-245.84)	<0.001
BAI	27.88 (22.60-38.40)	31.45 (22.96—55.78)	0.001
BRI	2.26 (1.03-6.49)	4.04 (1.59-10.33)	<0.001
VAI	0.85 (0.30 – 6.67)	1.45 (0.37 – 9.53)	<0.001
AVI	9.80 (7.44 – 15.84)	14.96 (8.45 – 29.28)	<0.001
BMI	20.56 (15.94-34.53)	26.64 (17.36-48.49)	<0.001

HDL: high density lipoprotein, LDL: low density lipoprotein, HOMA-IR: homeostasis model assessment formula, CIMT: carotid intima media thickness, VAI: visceral adiposity index, LAP: lipid accumulation product, BAI: body adiposity index, AVI: abdominal volume index, BRI: body roundness index, ABSI: body shape index, BMI: body mass index

When the anthropometric measurements of all the participants were evaluated with PCOS status, all the measurements were found to be correlated with a positive PCOS status. ABSI was the poorest correlated antropometric measurement (r:0.178; p:0.044). The highest correlation with PCOS was seen with the waist-hip ratio measurement (r:0.818; p<0.001). When the anthropometric measurements were evaluated with CIMT, with the exception of ABSI and BAI, all the other measurements were found to be correlated. When anthropometric measurements were evaluated with hsCRP, with the exception of ABSI, BRI, and waist-hip ratio, all other measurements were found to be correlated. When anthropometric measurements were evaluated with HOMA, with the exception of ABSI, all other measurements were found to be correlated (**Table 3**).

Table 3. Correlations of PCOS status, CIMT, hsCRP and HOMA-IR, with anthropometric measurements (all participants)

		PCOS	CIMT	CRP	HOMA
BRI	r	0.615	0.297	0.206	0.626
	p	<0.001	0.001	0.053	<0.001
VAI	r	0.421	0.264	0.250	0.486
	p	<0.001	0.004	0.018	<0.001
LAP	r	0.572	0.278	0.266	0.582
	p	<0.001	0.002	0.012	<0.001
BAI	r	0.331	0.110	0.194	0.497
	p	<0.001	0.264	0.069	<0.001
AVI	r	0.697	0.304	0.238	0.574
	p	<0.001	-0.076	0.025	<0.001
ABSI	r	0.178	0.411	0.036	0.121
	p	0.044	0.875	0.736	0.211
BMI	r	0.590	0.351	0.253	0.610
	p	<0.001	<0.001	0.016	<0.001
WHR	r	0.816	0.330	0.163	0.530
	p	<0.001	<0.001	0.128	<0.001

VAI: visceral adiposity index, LAP: lipid accumulation product, BAI: body adiposity index, AVI: abdominal volume index, BRI: body roundness index, ABSI: body shape index, BMI: body mass index , WHR: waist/hip ratio

When the anthropometric measurements of only PCOS patients were evaluated, only BMI was correlated with CIMT (r:0.285; p:0.031). There was no correlation of CRP with any anthropometric measurement (**Table 4**). When the PCOS patients anthropometric measurements were evaluated with HOMA, with the exception of waist-hip ratio, all other measurements were found to be correlated. The poorest correlation with HOMA was seen with ABSI and the highest correlation was seen with BMI (**Table 4**).

Table 4. Correlations of CIMT, hsCRP and HOMA-IR with anthropometric measurements (PCOS patiens)

		CIMT	CRP	HOMA
BRI	r	0.182	0.112	0.401
	p	0.184	0.516	0.002
VAI	r	0.001	0.132	0.531
	p	0.993	0.553	<0.001
LAP	r	0.040	0.049	0.450
	p	0.771	0.778	0.001
BAI	r	0.034	0.226	0.415
	p	0.805	0.186	0.002
AVI	r	0.217	0.114	0.346
	p	0.111	0.508	0.010
ABSI	r	0.256	0.175	0.305
	p	0.059	0.307	0.024
BMI	r	0.285	0.244	0.547
	p	0.031	0.140	<0.001
WHR	r	0.174	0.009	0.129
	p	0.204	0.960	0.347

