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Metabolic Concomitants of Obese and Nonobese Women With Features of Polycystic Ovarian Syndrome

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Context: Polycystic ovarian syndrome (PCOS) is often associated with obesity and diabetes.

Objective: The present study measured body fat distribution and metabolic risk factors in women with features of PCOS.

Design: Cross-sectional, multiethnic study of cardiovascular risks.

Setting: General community.

Study Participants: 145 PCOS and 344 non-PCOS women.

Exposure Measures: Body composition by dual x-ray absorptiometry; abdominal fat masses measured by magnetic resonance imaging and hepatic triglyceride by magnetic resonance spectroscopy.

Outcomes Measures: Body composition, liver fat content, homeostatic model assessment for insulin resistance (HOMA-IR), revised, and metabolic syndrome components.

Results: PCOS women had a higher free androgen index compared with the non-PCOS women. Nonobese PCOS and non-PCOS women had a similar body fat content and distribution, HOMA-IR, and hepatic triglyceride content. Obese PCOS women had a similar total body fat percentage compared with their non-PCOS counterparts (41.4% and 41.4% respectively). Both obese groups had similar intraperitoneal fat (1.4% of total body mass in PCOS vs 1.4% in non-PCOS). However, obese PCOS women had a greater ratio of truncal/lower body fat (1.42 vs 1.27; $P < 0.016$). They also had greater insulin resistance (HOMA-IR: PCOS, 2.24% vs non-PCOS, 1.91%; $P < 0.016$), higher liver triglyceride content (6.96% in PCOS vs 4.44% in non-PCOS; $P < 0.016$), and a greater incidence of hypertension (33% vs 24%; $P < 0.05$). No differences were observed in other metabolic risk factors.

Conclusions: Both obese and nonobese women with PCOS features had a greater free androgen index compared with non-PCOS women, but neither had greater intraperitoneal fat or abnormal lipid levels. Obese, but not nonobese, women with PCOS had a greater truncal/lower extremity fat ratio, HOMA-IR, and liver triglyceride content.

Polycystic ovarian syndrome (PCOS) is a common endocrinopathy in women. PCOS was first described by Stein and Leventhal [1]. PCOS is characterized by androgen excess and oligo-anovulation and polycystic ovaries [2]. The syndrome is frequently accompanied by hirsutism,

Abbreviations: BMI, body mass index; CRP, C-reactive protein; DHS I, Dallas Heart Study I; DXA, dual x-ray absorptiometry; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment insulin resistance; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; PCOM, polycystic ovarian morphology; PCOS, polycystic ovarian syndrome; RWS, Reynolds Women Study; SHBG, sex hormone-binding globulin (testosterone-estrogen binding globulin); US, ultrasonography.

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acne, and male pattern baldness. Android body fat distribution has been reported [3, 4]. Obesity, insulin resistance, and other features of the metabolic syndrome are frequently present as well [5–9].

Clinically, PCOS is usually defined using the Rotterdam consensus criteria [10]. These criteria include (1) clinical and/or biochemical evidence of hyperandrogenism; (2) evidence of oligo-anovulation; and (3) ultrasound evidence of a polycystic ovary. These criteria focus more on the endocrine abnormality than on metabolic disorders. An unresolved question concerns the influence of androgens on body fat distribution and the metabolic consequences. For example, men typically have a body fat pattern characterized by predominant upper body fat and more intra-abdominal (visceral or intraperitoneal) adipose tissue than women [11]. Women, in contrast, typically have predominantly lower body fat. Because upper body fat is associated with insulin resistance, metabolic syndrome, and diabetes, it is possible that elevated androgens contribute to the typical body fat pattern of men and its associated metabolic abnormalities.

The present study was performed in a subgroup of women participating in the Dallas Heart Study I (DHS I) [12]. The latter is an investigation into the causes of cardiovascular disease in a large multiethnic population [13]. Premenopausal women were screened for features of PCOS, and the metabolic parameters were examined in obese and nonobese women with and without this endocrine disorder. The present study was performed to determine whether women with PCOS features have abnormalities of body fat distribution, metabolic risk factors, and liver triglyceride content that is independent of the percentage of body fat content.

