

POLİKİSTİK OVER SENDROMUNDA TANI ve FENOTİPLER

Öğr. Gör. Uzm. Dr. R Emre OKYAY

**DEUTF Hastanesi Kadın Hastalıkları ve Doğum AD
Reprodüktif Endokrinoloji ve İnfertilite Bilim Dalı**

Polycystic ovary syndrome: an ancient disorder?

Ricardo Azziz, M.D., M.P.H., M.B.A.,^{a,d,e} Daniel A. Dumesic, M.D.,^{a,f} and Mark O. Goodarzi, M.D., Ph.D.^{a,b,c,d}

^a Department of Obstetrics and Gynecology, ^b Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, and ^c Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, California; ^d Department of Medicine, and ^e Department of Obstetrics and Gynecology, the David Geffen School of Medicine at UCLA, Los Angeles, California; and ^f National Primate Research Center, University of Wisconsin, Madison, Wisconsin

Is polycystic ovary syndrome (PCOS) an ancient disorder? Or is it a disorder of recent development, the consequence of rising metabolic stress in an increasingly obese society? And if it is ancient, why has it persisted despite its reproductive disadvantage? And can the antiquity and evolutionary history of PCOS inform our efforts to unravel its genetic makeup?



PKOS varlığı paleolitik çağa kadar uzanıyor

- Avcı toplumda enerji depolayabilenlerin survivalı daha yüksekti.

PCOS'lu kadınlar besinin bol olduğu zamanlarda enerjiyi depoluyor / Doğum yapmıyor veya az doğum yapıyorlar / Açlık zamanlarında zayıflayarak doğuruyorlar /

*Az doğum yaptıkları için doğum sebepli ölümlerin çok olduğu zamanlarda az doğum yapıp yaşıyorlar. Bu da, sahip oldukları “**thrifty**” genler sayesinde oluyor.....*

Son 20 yılda.....

✓ **Androjen fazlalığı** hastalıklarına ait çalışmaların büyük çoğunluğu

POLİKİSTİK OVER SENDROMU (PKOS) üzerine odaklanmıştır.....

PATOGENEZ

FENOTİP

TEDAVİ



TANIDA HETEROJENİTE.....

- **Stein I, Leventhal M.** Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol **1935**;29:181–5.

➤ **PKOS'un ilk tanımlanması** →



- Değişen derecede büyümüş overler
- Obezite
- Hirsutismus
- Kronik anovulasyon



- Uygunsuz gonadotropin sekresyonu
- Hiperandrojenemi



- Ovaryan morfoloji



- İnsülin rezistansı/Hiperinsülinemi
- Karbonhidrat metabolizma bozukluğu
- Kardiyovasküler komplikasyonlar
- Metabolik bozukluklar



**National Institutes of Health
(NIH) criteria***

ASRM/ESHRE features**

**AE-PCOS Society
Task Force*****

Drs. Zawadzki and Dunaif

1. Hiperandrojenizm ve/veya hiperandrojenemi
2. Menstrual disfonksiyon

1. Oligo ve/veya anovulasyon
2. Klinik ve/veya biyokimyasal hiperandrojenizm
3. **Polikistik overler**

1. **Hiperandrojenizm**
2. Ovaryan disfonksiyon
Oligo-anovulasyon ve/veya polikistik overler

Diğer hiperandrojenemi ile ilişkili hastalıkların dışlanması

21-hidroksilaz eksikliği Non-klasik KAH, Tümörler, İlaçlar, Cushing Sendromu, HAIR-AN Sendromu, Tiroid bozuklukları ve hiperprolaktinemi

1990

2003

2006 ve 2009

%6-8¹

% 15-18¹

%12¹

* Zawadzki JK, Dunaif A. Diagnostic criteria for polycystic ovary syndrome: towards a rational approach. In: Dunaif A, Givens JR, Haseltine FP, Merriam GR, eds. Polycystic ovary syndrome. Boston, MA: Blackwell Scientific Publications, 1992:377-84.

** ESHRE/ASRM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19-25.

*** Azziz R, Carmina E, Dewailly D, et al.; Task Force on the Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PCOS Society. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91(2):456-88.

¹ Shannon M, Wang Y. Polycystic ovary syndrome: a common but often unrecognized condition. J Midwifery Womens Health. 2012;57(3):221-30

Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria

Bulent Okan Yildiz¹, Gurkan Bozdag², Zuhai Yapici², Ibrahim Esinler², and Hakan Yarali^{2,*}

¹Endocrinology and Metabolism Unit, Department of Internal Medicine, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey; ²Department of Obstetrics and Gynecology, Faculty of Medicine, School of Medicine, Hacettepe, 06100 Ankara, Turkey

Table II Prevalence of PCOS according to BMI.

	Whole group	NIH	Rotterdam	AE-PCOS
Total prevalence	392 (100)	24 (6.1)	78 (19.9)	60 (15.3)
Non-obese (<30 kg/m ²)	352 (89.8)	18 (5.1)	66 (18.8)	51 (14.5)
Obese (≥30 kg/m ²)	40 (10.2)	6 (15.0)	12 (30.0)	9 (22.5)

Percentages are given in parentheses.

Table V Prior studies evaluating the prevalence of PCOS.

Author, year (country)	NIH (%)	Rotterdam (%)	AE-PCOS (%)
Knochenhauer et al., 1998 (USA)	4.0		
Diamanti-Kandarakis et al., 1999 (Greece)	8.8		
Michelmore et al., 1999 (UK)	8.0		
Asuncion et al., 2000 (Spain)	6.5		
Azza et al., 2004 (USA)	6.6		
Chen et al., 2008 (China)		2.4	2.2
Kumarapeli et al., 2008 (Sri Lanka)		6.3	
March et al., 2010 (Australia)	8.7 ± 2.0	11.9 ± 2.4	10.2 ± 3.2
Moran et al., 2010a (Mexico)	6.0	6.6	6.0
Boyle et al., 2012 (Australia)	15.3	20.9	
Sanchon et al., 2012 (Spain and Italy)	5.4		
Our data (Turkey)	6.1	19.9	15.3

Phenotypes for polycystic ovary syndrome based on 2003 Rotterdam criteria

	Severe PCOS	Hyperandrogenism and chronic anovulation	Ovulatory PCOS	Mild PCOS
Periods	Irregular	Irregular	Normal	Irregular
Ovaries on ultrasonography	Polycystic	Normal	Polycystic	Polycystic
Androgen concentrations	High	High	High	Mildly raised
Insulin concentrations	Increased	Increased	Increased	Normal
Risks	Potential long-term	Potential long-term	Unknown	Unknown
Prevalence in affected women ¹⁰	61%	7%	16%	16%

PCOS=polycystic ovary syndrome.

Table 1: Phenotypes for polycystic ovary syndrome based on 2003 Rotterdam criteria

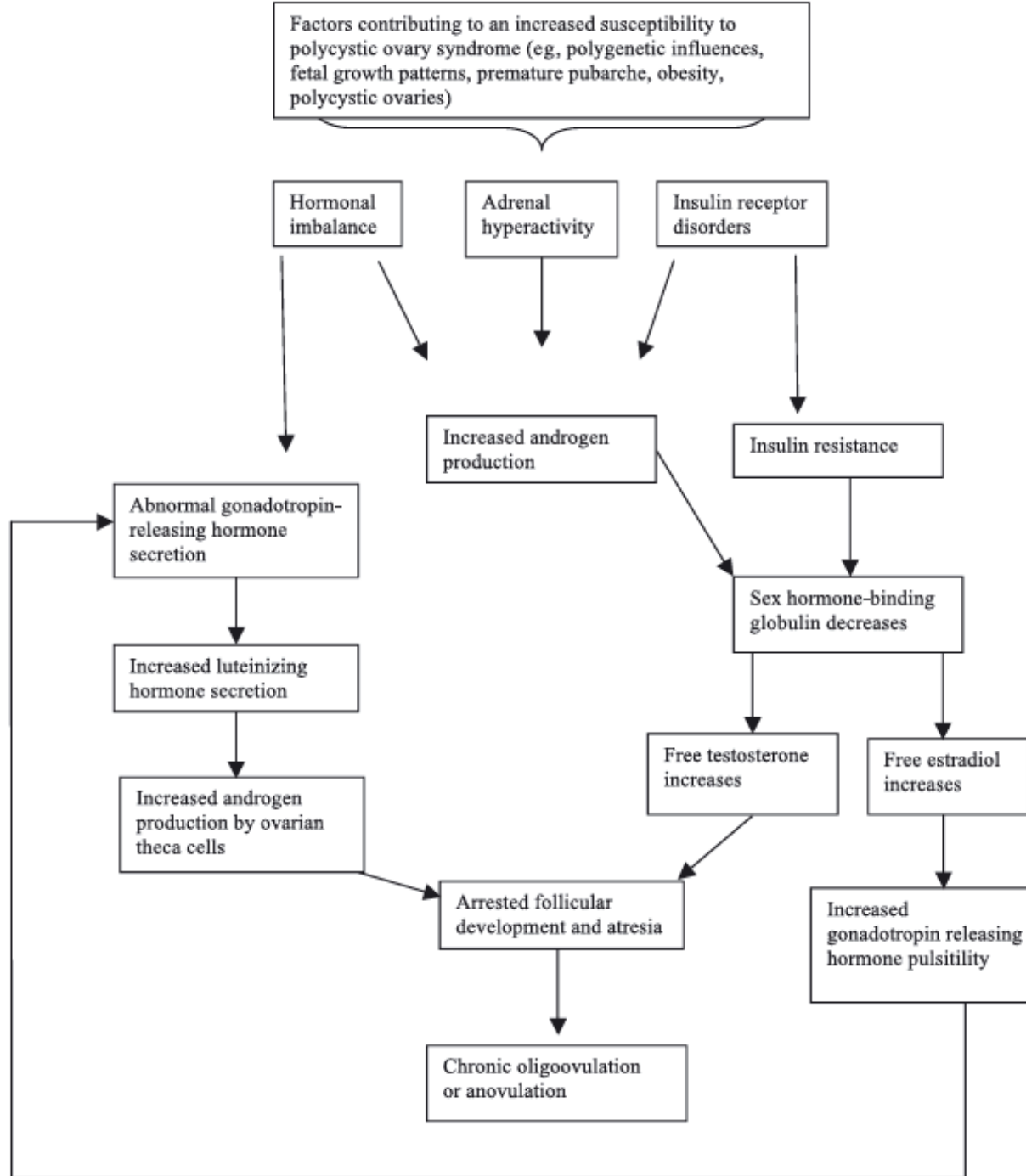


Figure 1. Pathophysiology of Polycystic Ovary Syndrome

Reprodüktif, obstetrik, endokrin, metabolik , psikolojik özelliklerle ilişkilidir....

- **Hiperandrojenizm** (Hirsutismus, akne, alopesi)

- **Hiperandrojenemi**

PKOS bir androjen fazlalığı hastalığıdır.....???????

4 esas
özellik

- **Menstrual ve ovulatuvar disfonksiyon**

- **Polikistik overler**

- **Anovulatuvar infertilite**

- **Gonadotropik bozukluklar (LH/FSH)**

- **İnsülin rezistansı/hiperinsülinemi**

- **Metabolik özellikler**

Metabolik sendrom, dislipidemi, Tip 2 DM, IGT, Obezite, KVSH vs

- **Obstetrik özellikler**

Erken gebelik kaybı, GDM, PIH, neonatal komplikasyonlar

TANISAL DEĞİL
ANCAK
METABOLİK
FENOTİPTE
ÖNEMLİ.....