VAI: visceral adiposity index, LAP: lipid accumulation product, BAI: body adiposity index, AVI: abdominal volume index, BRI: body roundness index, ABSI: body shape index, BMI: body mass index, WHR: waist/hip ratio

DISCUSSION

The results of the current study demonstrated that obesity, insulin resistance, and subclinical atherosclerosis increase in PCOS patients. In addition, atherosclerotic deterioration was observed in the lipid profile. It was also determined that waist circumference is increased and visceral obesity is seen at a higher rate in PCOS patients. This situation was shown through many anthropometric measurements. With the exception of ABSI, the anthropometric measurements were found to be generally correlated with each other. All the anthropometric measurements were found to be correlated with PCOS status. Waist-hip ratio showed the highest correlation with PCOS status, while BMI showed the highest correlation with insulin resistance, and subclinical atherosclerosis. However, ABSI showed the poorest correlation. None of the anthropometric measurements were correlated with proinflammatory status in PCOS patients.

Central obesity and dyslipidemia are thought to contribute to the aggravated risk of atherogenesis in women with PCOS (6,7). CIMT has recently been used as a indicator of the progress of subclinical atherosclerosis, and studies have reported that increased CIMT is a strong predictor of the risk of stroke, myocardial infarction, and cardiovascular death (25,26). Altın et al. (27) declared that both early atherosclerotic changes and CIMT were significantly ameliorated following sleeve gastrectomy in obese cases. In the current study, CIMT was meaningfully elevated in cases with PCOS.

Correlations were determined between CIMT and AVI, BRI, LAP, VAI, BMI, and waist-hip ratio. However, no correlation was found between CIMT and ABSI and BAI. In a recent study of 62 PCOS patients, no correlation was found between ABSI measurement and CIMT, similar to the findings of the current study (13). This indicates that new anthropometric measures other than ABSI and BAI can be considered to prognosticate atherosclerotic risk in patients with PCOS.

It has been stated in some studies that subclinical inflammation is the ongoing process in patients with PCOS (5,30). According the current study, the hsCRP levels did not differ between the groups. Although correlations between hsCRP and AVI, BAI, LAP, VAI, BMI, and waist/hip ratio were detected in the whole sample, when only the PCOS group was evaluated this correlation was lost. This indicates that hsCRP elevation is mainly affected by visceral adiposity in the general population. However, other factors that affect the proinflammatory state in PCOS patients need to be considered.

A strict relationship between insulin resistance and splanchnic adiposity has been previously demonstrated (28,29). Similarly, significantly increased HOMA was seen in the current study PCOS patients. Correlations were determined between HOMA and AVI, BAI, BRI, LAP, VAI, and BMI. However, no correlation was found between HOMA and ABSI. The increased visceral adipose tissue in the current study was associated with increased insulin resistance in these patients. These results were compatible with those of other recent studies conducted in Turkey (13,14). Consequently, visceral adiposity can be accepted as an important determinant of insulin resistance in PCOS.

The main limitation of this study was the small number of participants. Besides that, the retrospective design and that there was no long-term patient follow-up reduce the power of the study. Multiple regression analyses could not performed because the main outcome criteria of this study, such as HOMA, CIMT, and hsCRP, were non-parametric linear variables. Therefore, the inability to evaluate the anthropometric predictors of the main outcome measures can be considered a limitation of the study. More information on the development of cardiometabolic events in PCOS will be able to be obtained with further prospective studies with larger numbers of participants.

CONCLUSION

The results of this study demonstrated that anthropometric measurements may be functional in predicting PCOS-related subclinical atherosclerosis and insulin resistance. However, it was observed that ABSI measurements may not be suitable for use in PCOS patients. Visceral adiposity was found to be predictive for insulin resistance and subclinical atherosclerosis in PCOS patients. The highest correlation with CIMT was obtained in the BMI measurement, and the highest correlation with HOMA was obtained in the BRI measurement. Anthropometric measurements were not found to be correlated with proinflammatory status in PCOS patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Researches Ethics Committee (Date: 18.10.2021, Decision No: 122/4).

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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