1. Methods

A. Study Population

From 2000 to 2002, the DHS I recruited a probability-based cohort of adults in the Dallas county [13] to evaluate the risk of cardiovascular disease in the community. A nested cohort of the DHS I consisted of women in the age range of 35 to 49 years. These women provided reproductive health and menstrual cycle information by self-administered questionnaires, hormonal measurements, and pelvic imaging, as detailed previously [12]. The substudy was named the Reynolds Women Study (RWS).

In the present study, we analyzed the imaging data collected from the RWS cohort. Initially, 1179 women participated in the first visit of RWS. Of these, 489 met the inclusion criteria for participation in the study. The inclusion criteria were complete pelvic magnetic resonance imaging (MRI) examination for polycystic ovary morphology (PCOM) and analysis of body composition using dual x-ray absorptiometry (DXA).

The criteria for PCOS features included two or more of the following factors: hyperandrogenism, hirsutism, oligomenorrhea, and ovarian cysts [10]. A detailed clinical evaluation was performed, as described previously, to identify each PCOS feature [12]. Hyperandrogenism [14, 15] included "treatment of unwanted hair" on chin, chest, abdomen, or back and/or elevated testosterone levels ($\geq$2.78 nmol/L; this cutpoint was derived from the upper quartile of women in the DHS I aged 35 to 49 years [12]. Oligomenorrhea was identified from self-reported irregular periods, with the smallest cycle length $>$45 days or cycle length averaging $>$45 days from the age of 20 to 30 years. Ovarian size and structure were assessed noninvasively using pelvic MRI, as detailed previously [12, 13]. MRI was used in lieu of ultrasonography (US) for research purposes. The method is more sensitive than US and has been shown to provide adequate resolution for evaluation of PCOM. MRI can also be used to evaluate infertility beyond PCOS [14–16]. However, by consensus, the clinical guidelines have endorsed US for evaluation of PCOM [10]. A paucity of data are available comparing US and MRI directly in adults to establish equivalency of the number of follicles required to define PCOM using two imaging methods. Therefore, in the present research study, we used the designation of "women with PCOS features" to classify women who met the criteria of

hyperandrogenism (hirsutism or hyperandrogenemia) and ovarian dysfunction (oligomenorrhea, anovulation, and or PCOM using MRI). Furthermore, in the present research study, women were considered to be non-PCOS and were designated as a reference group, if they had fewer than two of the criteria for PCOS features.

From the cohort of 489 women, 145 women had two or more PCOS features, 176 women had only one feature, and 168 women did not have any PCOS features. Data from the women with one feature of PCOS and women with no PCOS features were combined to be used as the reference group and henceforth have been designated as non-PCOS. Eighty-six percent of all women with PCOS features had hyperandrogenism, combined with PCOM (48%) or oligomenorrhea (25%) or oligomenorrhea plus PCOM (13%). Thus, most of the PCOS cohort had hyperandrogenism. A small fraction of PCOS women were perimenopausal; of these, 67% had PCOM combined with hirsutism (49%) or oligomenorrhea (9%) or hirsutism plus oligomenorrhea (9%). In addition, 9 PCOS women and 10 non-PCOS women were receiving hormonal therapy. None of the PCOS women was taking metformin at the time of the study.

The women with PCOS features and the non-PCOS women were both subgrouped into nonobese and obese using a percentage of body fat ≥35% as the cutpoint for obesity [17, 18]. Comparisons of body composition and metabolic parameters were performed within the nonobese and obese subgroups.

The institutional board for investigation in humans approved the DHS and RWS substudies, and the participants gave informed written consent.

B. Body Composition Analysis by DXA

Body composition analysis was performed using DXA [11], abdominal adipose tissue was measured using MRI [19], and liver fat was assessed using magnetic resonance spectroscopy (MRS) [20, 21]. The total fat and fat-free masses were quantified using DXA in the trunk, upper and lower extremities, and head, as previously described [11] (Delphi W scanner; Hologic Inc., Bedford, MA; and Discovery software, version 12.2; Hologic Inc., Bedford, MA). The truncal fat was defined as the region below the chin, the region delineated by the vertical lines within the left and right glenoid fossae and bordering laterally to the ribs, and the region delineated by oblique lines that cross the femoral necks and converge below the pubic symphysis. The lower body fat included all fat below these oblique lines. The weight, height, and waist and hip girth were measured as detailed previously [11].