4 Esas Özellik +/- Açısından Olası Tüm Fenotipler

Features	Potential Phenotypes															
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Hyperandrogenemia	+	+	+	+	-	-	+	-	+	-	+	-	-	-	+	-
Hirsutism	+	+	-	-	+	+	+	+	-	-	+	-	-	+	-	-
Oligo-anovulation	+	+	+	+	+	+	-	-	-	+	-	-	+	-	-	-
Polycystic ovaries	+	-	+	-	+	-	+	+	+	+	-	+	-	-	-	-
NIH 1990 criteria	✓	✓	✓	✓	✓	✓										
Rotterdam 2003 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						
AE-PCOS 2006 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						

Atz: AE-PCOS Society report on PCOS phenotype. Fertil Steril 2009.

Klasik PKOS

Ovulatuvar PKOS

Non-HA Anovulatuvar PKOS

İki yeni PKOS fenotipi : 1. Hiperandrojenik ovulatuvar PCO'lu kadınlar
2. Non-hiperandrojenik anovulatuvar PCO'lu kadınlar

Reproduktif Tanı Kriterlerine Göre Farklı PKOS Fenotipleri*

Features:	Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenism (biochemical or clinical)	+	+	+	-	+	-	-
Oligo- or anovulation	+	+	-	+	-	-	+
Polycystic ovaries	+	-	+	+	-	+	-
<u>NIH criteria</u>	✓	✓					
ESHRE/ASRM criteria	✓	✓	✓	✓			
AES criteria	✓	✓	✓				

NIH PKOS

(HA +)

- Fenotip A (PKO +)
- Fenotip B (PKO -)

non-NIH PKOS

(PKO +)

- Fenotip C (HA +)
- Fenotip D (HA -)

Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria

Bulent Okan Yildiz¹, Gurkan Bozdogan², Zuhar Yapici², Ibrahim Esinler², and Hakan Yarali^{2*}

¹Endocrinology and Metabolism Unit, Department of Internal Medicine, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey; ²Departments of Obstetrics and Gynecology, Hacettepe University School of Medicine, Hacettepe, 06100 Ankara, Turkey

Table I Prevalence of the component and composite phenotypes in PCOS.

Phenotype	n	%
All normal	190	48.5
PCO only	69	17.6
Hyperandrogenism only	37	9.4
Hirsutism only	6	1.5
Hyperandrogenemia only	26	6.6
Hirsutism and hyperandrogenemia	5	1.3
OD only	18	4.6
Hyperandrogenism + PCO	36	9.2
Hyperandrogenism + PCO + OD	20	5.1
OD + PCO	18	4.6
Hyperandrogenism + OD	4	1.0

Relative Prevalence of Different Androgen Excess Disorders in 950 Women Referred because of Clinical Hyperandrogenism

The Journal of Clinical Endocrinology & Metabolism 91(1):2-6
Copyright © 2006 by The Endocrine Society
doi: 10.1210/jc.2005-1457

E. Carmina, F. Rosato, A. Janni, M. Rizzo, and R. A. Longo

Departments of Endocrinology (E.C., F.R., A.J.) and Clinical Medicine (E.C., M.R., R.A.L.), University of Palermo, 90139 Palermo, Italy

TABLE 1. Prevalence of different androgen excess disorders in 950 women referred because of clinical hyperandrogenism

	No. of patients	% of total no. of patients
Classic PCOS	538	56.6
Ovulatory PCOS	147	15.5
Idiopathic hyperandrogenism	150	15.8
Idiopathic hirsutism	72	7.6
NCAH	41	4.3
Androgen-secreting tumors	2	0.2

%72

Specific dermatologic features of the polycystic ovary syndrome and its association with biochemical markers of the metabolic syndrome and hyperandrogenism

SUNA ÖZDEMİR¹, MUSTAFA ÖZDEMİR², HÜSEYİN GÖRKEMLİ³, AYSEL KIYICI³ & SAİT BODUR⁴

¹Department of Gynecology and Obstetrics, ²Dermatology, ³Biochemistry, and ⁴Public Health, Meram Medical Faculty, Selçuk University, Konya, Turkey

Acta Obstetricia et Gynecologica. 2010; 89: 199–204

Table 2. Prevalence of the cutaneous features in women with PCOS.

Skin features	Women with PCOS (n = 115) N (%)
Acne	61 (53)
Hirsutism	85 (73.9)
Seborrhea	40 (34.7)
Female pattern hair loss	40 (34.7)
Acanthosis nigricans	6 (5.2)

Note: PCOS, polycystic ovary syndrome.

Akne

- PKOS'lu olguların %15-25 ini etkiler
- PKOS'ta prevalansının daha yüksek olduğu net değil
- Akne şikayeti olan kadınların %20-40'ında PKOS (+)

Alopesi

- PKOS'un bulgularından birisi olarak tanımlanmıştır
- PKOS'ta prevalansı net değil (%5 - %50)
- Alopesi olan kadınların ise %10'unda PKOS (+)

The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report

Ricardo Azziz, M.D., M.P.H.,^a Enrico Carmina, M.D.,^b Didier Dewailly, M.D.,^c

Evanthia Diamanti-Kandarakis, M.D.,^d Héctor F. Escobar-Morreale, M.D., Ph.D.,^e

Walter Futterweit, M.D.,^f Orno E. Janssen, M.D.,^g Richard S. Legro, M.D.,^h

Robert J. Norman, M.D.,ⁱ Ann E. Taylor^j and Selma F. Witchel, M.D.,^k (Task Force on the Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PCOS Society*)

Prevalence of hyperandrogenemia and hirsutism in the polycystic ovary syndrome (PCOS).

Study	Reference	Total No. PCOS	No. with elevated Total T	% with elevated Total T	No. with elevated Free T	% with elevated Free T	No. with elevated DHEAS	% with elevated DHEAS	No. with Hirsutism ^c	% with Hirsutism ^c
Ferrman & Purdie, 1983	83	280							230	82.14%
Conway et al., 1989	84	556	110	22.30% ^a					320	57.55%
Kiddy et al., 1990	85	263							129	49.05%
Rajkhowa et al., 1995	86	153							123	80.39%
Balen et al., 1995	87	1741	503	28.90%					1153	66.23%
Norman et al., 1995	109	122							103	84.43%
Falsetti & Eleftheriou, 1996	88	240							92	38.33%
Khoury et al., 1996	89	112							20	17.86%
Talbott et al., 1998	90	244							105	43.03%
Alborzi et al., 2001	92	371							300	80.86%
Williamson et al., 2001	93	162							147	90.74%
Amer et al., 2002	95	161							53	32.92%
Orio et al., 2003	97	100	33	33.00%			27	27.00%	100	100.00%
Azziz et al., 2004	47	873							517	72.20%
Chang et al., 2005	98	316	122	38.60%	216	68.40%	71	22.50%	224	70.89%
Hahn et al., 2005	99	200	162	81.00%			76	38.00%	129	64.50%
Legro et al., 2006	110	626	373	60.80% ^b					505	80.67%
Diamanti-Kandarakis & Danidis, 2007	100	634	535	84.38%			70	11%	441	69.55%
Total		6281	1838	29.26%	216	3.44%	244	3.88%	4691	74.69%



1. En sık görülen androjenik dermatolojik fenotip **HİRSUTİSMUS**
2. Alopesi/Akne ile biyokimyasal HA düzeyi açısından fark yok
3. Alopesi/akne varlığı ile menstruasyon disfonksiyonu açısından korelasyon yok
4. Hirsutismuslu kadınların **%70-80'i**
Akneli kadınların **%20-40'ı**
Alopesili olguların ise sadece **%10'u** PKOS
5. PKOS'lu olgularda **%70** serbest T yüksek
6. Total T, androstenedion ve DHEAS ölçümlerinin diagnostik değeri kısıtlı

Hafif Tip Androjen Fenotipleri

- Ovulatuvar bozukluğun saptanmadığı androjen fenotipin hafif olduğu kadınları ifade eder
- Sık görülen HA formudur
- Erişkin kadınların %2-4'ünü etkiler
- HA olguların %12'sini oluşturur.
- 3 ana neden ayırıcı tanıda düşünülmelidir

– **Ovulatuvar PCOS**

– **İdiopatik Hirsutismus**

– **İdiopatik Hiperandrojenemi**

Klinik HA olgularının %23'ünü oluşturur

Hafif Hiperandrojenik Fenotipler

Features	Potential Phenotypes															
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Hyperandrogenemia	+	+	+	+	-	-	+	-	+	-	+	-	-	-	+	-
Hirsutism	+	+	-	-	+	+	+	+	-	-	+	-	-	+	-	-
Oligo-anovulation	+	+	+	+	+	+	-	-	-	+	-	-	+	-	-	-
Polycystic ovaries	+	-	+	-	+	-	+	+	+	+	-	+	-	-	-	-
NIH 1990 criteria	✓	✓	✓	✓	✓	✓										
Rotterdam 2003 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						
AE-PCOS 2006 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						

Atz: AE-PCOS Society report on PCOS phenotype. Fertil Steril 2009.

Ovulatuvar
PKOS

İdiopatik
Hiperandrojenizm



- Klinik fenotip klasik PKOS'a benzer
- PCO her zaman (+)
- Ovulasyon bozukluğunun olmaması önemli
- Sadece menstruasyon düzenli değil ovulasyon da düzenli
- Fertilité problemi (-)

Mild androgen phenotypes

Enrico Carmina* MD

Professor and Head of Endocrine Unit

Department of Clinical Medicine, University of Palermo, Via delle Croci 47, 90139 Palermo, Italy

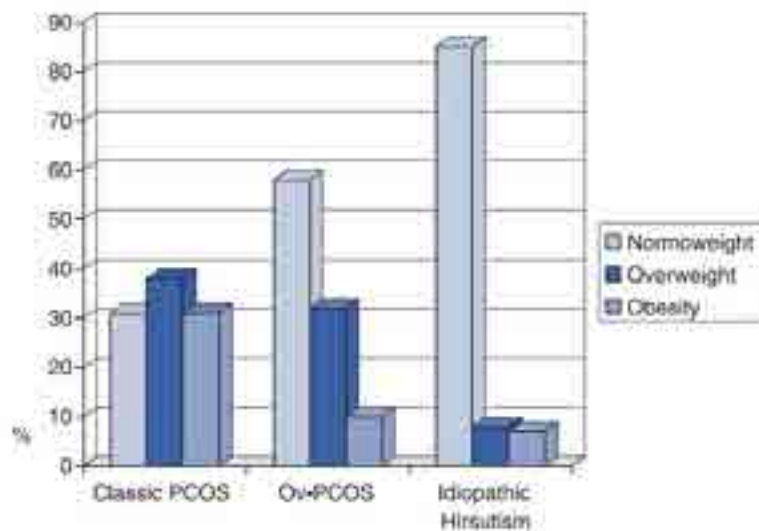


Figure 1. Distribution of body weight in women with classic (anovulatory) polycystic ovary syndrome (PCOS), ovulatory PCOS (ov-PCOS), and idiopathic hirsutism. Normalweight, BMI 19–24.9; overweight, BMI 25–29.9; obesity, BMI ≥ 30 .

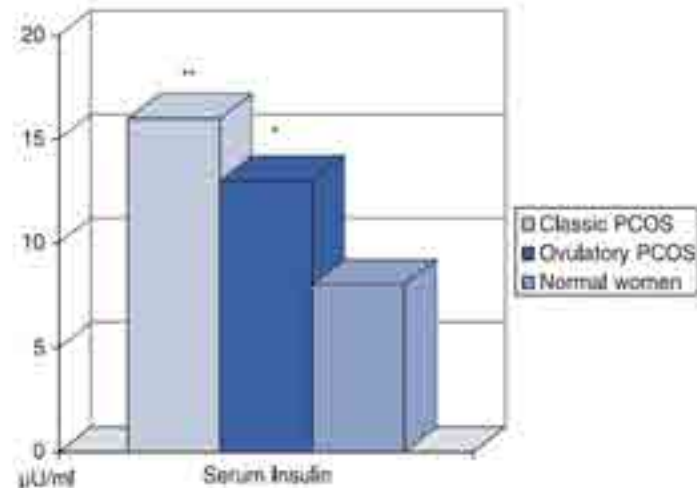


Figure 2. Fasting serum insulin in normal women and in patients with classic (anovulatory) polycystic ovary syndrome (PCOS) and with ovulatory PCOS. ** $P < 0.01$ versus ovulatory PCOS and normal women; * $P < 0.01$ versus normal women. Modified from Carmina et al (2005, *Journal of Clinical Endocrinology and Metabolism*, 90: 2545–2549) with permission.