C. Measurement of Abdominal Fat Using MRI

Measurements of the abdominal compartments of body fat were performed using a 1.5-Tesla MRI scanner (Intera; Philips Medical Systems, Best, Netherlands). The entire abdomen from the diaphragm to the pelvis was scanned using contiguous axial 10-mm slices, as previously described [18]. We have previously shown that a single MRI slice at the L2-L3 level accurately predicts the total subcutaneous, intraperitoneal, and retroperitoneal adipose tissue mass in men and women with a body mass index (BMI) representative of the total range of BMIs and ethnic distribution of the DHS cohort [11]. Areas of designated anatomical regions were measured and converted to kilograms using an algorithm detailed previously [19].

D. Measurement of Liver Fat

The liver fat measurement was performed using MRS, as detailed previously [20, 21]. A high liver fat content was defined as ≥5.5% [19, 20]. In brief, a histogram of the liver fat content measured in 345 DHS I participants who were relatively healthy was constructed, and the 95th percentile corresponded to a 5.5% liver fat content. This definition of elevated liver fat was also used in the present study.

E. Hormonal Levels and Other Analytes

Total testosterone was measured using a competitive radioimmunoassay, as detailed previously [12]. Measurements of testosterone-estrogen binding globulin [or sex hormone-binding globulin (SHBG)] were measured using a two-site immunoradiometric sandwich assay. All these measurements were performed at the Diagnostics Systems Laboratory (Webster, TX) [12]. For the total testosterone measurements, the coefficient of variation was 7.7% [12]. SHBG was measured using a two-site immunoradiometric sandwich assay, and calculated free testosterone was estimated using measured levels of albumin, total testosterone, and SHBG, as detailed previously [12]. The free androgen index was also calculated as detailed in the section on biostatistics.

The levels of plasma total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol were measured using enzymatic assays, as detailed previously [11]. The levels of insulin were measured immunochemically (Linco, Inc.). Adiponectin and leptin measurements were performed using enzyme-linked immunosorbent assay, as previously detailed [22].

F. Biostatistical Analysis

The free androgen index was calculated as 100 times the total testosterone/sex hormone-binding protein concentration ratio. The homeostatic model assessment for insulin resistance (HOMA-IR), revised, was calculated using the interactive program available from the University of Oxford website (available at: https://www.dtu.ox.ac.uk/homacalculator/download.php).

Descriptive statistics were used to summarize the subject demographic and clinical characteristics. The median and 95% confidence intervals (lower and upper limits) were used to summarize the independent variables. The χ^2 test was used to compare categorical variables. The body composition data, metabolic analytes, HOMA-IR, revised, and liver fat levels were compared between the nonobese women with PCOS features and the non-PCOS women and obese women with PCOS features and non-PCOS using a balanced design analysis of variance with *post hoc* analysis, as needed. Also, the interaction of the PCOS features with obesity status was examined. In some cases, the parameters were log transformed for the parametric analyses. An $\alpha \leq 0.05$ was considered to indicate statistical significance. Also, Spearman correlations were calculated for selected parameters of interest. The NCSS 9 Statistical Software (2013; NCSS, LLC, Kaysville, UT; available at: ncss.com/software/ncss) was used for the statistical analyses.

2. Results

The characteristics of women with and without PCOS features subgrouped according to the percentage of body fat category determined by DXA are listed in Table 1. Accordingly, women with a percentage of body fat <35% were designated as nonobese and women with a percentage of body fat ≥35% were designated as obese. The ages were dissimilar by ~1 year. The percentages of African-American women were similar among the groups. A high percentage of women with PCOS features had hirsutism, oligomenorrhea, and PCOM. The PCOS women had greater levels of total testosterone and calculated free testosterone and a lower level of SHBG compared with non-PCOS women, regardless of their obesity classification. The free androgen index was significantly greater in women with PCOS features than in non-PCOS women, regardless of their obesity status (Table 1).