Ovulatuar PKOS



- PKOS'un hafif bir fenotipidir
- Klinik ve biyolojik fenotip özellikleri;

1. Hiperandrojenizm VAR
2. Ovulatuar bozukluk YOK
3. Vücut ağırlığı HAFİF ARTMIŞ
4. Hiperinsülinemi HAFİF
5. İnsülin rezistansı HAFİF
6. Dislipidemi HAFİF

OLGU 1

- 19 yaşında
- BMI: 27.2
- Hirsutismus (+)
- Androjen seviyeleri artmış
- Normal ve ovulatuar siklusları var
- USG: Bilateral PCO
- Açlık serum insülin seviyesi: 13 μ U/mL

TANI: OVULATUAR PKOS

OLGU 2

- 23 yaşında
- BMI:33
- Hirsutismus (+)
- Androjen seviyeleri artmış
- Oligomenore/Kronik anovulatuar siklusları mevcut
- USG: Bilateral PCO
- Açlık serum insülin seviyesi: 19 μ U/mL

TANI: KLASİK PKOS

AYNI HASTA !!!!!.....



PKOS'ta ovulasyon bozukluğunun gelişmesinde tek başına hiperandrojenemiden ziyade, hiperandrojenemi ve orta-şiddetli hiperinsülineminin kombine etkisi gerekmektedir !!!...



PKOS'ta Reprodiktif Fenotipik Ekspresyon

- Ovulatuar ve Menstrual Disfonksiyon
- Polikistik Ovaryan Morfoloji

The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population

RICARDO AZZIZ, KESLIE S. WOODS, ROSARIO REYNA, TIMOTHY J. KEY,
 ERIC S. KNOCHENHAUER, AND BÜLENT O. YILDIZ

TABLE 1. Number of individuals with PCOS among 400 unselected women of reproductive age

Initial presentation ^a	n	Complete evaluation	No. of confirmed PCOS ^b	No. of possible PCOS ^c	Probability that patients with possible PCOS have PCOS ^d	No. of additional calculated PCOS ^e
Eumenorrhea without hirsutism	293	293	0	0	0	0
Menstrual dysfunction only	80	38	3	42	0.08 (3/38)	3.4
Hirsutism only	16	9	6	7	0.08 (6/9)	4.7
Menstrual dysfunction and hirsutism	11	7	6	4	0.67 (6/7)	3.4
Total	400	347	15	53	—	11.5

% 22.8

^a The initial presentation is based on the clinical features evident before the hormonal evaluation.

^b Confirmed PCOS was established by the presence of oligo- or anovulatory cycles (<26 d or >35 d in length; or anovulation demonstrated by a midluteal progesterone level <4 ng/ml if cycles were 26–35 d in length), with hyperandrogenemia and/or hirsutism (anF-G score ≥ 4), after the exclusion of related disorders (hypothyroidism, Cushing's disease, and NCAH). In individuals whose evaluations were complete.

2) Women with menstrual dysfunction only. Eighty women (20% of the total) had menstrual dysfunction without hirsutism (Table 1). Thirty-eight subjects had complete evaluations, and three of these had confirmed PCOS. The remaining 42 individuals with incomplete evaluations were designated as having possible PCOS. Their individual probability of PCOS was 0.08 (i.e. 3 of 38 in the group completing evaluation), and the total number of additional PCOS cases from this group was 3.4 (i.e. 0.08 × 42). The prevalence of PCOS in this phenotype was 8% (6.4 of 80).

The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria

Human Reproduction, Vol.25, No.2 pp. 544–551, 2010

Wendy A. March^{1,2}, Vivienne M. Moore³, Kristyn J. Willson¹,
 David I.W. Phillips³, Robert J. Norman¹, and Michael J. Davies^{1,4}

Table II Number of individuals with PCOS under the NIH, Rotterdam and AES criteria among 728 unselected women

PCOS criteria	Total known PCOS n (% ± CI)	Total + imputed polycystic ovaries ^a
1. NIH (Menstrual dysfunction + hirsutism and/or high free T)	63 (8.7 ± 2.0)	
2. Rotterdam Phenotypes	87 (11.9 ± 2.4)	129.5 (17.8 ± 2.8)
a. Menstrual dysfunction + hirsutism and/or high free T + polycystic ovaries	17 (2.3 ± 1.1)	27.4 (3.8 ± 1.4)
b. Menstrual dysfunction + hirsutism and/or high free T only (no polycystic ovaries)	21 (2.9 ± 1.2)	35.6 (4.9 ± 1.6)
a. or b. Menstrual dysfunction + hirsutism and/or high free T + polycystic ovaries (unknown if polycystic ovaries present as did not have an ultrasound)	25 (3.4 ± 1.3)	values added to phenotype a. or b.
c. Hirsutism and/or high free T + polycystic ovaries	11 (1.5 ± 0.9)	24.5 (3.4 ± 1.3)
d. Menstrual dysfunction + polycystic ovaries	13 (1.8 ± 1.0)	42.1 (5.8 ± 1.7)
3. Androgen Excess Society (a., b. or c.)	74 (10.2 ± 2.2)	87.5 (12.0 ± 2.4)

The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report

TABLE 2

Prevalence of menstrual dysfunction in the polycystic ovary syndrome (PCOS).

Study	Reference	Total No. PCOS	No. of PCOS patients with oligo-amenorrhea	% of PCOS patients with oligo-amenorrhea	No. of PCOS patients with eumenorrhea	% of PCOS patients with eumenorrhea
Ferriman & Purdie, 1983	83	280	237	84.60%	43	15.40%
Conway et al., 1989	84	556	395	71.00%	139	25.00%
Kiddy et al., 1990	85	263	203	77.20%	60	22.80%
Ardaens et al., 1991	65	144	105	72.90%	39	27.10%
Rajkhowa et al., 1995	86	153	129	84.30%		
Balen et al., 1995	87	1741	1043	59.90%	517	29.70%
Falsetti & Eleftheriou, 1996	88	240	207	86.30%	24	10.00%
Khoury et al., 1996	89	112	112	100.00%	0	0.00%
Talbott et al., 1998	90	244	229	93.90%	15	6.10%
Carmina et al., 1998	91	332	290	87.30%	42	12.70%
Alborzi et al., 2001	92	371	371	100.00%	0	0.00%
Williamson et al., 2001	93	162	144	88.90%		
Haddad et al., 2002	94	146	120	82.20%	26	17.80%
Amer et al., 2002	95	161	149	92.50%	12	7.50%
Glueck et al., 2003	96	138	138	100.00%	0	0.00%
Orio et al., 2003	97	100	100	100.00%	0	0.00%
Chang et al., 2005	98	316	265	83.90%	51	16.10%
Hahn et al., 2005	99	200	200	100.00%	0	0.00%
Carmina et al., 2006	46	685	538	56.60%	147	15.50%
Diamanti-Kandarakis & Danidis, 2007	100	634	545	85.90%	89	14.10%
Total		6978	5520	79.11% ^a	1204	17.25%

Do hyperandrogenic women with normal menses have polycystic ovary syndrome?

Enrico Carmina, M.D., and Rogério A. Lobo, M.D.

Result(s): Twelve (20.7%) of the hyperandrogenic women were anovulatory and met the usual criteria for the diagnosis of PCOS. The ovulatory patients had lower serum total and unbound testosterone levels. Thirty-one (53.4%) of the ovulatory women had polycystic ovaries on ultrasound examination and/or an increased 17-OHP response to leuprolide acetate, suggesting the diagnosis of PCOS despite the presence of ovulation. Considering both the anovulatory and ovulatory patients, 74% of the hyperandrogenic women studied could have PCOS.

Conclusion(s): The data suggest that most (74%) hyperandrogenic women who report normal menses have evidence for the diagnosis of PCOS. (*Fertil Steril*® 1999;71:319–22, ©1999 by American Society for Reproductive Medicine.)

FIGURE 1

Testosterone (T) and unbound testosterone levels in hyperandrogenic women with normal menses who were found to be ovulatory or anovulatory (□). Asterisks indicate statistically significant differences between the two groups ($P < .05$).

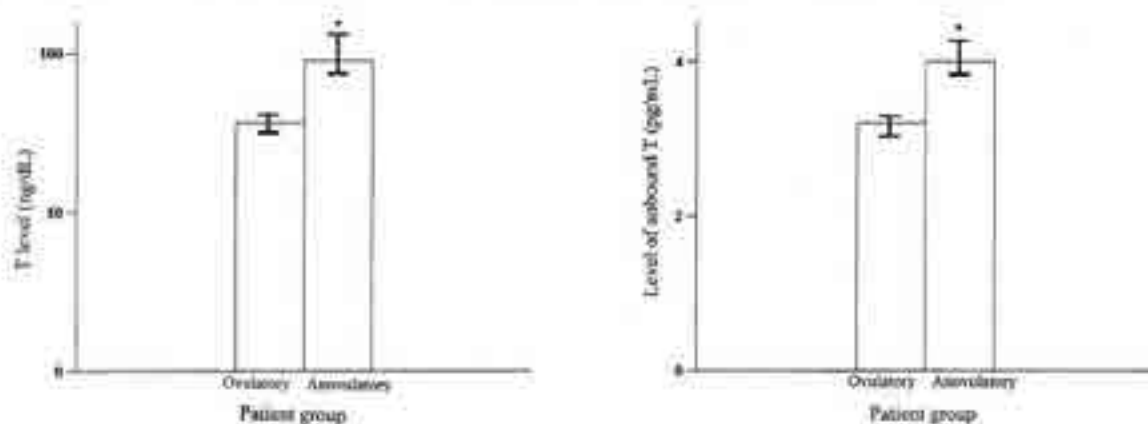
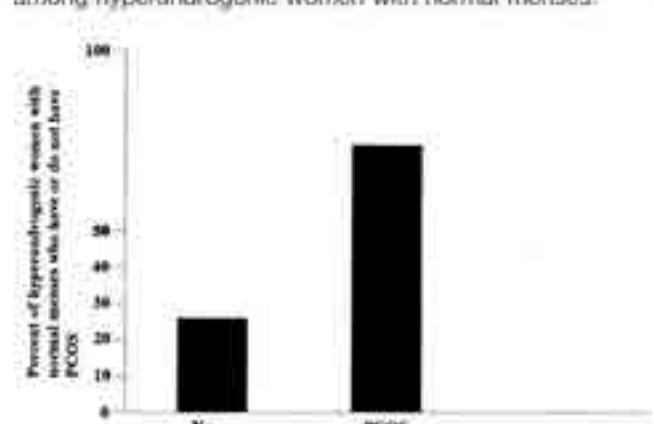


FIGURE 2

Suggested prevalence of polycystic ovary syndrome (PCOS) among hyperandrogenic women with normal menses.