The parameters for body composition are listed in Table 2 for the nonobese and obese women with and without PCOS features. In the nonobese groups, no differences in the percentage of total body fat or the distribution between upper and lower body fat was noted between those women with and without PCOS features.

In the obese women with and without PCOS, the percentage of total body fat was similar. The truncal body fat mass and percentage of truncal fat were significantly greater in women with PCOS features, as was the truncal/lower extremity fat ratio. The lean body mass was greater in the obese women with PCOS features than in their non-PCOS counterparts. The percentage of total body fat in the trunk was greater and the percentage of lower extremity fat

Table 1. Clinical Characteristics of Women With and Without Polycystic Ovarian Syndrome

	Nonobese		Obese	
Characteristic	**PCOS Features**	**Non-PCOS**	**PCOS Features**	**Non-PCOS**
Subjects, n	37	107	108	237
Age, y	40 (38, 41)[a]	41 (39, 42)	41 (39, 42)[b]	42 (41, 43)
BMI, kg/m^2	23.9 (23.0, 25.5)	23.9 (22.8, 24.9)	33.9 (32.5, 36.9)[b]	32.1 (30.9, 33.3)
Waist girth, cm	79 (77, 84)	79 (75, 82)	102 (98, 110)[b]	99 (96, 100)
Hip girth, cm	97 (94, 101)	98 (97, 102)	118 (114, 123)[b]	115 (113, 117)
Waist/hip ratio	0.82 (0.80, 0.86)	0.81 (0.79, 0.83)	0.87 (0.86, 0.88)	0.85 (0.84, 0.87)
Total testosterone, nmol/L	2.78 (2.08, 2.78)[a]	1.74 (1.74, 2.08)	2.78 (2.77, 3.12)[b]	2.08 (2.08, 2.08)
Calculated free testosterone, pmol/L	1.84 (1.51, 2.15)[a]	1.41 (1.26, 1.52)	2.19 (2.01, 2.37)[b,d]	1.73 (1.61, 1.84)
SHBG, nmol/L	149 (115, 188)[a]	169 (157, 186)	96 (91, 117)[b]	123 (114, 139)
Free androgen index	1.84 (1.08, 2.14)[a]	1.15 (0.96, 1.28)	2.83 (2.16, 3.12)[b,d]	1.58 (1.43, 1.75)
Prevalence of clinical features, %				
Hirsutism	81[c]	25	88[c]	25
Oligomenorrhea	73[c]	8	87[c]	8
Polycystic ovaries	78[c]	21	85[c]	17
African-American	57	39	47	50
Premenopausal	86	79	69	74

Data presented as median (95% confidence intervals).
[a]Significantly different between nonobese (body fat <35%) PCOS and nonobese non-PCOS ($P < 0.05$).
[b]Significantly different between obese (body fat ≥35%) PCOS and obese non-PCOS ($P < 0.05$).
[c]Significantly different from non-PCOS within nonobese and obese subgroups ($P < 0.05$; χ^2 test).
[d]Significantly greater in obese PCOS than in all other subgroups ($P = 0.04$).

was lower in obese PCOS women compared with their controls (Table 2). In non-PCOS women, the natural log of testosterone levels correlated weakly with the percentage of body fat (Spearman $r = 0.14$; $P < 0.01$); in the PCOS women, the correlation was not statistically significant ($r = 0.08$; $P = 0.31$).

The parameters for abdominal fat mass are listed in Table 3 for the nonobese and obese women with PCOS features and non-PCOS subgroups. Nonobese women with PCOS features did not have more intraperitoneal, subcutaneous, or retroperitoneal fat than did nonobese non-PCOS women. In the obese women, intraperitoneal fat was similar between the PCOS and non-PCOS groups (Table 3). However, obese PCOS women had significantly more subcutaneous and retroperitoneal fat.