Obesity, rather than menstrual cycle pattern or follicle cohort size, determines hyperinsulinaemia, dyslipidaemia and hypertension in ageing women with polycystic ovary syndrome

Mariet W. Elting, Ted J. M. Korse and Joop Schoemaker

Research Institute of Endocrinology, Reproduction and Metabolism, Department of Obstetrics, Gynaecology and Reproductive Medicine, Vrije Universiteit Medical Centre, Amsterdam, The Netherlands

Table 1 Characteristics of 53 PCOS women divided by their present menstrual cycle pattern (mean \pm SD or median + range)

	Total	Regular	Irregular	P-value
Characteristics	<i>n</i> = 53	<i>n</i> = 41	<i>n</i> = 12	
Age (years)	41.3 \pm 3.6	42.1 \pm 3.5	38.7 \pm 2.9	0.004
BMI (kg/m ²)	25.5 (19.2–48.8)	25.2 (19.7–44.3)	28.9 (19.2–48.8)	0.09
WHR (cm/cm)	0.82 \pm 0.08	0.82 \pm 0.08	0.84 \pm 0.08	NS
DBP (mmHg)	78.3 \pm 9.6	77.9 \pm 9.0	79.8 \pm 11.7	NS
SBP (mmHg)	120.3 \pm 13.8	121.4 \pm 14.0	116.8 \pm 13.1	NS
Ultrasound	<i>n</i> = 48	<i>n</i> = 36	<i>n</i> = 12	
Follicle count	5.8 \pm 3.1	5.1 \pm 2.6	7.8 \pm 3.7	0.009
Ovarian volume	6.5 \pm 2.8	6.0 \pm 2.7	7.9 \pm 2.7	0.05

NS, not significant.

1. Normal populusyonda menstrual siklus bozukluk prevalansı %18'dir. (%14.6-%22.9)



Bu olguların 1/4 veya 1/3 ünde PKOS mevcuttur...

2. PKOS'lu olguların %75-85 inde menstrual bozukluk vardır
3. Ancak oligo-amenoreik PKOS olgularında siklusların %30 u ovulatuardır...
4. PKOS ta menstrual sikluslar yaş ilerledikçe daha düzenli halme eğilimindedir
5. Menstrual bozukluk artmış AFS, BMI, metabolik risk ve daha siddetli PKOS fenotipleri ile ilişkilidir...

6. Düzenli menstruasyon kronik anovulasyon olmadığını göstermez....
7. Bu olgu grubu esas olarak hem klinik hem biyokimyasal HA ile ilişkilidir
8. Hiperandrojenizimli olguların yaklaşık %20 sinde menstruasyon normaldir. Ancak bu olguların **%20-50'sinde kronik anovulasyon** eşlik eder.
9. PKOS olgularının **%20-30'unda** menstruasyon düzenli iken kronik anovulasyon eşlik eder.....



Hiperandrojenik olgularda düzenli menstruasyon varlığında ovulatuvar fonksiyon ayrıca değerlendirilmelidir. Genellikle 20-24 P ölçümü değerlendirme için yeterlidir. Bu olguların yaklaşık %40 ında PKOS tanısı konacaktır....

PKOS'ta Reprodiktif Fenotipik Ekspresyon

- Ovulatuvar ve Menstrual Disfonksiyon
- Polikistik Ovaryan Morfoloji

Polikistik Over Tanımlama-1

- PKO tanımlaması için 3 kriter değerlendirilmiştir
 - Ovaryan boyut ve hacim (volume)
 - Stromal volume
 - Follikül boyut ve sayısı
- PKO'nun sonografik tanı kriterlerinin tanımlanması tartışmalıdır
- *Adams, J.M., Franks, S., Polson, D.W., et al. Multifollicular ovaries: clinical and endocrine features and response to pulsatile gonadotropin releasing hormone. Lancet 1985;2:1375±1378.*

- **İlk yapılan tanımlama**

- PKO ya ait 2 ana histolojik özelliği içerir:

1. Artmış follikül sayısı
"Multifollikül" olarak tanımlanmıştır
2. Stromal hipertrofi

Dens (ekojen) bir stroma etrafında
periferik yerleşimli
veya
Artmış bir stroma boyunca dağılmış
2-8 mm çaplı ≥ 10 kistlerin varlığı

- Bu kriterler,
 1. Subjektif
 2. Transvajinal USG uygulamaları
 3. Multifoliküler over ile olan karışıklıklar vs. nedeniyle

Dewailly et al. tarafından 2003 yılında revize edildi.

Ultrasound assessment of the polycystic ovary: international consensus definitions

Human Reproduction Update, Vol.9, No.6 pp. 505-514, 2003

Adam H.Balen^{1,4}, Joop S.E.Laven², Seang-Lin Tan³ and Didier Dewailly⁴

Table II. Receiver operating characteristic (ROC) curve data for the assessment of polycystic ovaries (Jonard *et al.*, 2003)

FNPO (mm)	Area under ROC curve	Threshold	Sensitivity (%)	Specificity (%)
2-5	0.924	10	65	97
		12	87	90
		15	42	100
6-9	0.502	3	32	69
		4	32.5	80
		5	71	80
2-9	0.937	10	86	90
		12	75	90
		15	88	100

FNPO = follicle number per ovary.

Günümüzde en sık kullanılan 2003 ESHRE/ASRM Rotterdam Consensus kriterleri ortaya atıldı.

ESHRE/ASRM Konsensus Kriterleri

Table III. Ultrasound assessment of the polycystic ovary (PCO): international consensus definitions

Definition

1. The PCO should have at least one of the following: either 12 or more follicles measuring 2–9 mm in diameter or increased ovarian volume (>10 cm³). If there is evidence of a dominant follicle (>10 mm) or a corpus luteum, the scan should be repeated during the next cycle.
2. The subjective appearance of PCOs should not be substituted for this definition. The follicle distribution should be omitted as well as the increase in stromal echogenicity and/or volume. Although the latter is specific to polycystic ovary, it has been shown that measurement of the ovarian volume is a good surrogate for the quantification of the stroma in clinical practice.
3. Only one ovary fitting this definition or a single occurrence of one of the above criteria is sufficient to define the PCO. If there is evidence of a dominant follicle (>10 mm) or corpus luteum, the scan should be repeated next cycle. The presence of an abnormal cyst or ovarian asymmetry, which may suggest a homogeneous cyst, necessitates further investigation.
4. This definition does not apply to women taking the oral contraceptive pill, as ovarian size is reduced, even though the 'polycystic' appearance may persist.
5. A woman having PCO in the absence of an ovulation disorder or hyperandrogenism ('asymptomatic PCO') should not be considered as having PCOS, until more is known about this situation.
6. In addition to its role in the definition of PCO, ultrasound is helpful to predict fertility outcome in patients with PCOS (response to clomiphene citrate, risk for ovarian hyperstimulation syndrome (OHSS), decision for in-vitro maturation of oocytes). It is recognized that the appearance of PCOs may be seen in women undergoing ovarian stimulation for IVF in the absence of overt signs of PCOS. Ultrasound also provides the opportunity to screen for endometrial hyperplasia.
7. The following technical recommendations should be respected:
 - State-of-the-art equipment is required and should be operated by appropriately trained personnel.
 - Whenever possible, the transvaginal approach should be preferred, particularly in obese patients.
 - Regularly menstruating women should be scanned in the early follicular phase (days 3–5). Oligo-/amenorrhoeic women should be scanned either at random or between days 3–5 after a progestogen-induced bleed.
 - If there is evidence of a dominant follicle (>10mm) or a corpus luteum, the scan should be repeated the next cycle.
 - Calculation of ovarian volume is performed using the simplified formula for a prolate ellipsoid ($0.5 \times \text{length} \times \text{width} \times \text{thickness}$).
 - Follicle number should be estimated both in longitudinal, transverse and antero-posterior cross-sections of the ovaries. Follicle size should be expressed as the mean of the diameters measured in the three sections.



MULTİFOLLİKÜLER OVER

- Subjektif, kesin tanı kriterleri net değil
- 4-10 mm çaplı tek planda ≥ 6 multipl kistler
- Over boyunca kistlerin dağıldığı gözlenir
- Stromal ve over volüm/ekojenite artışı görülmez
- Non-hirsute ovulatuvar kadınların en az bir overde MFO saptanma oranı yaklaşık %40

1. Hipotalamik amenore/anovulasyon

- a) Aşırı egzersiz
- b) Diyet kısıtlaması ve ani kilo verme
- c) Psikolojik stress

2. Orta-Geç normal puberte

3. Santral puberte prekoks

4. Hiperprolaktinemi

5. NORMAL ERİŞKİN KADIN ERKEN FOLLİKÜLER FAZ

- **Sadece bir overde**
- **Dominant follikülden önce**



Transvaginal ultrasound detection of multifollicular ovaries in non-hirsute ovulatory women

J. PHY*, S. FOONG*, D. SESSION*, A. THORNHILL*, L. TUMMON* and D. DUMESIC*†

*Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, †Division of Endocrinology, Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA

In conclusion, MFO may be identified by TVS in non-hirsute ovulatory women, in whom it is a common morphological variant of normal folliculogenesis rather than a consequence of hypothalamic dysfunction or abnormal ovarian steroidogenesis.

Table 1 Serum gonadotropin, steroid, glucose and insulin levels during day 6 of the menstrual cycle in non-hirsute ovulatory women with and those without multifollicular ovary (MFO)

Parameter	Without MFO (median (range)) (n = 20)	With MFO (median (range)) (n = 13)	P
FSH (IU/L)	5.9 (4.1-8.9)	5.6 (4.2-7.5)	0.4
LH (IU/L)	4.8 (2.7-10.8)	4.4 (2.7-7.1)	0.2
DHEAS ($\mu\text{mol/L}$)	2.7 (0.8-4.1)	3.3 (1.7-6.0)	0.1
Androstenedione (nmol/L)	5.2 (1.0-10.2)	5.2 (3.5-10.8)	1.0
Total testosterone (nmol/L)	1.4 (0.6-2.0)	1.2 (0.7-2.2)	0.6
Free testosterone (pmol/L)	3.8 (1.4-10.1)	3.8 (1.7-10.4)	0.8
Fasting glucose (mmol/L)	5.2 (4.3-5.8)	5.2 (4.7-5.8)	1.0
Fasting insulin (pmol/L)	28.9 (12.9-83.2)	23.0 (12.9-71.0)	0.2
Glucose/insulin ratio ($\text{mg}/10^{-4} \text{ U}$)	23.0 (9.0-50.0)	30.6 (8.6-51.6)	0.2
2-h postprandial glucose (mmol/L)	6.5 (4.0-7.9)	6.4 (5.1-8.3)	0.7
2-h postprandial insulin (pmol/L)	108.7 (57.4-266.9)	89.7 (35.2-796.4)	0.8
AUC glucose release (6-h $\text{mmol/L} \times \text{min}$)	367.1 (184.3-600.6)	344.7 (31.6-477.9)	0.3
AUC insulin release (6-h $\text{pmol/L} \times \text{min}$)	26 182.0 (8782.0-45 332.0)	19 875.0 (6063.0-10 6671.0)	0.3

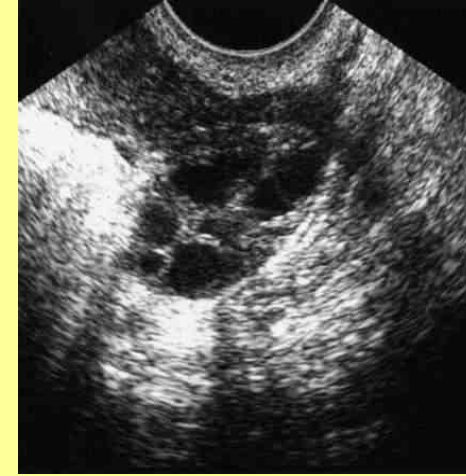
AUC, area under curve; DHEAS, dehydroepiandrosterone sulfate; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

MFO Farklar



NORMAL

- Folliküller genellikle daha büyük
- Folliküller arası stroma belirgin değil
- Folliküller birbirine daha yakın
- Over stroma ve ekojenitesinde artış yok
- Erken pubertal dönemde sık
- Pulsatil FSH sekresyonundaki hafif değişiklikler
- Hipotalamohipofizier disfonksiyon
- MFO (+)/MFO (-) kadınlar arasında;
Glukoz metabolizması,
LH/FSH düzeyi
Sex steroid seviyelerinde FARK YOK



MFO



PKO



Figure 1. Typical ultrasound evidence of PCO/PCOS of the peripheral cystic pattern: a high number of small subcapsular follicles (10 follicles with a maximum diameter <8 mm), increased ovarian volume (12.3 ml) and increased echodensity of the ovarian stroma.