Table 2. Body Composition of Women With and Without Polycystic Ovarian Syndrome

	Nonobese		Obese	
Body Composition (DXA)	**PCOS Features**	**Non-PCOS**	**PCOS Features**	**Non-PCOS**
Total body fat, kg	19.5 (16.7, 20.7)	19.3 (17.9, 20.5)	35.1 (32.7, 39.8)	33.6 (31.5, 36.1)
Total body fat, %	30.3 (28.3, 32.1)	31.2 (30.3, 32.1)	41.4 (40.0, 42.7)	41.4 (40.4, 42.0)
Truncal body fat, kg	8.1 (7.1, 9.4)	7.9 (7.1, 9.1)	17.4 (16.1, 20.4)[a]	15.9 (14.9, 17.2)
Truncal fat, %	12.2 (11.1, 14.7)	13.1 (12.0, 14.1)	20.4 (19.9, 21.2)[a]	19.4 (19.1, 20.0)
Upper extremity fat, kg	2.3 (1.8, 2.6)	2.2 (2.0, 2.5)	4.3 (4.0, 4.7)	4.0 (3.8, 4.2)
Upper extremity fat, %	3.6 (2.9, 4.0)	3.5 (3.4, 3.8)	5.1 (4.8, 5.2)	4.9 (0.48, 5.2)
Lower extremity fat, kg	11.0 (10.3, 12.0)	10.6 (10.1, 11.1)	14.7 (13.6, 15.6)	14.4 (13.7, 15.3)
Lower extremity fat, %	12.0 (11.4, 12.2)	12.1 (11.6, 13.0)	14.5 (13.9, 15.2)[a]	15.6 (15.2, 15.9)
Truncal/lower extremity fat ratio	1.08 (0.91, 1.20)	0.98 (0.91, 1.1)	1.42 (1.32, 1.48)[a]	1.27 (1.19, 1.30)
Lean mass, kg	42.3 (39.7, 44.5)	41.2 (39.7, 43.1)	49.4 (46.5, 50.6)[a]	46.7 (45.2, 48.4)
Lean mass, %	66.1 (64.3, 67.9)	65.1 (64.2, 65.9)	55.8 (54.3, 57.2)	55.8 (55.3, 56.6)

Data presented as median (95% confidence intervals).
[a]Significantly different between obese PCOS and obese non-PCOS ($P < 0.05$); obesity defined as body fat ≥35%.

Table 3. Abdominal Body Fat Composition of Women With and Without Polycystic Ovarian Syndrome

	Nonobese		Obese	
Abdominal Body Fat (MRI)	**PCOS Features**	**Non-PCOS**	**PCOS Features**	**Non-PCOS**
Subcutaneous fat mass, kg	3.2 (2.4, 3.5)	2.7 (2.4, 3.2)	6.6 (5.8, 8.3)[a]	5.9 (5.6, 6.4)
Subcutaneous fat, %	4.9 (3.9, 5.5)	4.5 (4.1, 4.9)	7.9 (7.3, 8.5)	7.4 (7.1, 7.7)
Intraperitoneal fat mass, kg	0.66 (0.52, 0.79)	0.69 (0.59, 0.77)	1.27 (1.16, 1.43)	1.24 (1.14, 1.32)
Intraperitoneal fat, %	1.0 (0.8, 1.2)	1.1 (1.0, 1.2)	1.4 (1.3, 1.6)	1.4 (1.3, 1.5)
Retroperitoneal fat mass, kg	0.44 (0.38, 0.52)	0.45 (0.41, 0.46)	0.75 (0.71, 0.80)[a]	0.68 (0.65, 0.72)
Retroperitoneal fat, %	0.70 (0.62, 0.81)	0.76 (0.67, 0.80)	0.87 (0.80, 0.93)[a]	0.81 (0.76, 0.85)

Data presented as median (95% confidence intervals).
[a]Significantly different between obese PCOS and non-PCOS ($P < 0.05$); obesity defined as body fat ≥35%.