Figure 2. General cystic pattern (GCP) in PCO/PCOS: the numerous ($n = 13$) small cysts are scattered through the entire ovarian parenchyma, the stroma is echodense and the volume is increased (14.0 ml).



Figure 3. Intra-ovarian stromal vascularization in PCO/PCOS: small stromal vessels with low downstream impedance (resistance index = 0.54).



Figure 4. Small-sized follicles (F) arranged around the echogenic stroma (\rightarrow) in the lower pole of the ovary. (The arrowheads are relative to the ultrasound image focus - displayed independently from the figure.)

Polikistik overler

- Genel olarak normal popülasyonun %20-30 unda (+)
- Yaşla beraber prevalansı azalır

The Polycystic Ovary Post-Rotterdam: A Common, Age-Dependent Finding in Ovulatory Women without Metabolic Significance

Erica B. Johnstone, Mitchell P. Rosen, Rebecca Neril, Deborah Trevithick, Barbara Sternfeld, Rosemary Murphy,Carolyn Addauan-Andersen, Daniel McConnell, Renee Reijo Pera, and Marcelle I. Cedars

J Clin Endocrinol Metab, November 2010, 95(11):4965–4972

PKO (+) olgularda PKOS prevalansı net değil

~ %20

Normal popülasyona göre 3 katlık risk artışı

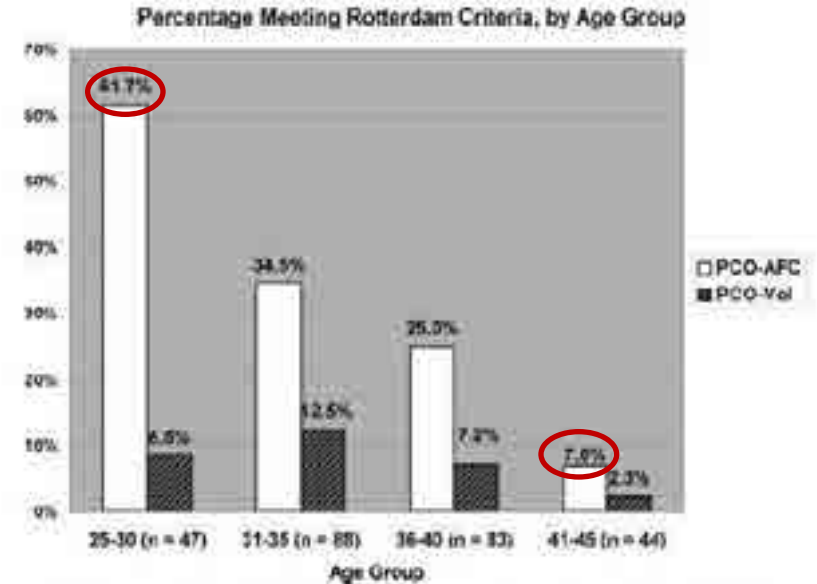
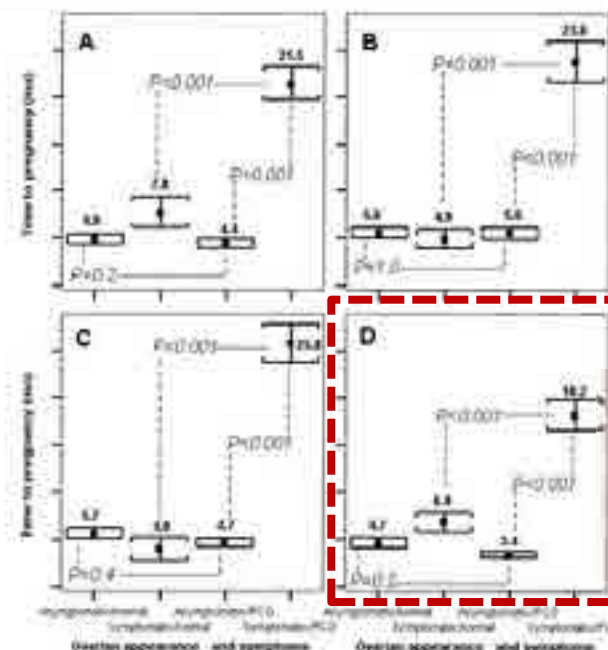


FIG. 1. Percentage of subjects meeting each portion of the Rotterdam Criteria, by age group.

Ultrasound diagnosis of polycystic ovaries in women who have no symptoms of polycystic ovary syndrome is not associated with subfecundity or subfertility

Mohamed A. M. Hassan, M.Sc., and Stephen R. Killick, M.D.

Academic Department of Obstetrics and Gynaecology, Women's and Children's Hospital, Hull Royal Infirmary, University of Hull, Hull, United Kingdom



Symptoms in study and control groups.

Symptoms	No. (%)		Odds ratio (CI)	P*
	PCO	Normal ov.		
Subfertility	135 (52.3)	47 (20.3)	2.6 (2.0-3.4)	<.001
Menstrual disturbances	139 (53.0)	35 (15.1)	3.8 (2.8-4.9)	<.001
History of obesity	118 (46.1)	46 (19.5)	2.3 (1.7-3.1)	<.001
Body mass index >29 kg/m ²	93 (36.1)	42 (18.6)	2.1 (1.5-2.8)	<.001
Acne	82 (35.0)	12 (5.2)	6.9 (3.5-12.3)	<.001
Hirsutism	68 (26.6)	33 (14.2)	1.9 (1.3-2.7)	.001
Androgens	102 (39.8)	42 (18.3)	2.2 (1.6-3.0)	<.001
Diseases (diabetes mellitus, hypertension)	24 (9.4)	10 (4.3)	2.2 (1.1-4.5)	.03
Miscarriage	38 (17.3)	34 (14.8)	1.2 (0.8-1.8)	.5
Family history of subfertility	52 (20.2)	22 (9.5)	2.1 (1.3-3.4)	.001
Family history of miscarriage	42 (16.3)	24 (10.3)	1.6 (1.0-2.5)	.06

Note: CI = 95% confidence interval.

* Fisher's exact test

Hassan. Effect of polycystic ovaries on fecundity. Fertil Steril 2005

Effect of symptoms on fecundity of women with a history of pregnancy in the study and control groups.

Symptoms	Groups (n)	TTP (months)			
		Unadjusted TTP		Adjusted TTP*	
		μ (CI)	P ^b	μ (CI)	P ^c
All four symptoms	1. Asymptomatic normal (122)	8.7 (2.8-8.7)	(2, 1) .2	7.4 (4.4-10.0)	(2, 1) .8
	2. Symptomatic normal (71)	6.0 (4.2-6.6)	(5, 1) .7	8.0 (5.4-10.0)	(5, 1) .1
	3. Asymptomatic PCO (72)	1.4 (0.8-6.1)	(4, 2) <.001	3.8 (0.6-7.1)	(4, 2) <.001
Menstrual pattern	4. Symptomatic PCO (124)	18.2 (10.2-20.2)	(4, 3) <.001	18.0 (12.0-21.1)	(4, 3) <.001
	1. Regular cycle/normal (110)	4.0 (2.5-6.0)	(2, 1) .2	3.5 (2.8-11.2)	(2, 1) 1.0
	2. Disturbed cycle/normal (90)	7.8 (5.8-11.7)	(3, 1) .7	8.5 (4.8-12.1)	(3, 1) .4
	3. Regular cycle/PCO (101)	4.4 (2.1-6.6)	(4, 2) <.001	5.4 (2.5-8.2)	(4, 2) <.001
Obesity (Body mass index >29)	4. Disturbed cycle/PCO (107)	21.5 (10.4-23.6)	(4, 3) <.001	19.7 (16.6-22.1)	(4, 3) <.001
	1. Thin women/normal (160)	5.0 (3.9-7.3)	(2, 1) .7	6.7 (4.9-6.6)	(2, 1) 1.0
	2. Obese women/normal (34)	4.9 (1.3-8.6)	(3, 1) 1.0	6.7 (4.1-9.4)	(3, 1) .68
	3. Thin women/PCO (121)	5.0 (3.6-7.3)	(4, 2) <.001	2.9 (1.4-6.4)	(4, 2) <.001
Androgens (acne/hirsutism)	4. Obese women/PCO (77)	25.8 (21.4-26.2)	(4, 3) <.001	24.1 (21.4-27.1)	(4, 3) <.001
	1. Nonandrogen/normal (161)	5.7 (4.1-7.2)	(2, 1) .4	7.6 (5.1-10.2)	(2, 1) .1
	2. Androgen/normal (39)	4.0 (0.8-7.2)	(3, 1) .4	5.8 (2.8-8.7)	(3, 1) .8
	3. Nonandrogen/PCO (122)	4.7 (2.9-6.5)	(4, 2) <.001	8.2 (4.8-13.5)	(4, 2) <.001
	4. Androgen/PCO (84)	25.8 (21.6-28.0)	(4, 3) <.001	29.3 (25.8-32.7)	(4, 3) <.001

Note: TTP = time to pregnancy; μ = mean; CI = 95% confidence interval; PCO = polycystic ovary.

* TTP adjusted for missing reasons, issues of subfertility-older than conception, history of gynecological diseases, the ages of the women and their partners, smoking, alcohol consumption, or parity.

^b Analysis of variance.

^c General linear model.

Hassan. Effect of polycystic ovaries on fecundity. Fertil Steril 2005

Endocrine abnormalities in ovulatory women with polycystic ovaries on ultrasound

E.Carmina¹, L.Wong², L.Chang², R.J.Paulson¹, M.V.Sauer¹, F.Z.Stanczyk² and R.A.Lobo^{1,3}

¹Department of Obstetrics and Gynecology, Columbia University College of Physicians & Surgeons, 630 West 168th Street, New York, NY 10032 and ²Department of Obstetrics and Gynecology, University of Southern California School of Medicine, Los Angeles, California, USA

Table 1. Serum androgens (mean \pm SE) in ovulatory NAO (normal-appearing ovaries) and PAO (polycystic-appearing ovaries)/PCO (polycystic ovaries) women, in obese polycystic ovarian syndrome (PCOS) and in normal weight PCOS patients

	Testosterone (nmol/l)	Unbound testosterone (pmol/l)	Androstenedione (nmol/l)	DHEAS (µmol/l)
NAO	1 \pm 0.1	11.8 \pm 1.4	6 \pm 0.3	4.7 \pm 0.5
PAO/PCO	1.2 \pm 0.1	15.9 \pm 3.5	7.7 \pm 0.7	4.7 \pm 0.4
Overweight PCOS	3.2 \pm 1.3 ^a	79.4 \pm 5 ^a	12.9 \pm 1 ^a	8.7 \pm 0.9 ^a
Normal weight PCOS	2.8 \pm 0.8 ^a	38 \pm 8 ^a	11.8 \pm 1 ^a	10 \pm 1.1 ^a

DHEAS = dihydroepiandrosterone sulphate.
^aP < 0.01 versus NAO and PAO/PCO women

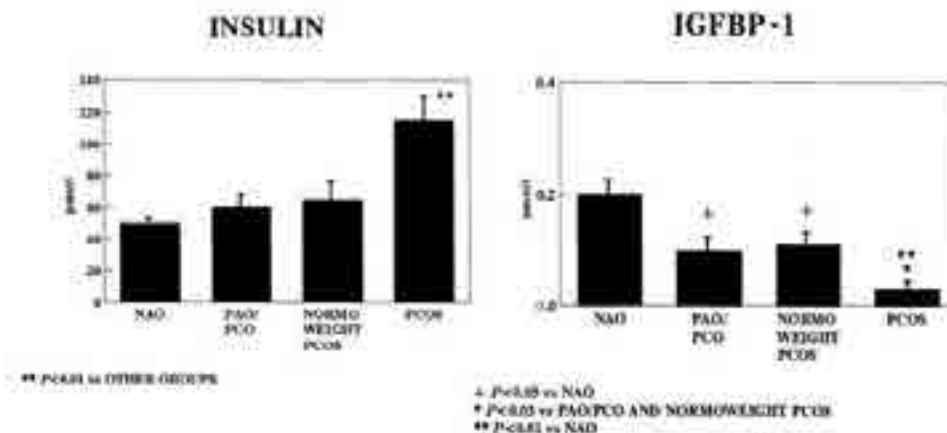
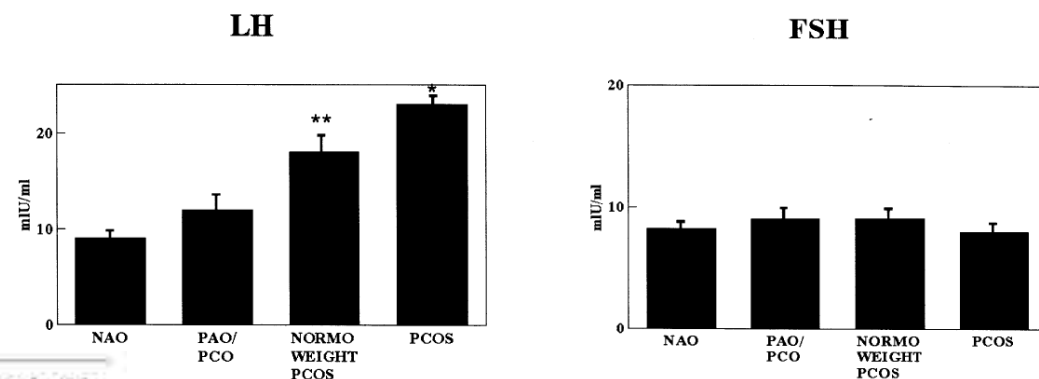


Figure 3. Serum concentrations (mean \pm SE) of insulin and insulin-like growth factor binding protein-1 (IGFBP-1) in ovulatory NAO and PAO/PCO women and in PCOS patients of normal and increased body weight. For abbreviations see Figure 1

Polycystic ovaries at ultrasound: normal variant or silent polycystic ovary syndrome?

S. CATTEAU-JONARD^{*,†}, J. BANCQUART^{*,†}, E. PONCELET^{†,‡}, C. LEFEBVRE-MAUNOURY^{*,†},
G. RORIN^{*,†} and D. DEWAILLY^{*,†}

Table 1 Clinical and metabolic characteristics of controls, women with polycystic ovaries (PCO) and women with polycystic ovary syndrome (PCOS)

Characteristic	Controls (n = 95)	PCO group (n = 95)	PCOS group (n = 95)	P _‡
Age (years)	29 (17–39)	29 (17–39)	29 (17–39)	NS
BMI (kg/m ²)	23.9 (17.3–44.0)	23.0 (17.0–43.4)	26.5 (15.0–53.0)	b,c
Systolic BP (mmHg)	110 (95–150)	110 (90–140)	110 (90–150)	NS
Diastolic BP (mmHg)	70 (50–93)	70 (50–97)	70 (50–90)	NS
Waist circumference (cm)	75 (59–131)	76 (61–123)	88 (61–142)	b,c
SHBG (nmol/L)	83.6 (15.6–132.0)	43.9 (8.3–143.0)	33.8 (6.9–97.9)	b,c
Glycemia (g/L)*	0.86 (0.59–1.14)	0.84 (0.62–1.25)	0.81 (0.62–1.06)	<
Insulin (mU/L)	3.6 (0.7–19.7)	4.5 (0.7–20.6)	6 (0.7–20.9)	b,c
QUICKI	0.69 (0.44–1.28)	0.83 (0.41–1.33)	0.61 (0.43–1.34)	b,c
Glycemia/insulin	0.24 (0.05–1.29)	0.18 (0.04–1.11)	0.14 (0.04–1.13)	b,c
HDL cholesterol (g/L)	0.60 (0.31–1.31)	0.60 (0.34–1.53)	0.52 (0.29–0.81)	b,c
LDL cholesterol (g/L)	0.99 (0.38–2.34)	0.99 (0.47–1.76)	1.90 (0.49–2.48)	b,c
Triglycerides (g/L)	0.57 (0.22–2.72)	0.59 (0.26–2.20)	0.72 (0.29–3.51)	b,c

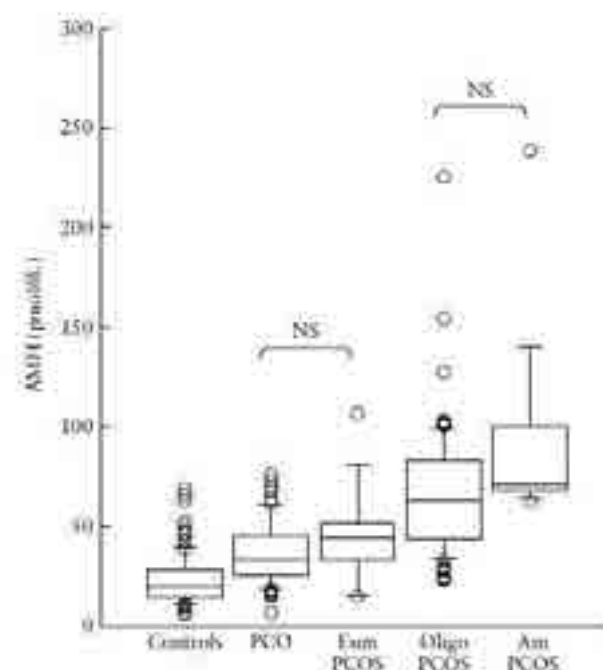
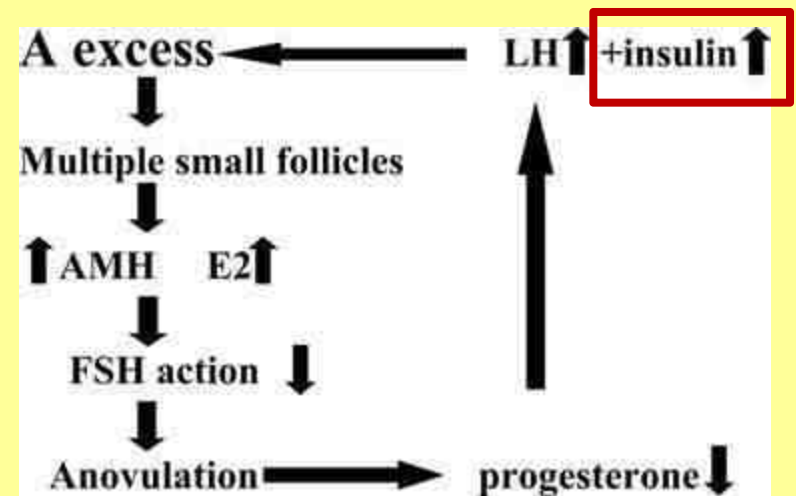
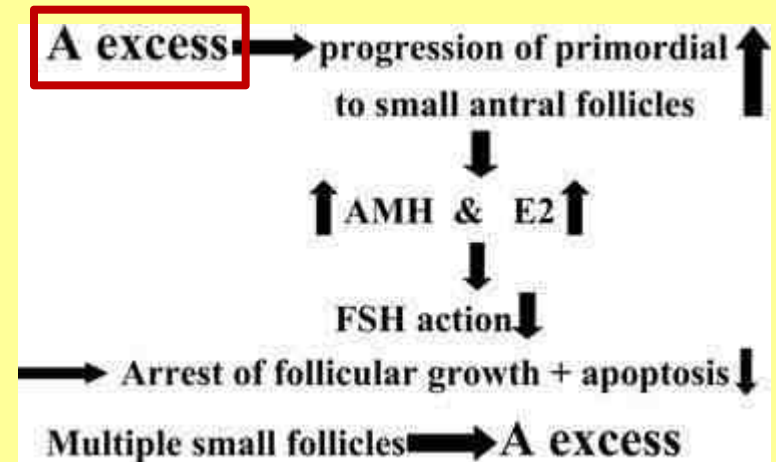


Table 2 Hormonal and ovarian characteristics of controls, women with polycystic ovaries (PCO) and women with polycystic ovary syndrome (PCOS)

Characteristic	Controls (n = 95)	PCO group (n = 95)	PCOS group (n = 95)	P _‡	P _‡ adjusted for BMI, WC or I	P _‡ adjusted for 2–9 FN
Testosterone (nmol/L)	0.79 (0.17–1.84)	0.90 (0.14–1.80)	1.39 (0.17–3.57)	b,c	b,c	b,c
FAI	5.41 (1.09–14)	5.99 (1.12–20)	13.3 (2.8–51)	b,c	b,c	b,c
Androstenedione (nmol/L)	4.37 (0.63–7.66)	5.25 (1.57–7.7)	6.09 (2.1–17.36)	b,c	b,c	b,c
17-OH-P (ng/mL) [§]	0.48 (0.21–1.86)	0.52 (0.17–1.46)	0.64 (0.24–1.49)	b,c	b,c	b,c
DHEAS (μmol/L)	4.0 (0.8–12)	4.6 (1.5–10.4)	5.1 (0.6–14)	NS	NS	NS
LH (IU/L)	3.8 (1.3–12.5)	4.3 (1.2–9.4)	5.7 (1.3–19.1)	b,c	b,c	b,c
FSH (IU/L)	6.5 (3.8–12)	5.9 (2.9–10.9)	5.5 (3.1–11.1)	a,c	c	c
E2 (pg/mL)	33 (19–80)	34 (13–79)	35 (15–69)	NS	NS	NS
AMH (pmol/L)	19.8 (6.6–69)	33.6 (6.9–75.9)	63.3 (15.4–239.6)	a,b,c	a,b,c	a,b,c
Ovarian area (cm ²)	7.4 (3.6–16.6)	9.6 (6.2–15.8)	10.8 (6–23.4)	a,b,c	a,b,c	a,b,c
2–9 FN	15 (4–23)	35 (14–67)	45 (25–140)	a,b,c	a,b,c	NA



- **Asemptomatik PKO'nun hafif hiperandrojenemi ve insülin sensitivite bozuklukları ile ilişkili olduğu öne sürülmektedir**



A new ultrasound criterion for the diagnosis of polycystic ovary syndrome: the ovarian stroma/total area ratio

FERTILITY AND STERILITY
VOL. 78, NO. 2, 40-45, 2002
Copyright © 2001 American Society for Reproductive Medicine
Published by Elsevier Science
Printed on acid-free paper

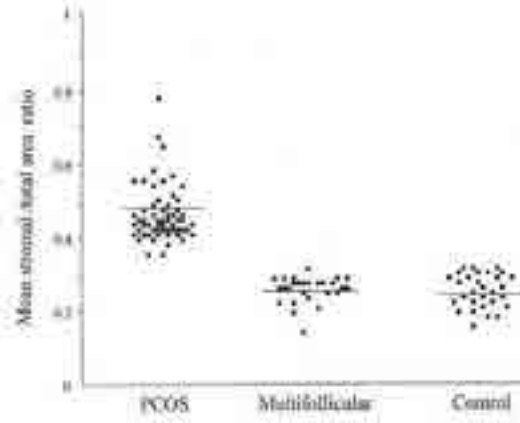
FIGURE 1

The three different examples of stromal/total area ratio in pathological and normal ovaries. (A) Polycystic ovary. (B) Multifollicular ovary. (C) Normal ovary. All figures were obtained with a transvaginal approach. The values on the left side represent the circumference of the ovary and of the stroma; those on the right represent the total area of the ovary and the area of the stroma.

The following parameters were evaluated echographically:

1. Ovarian volume, estimated according to the formula $1/2 (A \times B \times C)$, where A is the longitudinal diameter, B the anteroposterior diameter, and C the transverse diameter of the ovary (10).
2. Ovarian area, evaluated by outlining with the caliper the external limits of the ovary in the maximum plane section.
3. Ovarian stromal area, evaluated by outlining with the caliper the peripheral profile of the stroma, identified by a central area slightly hyperechoic with respect to the other ovarian area.
4. The stromal/total area ratio (S/A).

Mean and single values of the stromal/total area ratio PCOS patient, in multifollicular ovary patients, and in control women.



- Fulghesu et al. (2001) PKOS fenotipi ve metabolik etkilerini belirlemeye yardımcı olarak bir ovaryan stroma analiz yöntemi öne sürmüştür.
- Over Stroma/Over Yüzey Alanı (S/A) oranı için eşik değeri : **0.34**
- S/A oranı ile Adams kriterlerinin (≥ 10 follükül 2-8 mm + Ekodens santral ovaryan stroma) ovaryan stroma açısından objektif olarak değerlendirildiği belirtilmiştir
- **> 0.34 ve ≥ 10 adet 2-8 mm follükül ;** PKOS açısından (+) kabul edilmiştir

Table V. Linear relationships between ultrasound parameters and clinical, endocrine and metabolic data in the studied population.

	Ovarian volume		Stromal area		Stromal area/total area ratio		Total area
	R	P	R	P	R	P	NS
BMI	NS	NS	NS	NS	0.28	<0.01	NS
Testosterone	0.27	<0.04	0.34	<0.0001	0.39	<0.0001	NS
Androstenedione	NS	NS	0.30	<0.0001	0.38	<0.0001	NS
17-OHP	NS	NS	NS	NS	0.29	<0.0001	NS
DHEAS	NS	NS	NS	NS	NS	NS	NS
Cortisol	NS	NS	NS	NS	NS	NS	NS
FAI	NS	NS	0.30	<0.0001	0.39	<0.0001	NS
Fasting insulin	NS	NS	NS	NS	0.25	<0.0001	NS
AUC insulin	NS	NS	NS	NS	0.25	<0.0001	NS
Fasting glucose:fasting insulin	NS	NS	NS	NS	NS	NS	NS

17-OHP, 17-hydroxyprogesterone; AUC, area under curve; DHEAS, dehydroepiandrosterone sulphate; FAI, free androgen index; NS, not significant.

Diagnosis of polycystic ovary syndrome (PCOS): revisiting the threshold values of follicle count on ultrasound and of the serum AMH level for the definition of polycystic ovaries

D. Dewailly^{1,4}, H. Gronier¹, E. Poncelet², G. Robin¹, M. Leroy¹, P. Pigny¹, A. Duhamel⁴, and S. Catteau-jonard¹

Human Reproduction, Vol.26, No.11 pp. 3123-3129, 2011
Advanced Access publication on September 16, 2011 doi:10.1093/humrep/der297

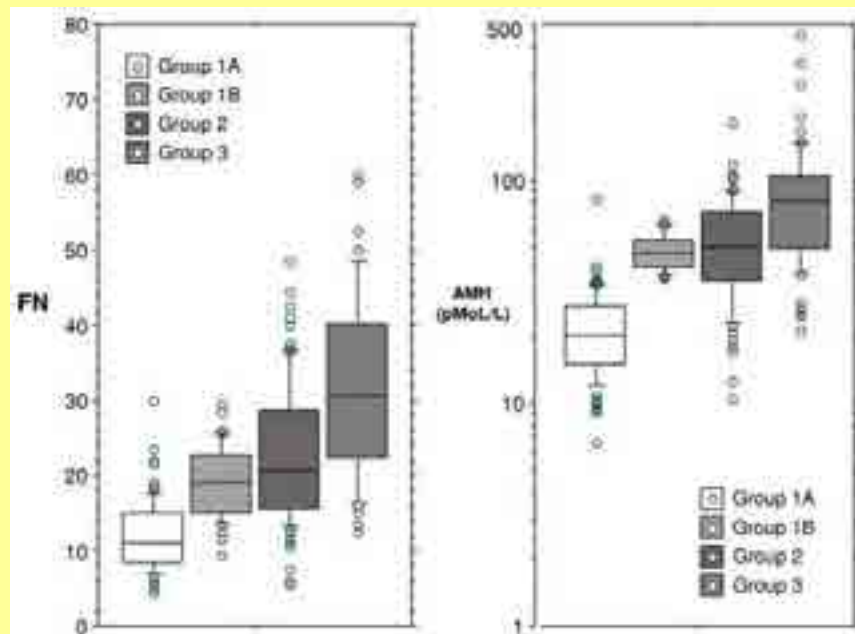


Figure 1 Picture of a PCOM with old (2001) (left) and new (2009) (right) equipment. Small follicles ≤ 2 mm (arrows) can be visualized and counted with the new equipment.

Table II Results of ROC analysis using a population consisting of groups 1A and 3 (non-PCOM non-PCOS women and those with PCOS, respectively).

	AUC (95% CI)	Threshold	Sensitivity (%)	Specificity (%)
Follicle number	0.949 (0.915–0.982)	17	87	83
		19	81	92
		21	78	92
Ovarian volume	0.923 (0.874–0.973)	7 ml	87	89
		8 ml	75	92
		9 ml	63	95
		10 ml	50	99.5
Serum AMH	0.973 (0.947–0.998)	30 pmol/l	92	82
		35 pmol/l	92	97
		40 pmol/l	85	100

AUC, area under the ROC curve; CI, confidence interval.

Bold values indicate best compromise between sensitivity and specificity.

Table III Adaptation of the previous classifications for the diagnosis of PCOS, proposing an excessive FN of >19 or serum AMH concentration >35 pmol/l or >5 ng/ml as a surrogate when either oligo-anovulation or HA is missing.

Oligo- anovulation	Clinical and/or biological HA	FN > 19 and/or serum AMH ^a > 35 pmol/l (5 ng/ml)	Diagnosis
+	+	(+/-) ^b	PCOS
+	-	+	PCOS
-	+	+	PCOS
-	-	+	Normal woman with PCOM ^c
+	-	-	Idiopathic anovulation
-	+	-	Idiopathic hyperandrogenism

As with the previous classifications, other causes of oligo-anovulation and/or HA must be excluded before applying this classification.

^aTo be used preferentially.

^bNot necessary for the diagnosis.

^cConsider the risk for OHSS.

PKOS'ta Gonadotropin Bozuklukları

- GnRH/LH pulsasyonundaki akselerasyon
- Artmış LH/FSH oranı
Zayıf PKOS olgularında daha belirgin
- Bazal LH/FSH ölçümleri tanı kriteri değil.
- Olguların %75'inde gonadotropik disfonksiyon (+)

PKOS'ta Metabolik Özellikler

- **Hiperinsülinemi / İnsülin Rezistansı (IR)**
 - *Patofizyolojide önemli ancak tanı kriteri değil.....*
 - *Teka androjen yapımını arttırır / SHBG seviyesini azaltır*
 - *%50 – 70' inde IR (+)*
- **Metabolik Sendrom**
- **Dislipidemi**
- **Obezite**
 - *Reproduktif ve metabolik fonksiyonlar üzerine olumsuz etkiye sahip*
- **Hipertansiyon**
- **Obstruktif sleep apne**
- **Artmış KVS hastalık riski**

PKOS Fenotipleri*

Features	Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenism (biochemical or clinical)	+	+	+	-	+	-	-
Oligo- or anovulation	+	+	-	+	-	-	+
Polycystic ovaries	+	-	+	+	-	+	-
<u>NIH criteria</u>	✓	✓					
ESHRE/ASRM criteria	✓	✓	✓	✓			
AES criteria	✓	✓	✓				

NIH PKOS

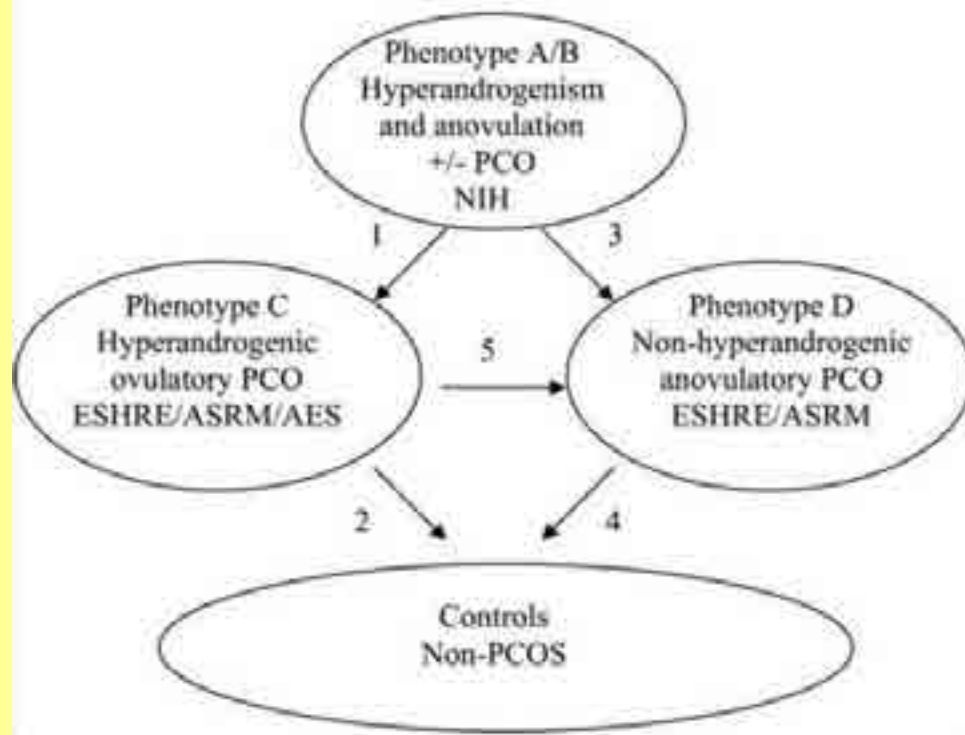
(HA +)

- Fenotip A (HA+O+PCO)
- Fenotip B (HA+O+PKO-)

non-NIH PKOS

(PKO +)

- Fenotip C (HA +PCO)
- Fenotip D (O+PCO)



PKOS reproduktif fenotiplerine göre metabolik özelliklerde herhangi bir deęişiklik oluyor mu ???.....

Metabolic features of the reproductive phenotypes of polycystic ovary syndrome

Lisa Moran^{1,3,†} and Helena Teede^{1,2,†}

¹The Juel Jansen Foundation for Women's Health Research Unit, Monash Institute of Health Services Research, Monash University, Locked Bag 246, Clayton, VIC 3168, Australia; ²Diabetes Unit, Southern Health, Clayton, VIC 3168, Australia

³Correspondence address: Tel: +61-3-9594-7592; Fax: +61-3-9594-7550; E-mail: lisa.moran@med.monash.edu.au

BACKGROUND: Polycystic ovary syndrome (PCOS) is a common condition in women of reproductive age with well established metabolic abnormalities. There are numerous diagnostic criteria generating several reproductive diagnostic phenotypes [National Institute of Health (NIH) hyperandrogenic anovulatory PCOS and non-NIH PCOS including hyperandrogenic ovulatory or non-hyperandrogenic anovulatory PCOS]. There is ongoing debate regarding the optimal diagnostic criteria for PCOS and on the metabolic implications of newer non-NIH PCOS phenotypes.

METHODS: We reviewed the literature on the presence of risk factors for type 2 diabetes (DM2) and cardiovascular disease (CVD) across the reproductive diagnostic phenotypes of PCOS with the aims of comparing the metabolic features of the NIH and non-NIH groups and identifying potential high metabolic risk phenotypes of PCOS.

RESULTS: NIH PCOS patients present with greater obesity, abdominal obesity, insulin resistance (IR) and risk factors for DM2 and CVD compared with non-NIH ovulatory and non-hyperandrogenic PCOS patients. Where differences in metabolic features exist between the phenotypes, they are generally related to the degree of total and abdominal obesity. There is emerging evidence suggesting ovulatory and non-hyperandrogenic PCOS have greater metabolic abnormalities than controls primarily linked to abdominal adiposity. There is currently no evidence that non-hyperandrogenic PCOS is associated with a less adverse metabolic profile than ovulatory PCOS.

CONCLUSIONS: Current metabolic evidence appears to justify the inclusion of both non-NIH PCOS groups (ovulatory and non-hyperandrogenic) as PCOS subgroups. NIH PCOS is associated with a more adverse metabolic profile including greater total and abdominal obesity, IR and risk factors for CVD and DM2 than non-NIH phenotypes.

Key words: polycystic ovary syndrome / diagnostic criteria / insulin resistance / hyperandrogenism

SORU: NIH-PKOS (Fenotip A/B) ile kıyaslarsak hiperandrojenik (HA) ovulatuvar PKOS'lu kadın benzer metabolik risklere mi sahiptir ?

■ CEVAP

1. Genetik olarak

2. Androjen oranı

benzerdir.

Features	Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenism (biochemical or clinical)	+	+	+	-	+	-	-
Oligo- or anovulation	+	+	-	+	-	-	+
Polycystic ovaries	+	-	+	+	-	+	-
NIH criteria	✓	✓					
ESHRE/ASRM criteria	✓	✓	✓	✓			
AES criteria	✓	✓	✓				

irirler.

al yağ

ofili



Benzer kilo ve BMI'ya sahip hiperandrojenemik iki PKOS olgusu arasında ovulasyonun olup olmamanın metabolik risk profilini etkilemez !!!!!

SORU: Hiperandrojenik ovulatuar PKOS'lu olgularda (Fenotip C) PKOS olmayan olgulara göre artmış metabolik risklere mi sahiptir ?

■ **CEVAP**



- 1. Ovulatuar PKOS olgularında, kontrol grubuna göre bozulmuş glukoz metabolizması prevalansında hafif bir artış olduğu belirtilse de metabolik risk artışı varlığı genel olarak gözlenmemiştir.**
- 2. Metabolik risk artışında esas belirleyici abdominal yağlanmadır.**

SORU: NIH-PKOS (Fenotip A/B) ile kıyaslarsak non-HA anovulatuvar PKOS'lu (fenotip D) bir olgu benzer metabolik risklere mi sahiptir ?

■ CEVAP

1. Genetik profil

2. Obezite

3. IR için esas belirleyici abdominal yağlanma miktarıdır.

Features	Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenism (biochemical or clinical)	+	+	+	-	+	-	-
Oligo- or anovulation	+	+	-	+	-	-	+
Polycystic ovaries	+	-	+	+	-	+	-
NIH criteria	✓	✓					
ESHRE/ASRM criteria	✓	✓	✓	✓			
AES criteria	✓	✓	✓				



olik

SORU: Non-HA anovulatuvar PKOS'lu olgularda (Fenotip D) PKOS olmayan olgulara göre metabolik risk artışı var mıdır ?

■ **CEVAP**



- 1. Abdominal obezite açısından fark olmadıkça, kontrol grubuna göre bu olguların metabolik risk artışına sahip olduğunu gösteren çok az kanıt vardır.**

SORU: HA ovulatuar PKOS'lu (Fenotip C) olgular ile non-HA anovulatuar PKOS (Fenotip D) olguları arasında metabolik risk açısından fark var mıdır ?

■ CEVAP:

1. Non-HA olguların

metabolik risk

2. Ancak HA olguların

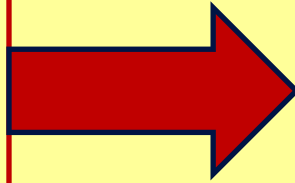
Features	Phenotypes						
	A	B	C	D	E	F	G
Hyperandrogenism (biochemical or clinical)	+	+	+	-	+	-	-
Oligo- or anovulation	+	+	-	+	-	-	+
Polycystic ovaries	+	-	+	+	-	+	-
NIH criteria	✓	✓					
ESHRE/ASRM criteria	✓	✓	✓	✓			
AES criteria	✓	✓	✓				



Ovulatuar PKOS olgularını artmış dislipidemi ve IR prevalansı ile birliktelik gösterse de, non-HA olgular benzer bir metabolik profile sahiptirler

PKOS'ta Metabolik Özellikler

- **Hiperinsülinemi / İnsülin Rezistansı (IR)**
 - *Patofizyolojide önemli ancak tanı kriteri değil.....*
 - *Teka androjen yapımını arttırır / SHBG seviyesini azaltır*
 - *%50 – 70' inde IR (+)*
- **Metabolik Sendrom**
- **Dislipidemi**
- **Obezite**
- **Hipertansiyon**
- **Obstruktif sleep apne**
- **Artmış KVS hastalık riski**



**SEMPATİK SİSTEM
AŞIRI AKTİVASYONU**

REVIEW ARTICLE

The sympathetic nervous system in polycystic ovary syndrome: a novel therapeutic target?

Andrew Lansdown* and D. Aled Rees*

*Centre for Endocrine and Diabetes Sciences, Institute of Experimental and Molecular Medicine, School of Medicine, Cardiff University, Cardiff, UK

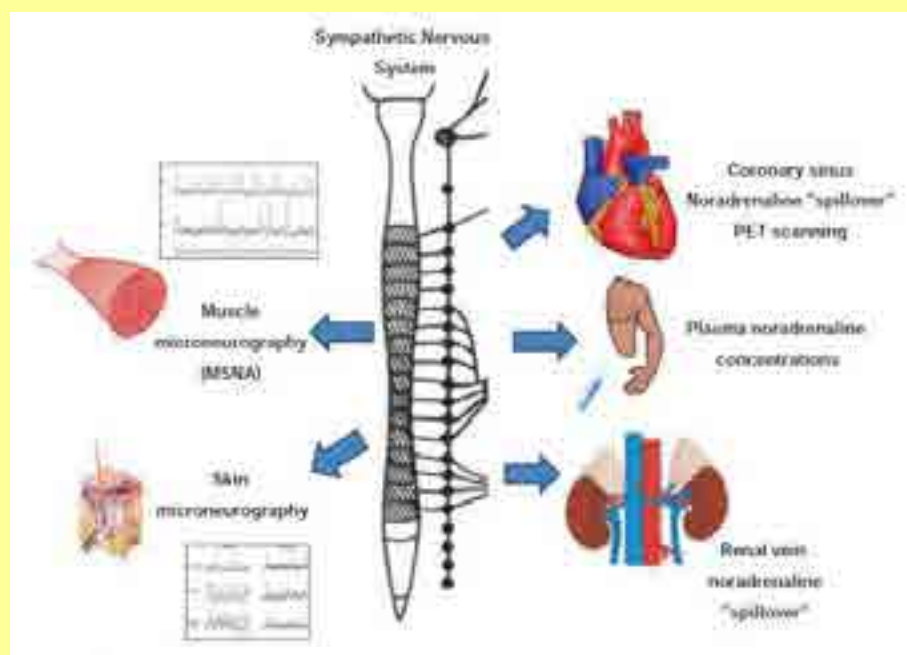


Fig. 2 Methods for measuring sympathetic nervous system activity.

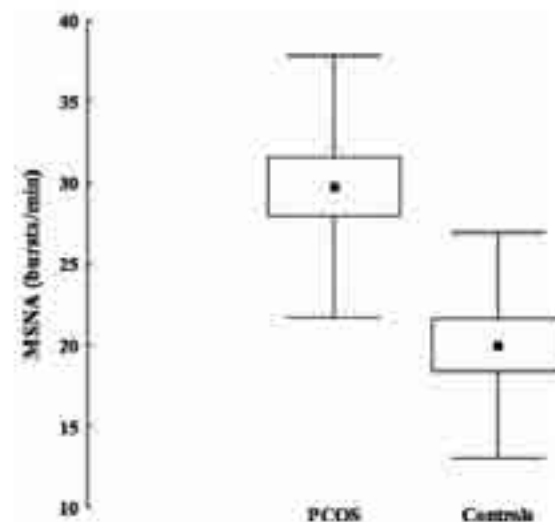


Fig. 3 Muscle sympathetic nerve activity (MSNA) expressed as burst frequency (bursts/min) in women with polycystic ovary syndrome (PCOS) and in healthy matched controls ($P < 0.0003$). Reproduced with permission from Jørgensen *et al.*²⁸

Conclusions





- ✓ PKOS için riskte olan populasyon
 - a. Anovulatuvar infertilite
 - b. Androjenik dermatolojik bulgular
 - c. Menstrual bozukluk
 - d. Oligo-ovulatuvar infertilite
 - e. PKO
 - f. IR/Hiperinsülinemi

- ✓ En sık görülen androjenik dermatolojik bulgu **HİRSUTİSM**'dir ve HA için iyi bir belirteçtir.

- ✓ PKOS heterojen bir hastalıktır. En sık görülen fenotipik özellikler:
 - a. Menstrual-ovulatuvar disfonksiyon
 - b. Hiperandrojenemi
 - c. Hirsutism
 - d. PKO
 - e. IR/Hiperinsülinemi




- ✓ PKOS bir hiperandrojenik hastalıktır.
- ✓ Klasik PKOS'un bir özelliđi olan anovulasyon için, tek başına androjen fazlalığı yanında IR ve hiperinsülinemi kritik rol oynar
- ✓ PKOM, PKOS olgularının %75-%90'ında saptanır
- ✓ HA olgularda normal mens, normal ovulasyonun varlığı açısından güvenli bir parametre deđil.
- ✓ PKOS'ta menstrual siklus yaş ilerledikçe daha düzelme eğilimindedir
- ✓ Menstrual irregülarite belirginleştikçe PKOS fenotipi daha şiddetlidir



- ✓ Etnik orijin ve kültür PKOS fenotipinin farklılığında rol oynar
- ✓ Artmış BMI ve obezite; menstruasyon bozukluğu, HA ve hirsutizm ile ilişkilidir
- ✓ Tüm PKOS fenotipleri benzer metabolik risk taşımaz
- ✓ HA + Oligomenore (klasik PKOS) metabolik risk oranı en yüksek fenotiptir
- ✓ PKOS herhangi bir yaş için daha büyük KVH risk oranı içerir
- ✓ Dislipidemi, IGT, Tip 2 DM (*ASKH için klasik risk belirteçleridir*) tümünün prevalansı artar



- Üreme çağında en sık endokrinopati
- Tanı kriterleri universal değildir, tanı kriterine göre fenotipler farklılıklar göstermektedir
- AMH tanı kriterleri arasına girecek gibi gözükmemektedir
- Prevelansı uygulanan tanı kriterine göre değişiklik göstermektedir (%5-20)
- Multisistemiktir, multidisipliner yaklaşım gerektirir



"Hiç bir şeye ihtiyacımız yok,
yalnız bir şeye ihtiyacımız vardır;
çalışkan olmak!"

K. Atatürk

Teşekkürler

ATAM İZİNDEYİZ...