The metabolic characteristics of the women with PCOS features and non-PCOS women are listed in Table 4. Among the nonobese women, no differences were found in the levels of fasting glucose, fasting insulin, HOMA-IR, fasting lipid, C-reactive protein (CRP), leptin, adiponectin, or average liver fat content (Table 4). Among the obese women, those with PCOS features had higher fasting insulin and HOMA-IR but not higher fasting glucose levels than those of the controls. No differences were noted for fasting lipid levels. CRP levels were greater in PCOS women, as was the average liver triglyceride content (Table 4). Hypertension was more prevalent in PCOS women than in non-PCOS.

3. Discussion

Several reports have indicated that women with PCOS frequently exhibit features of the metabolic syndrome [23–25]. The present study was performed to determine whether

Table 4. Metabolic Traits of Women With and Without Polycystic Ovarian Syndrome

	Nonobese		Obese	
Variable	**PCOS Features**	**Non-PCOS**	**PCOS Features**	**Non-PCOS**
Glucose, mg/dL	86 (80, 90)	86 (82, 89)	95 (91, 97)	93 (91, 95)
Insulin, mU/mL	8.3 (6.2, 10.2)	7.8 (6.3, 8.9)	17.3 (15.2, 19.4)[a]	14.8 (13.4, 16.5)
HOMA-IR, %	1.04 (0.78, 1.32)	1.01 (0.84, 1.15)	2.24 (1.94, 2.49)[a]	1.91 (1.75, 2.15)
Triglycerides, mg/dL	68 (51, 81)	69 (59, 85)	88 (81, 97)	89 (83, 99)
Total cholesterol, mg/dL	164 (150, 180)	168 (163, 174)	175 (162, 185)	174 (166, 178)
VLDL cholesterol, mg/dL	14 (10, 16)	14 (12, 17)	18 (16, 19)	18 (17, 20)
LDL cholesterol, mg/dL	91 (84, 98)	95 (86, 101)	102 (89, 112)	103 (99, 107)
HDL cholesterol, mg/dL	56 (49, 60)	57 (52, 62)	50 (47, 51)	47 (46, 49)
CRP, mg/L	1.1 (0.6, 2.0)	1.2 (0.08, 1.9)	5.3 (3.9, 6.9)[a]	4.0 (3.0, 4.6)
Leptin, mg/L	10.5 (8.3, 14.2)	9.4 (7.9, 11.2)	29.3 (26.4, 31.8)	26.7 (24.9, 29.2)
Adiponectin, ng/mL	9.0 (6.3, 10.6)	9.7 (8.1, 10.6)	5.9 (5.4, 6.8)[a]	6.8 (6.1, 7.4)
Liver fat, %	2.55 (1.49, 3.63)	2.56 (2.08, 3.19)	6.96 (5.37, 8.55)[a]	4.44 (3.74, 4.94)
Prevalence of clinical features, %				
Hypertension	27[b]	12	33[c]	24
Type 2 diabetes mellitus	0	5	13	11
Metabolic syndrome	19[b]	13	46[c]	39
Current smoker	54[b]	28	17	20

Data presented as median (95% confidence intervals).
Abbreviations: LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.
[a]Significantly different between obese PCOS and non-PCOS ($P < 0.05$).
[b]Significantly different between nonobese PCOS and non-PCOS ($P < 0.05$; χ^2 test).
[c]Significantly different between obese PCOS and non-PCOS ($P < 0.05$; χ^2 test).

premenopausal women with PCOS have abnormalities in body fat distribution and are prone to metabolic risk factors.

It has been widely reported that women with PCOS commonly are obese [26, 27]. In the DHS I, more obese than nonobese women had PCOS features. In the DHS as a whole, the proportion of women in the obese category exceeded that in the nonobese group [28]. We, therefore, could not determine with certainty that PCOS predisposes to excessive body fat. Compared with the obese controls without PCOS, the obese group with PCOS had a similar percentage of body fat and leptin levels. However, the lean mass was significantly higher in the PCOS than in the non-PCOS women.

Several reports have suggested that PCOS predisposes to upper body obesity [26, 27, 29]. In the present study, obese PCOS women had significantly greater truncal/lower extremity fat ratios than the obese non-PCOS women. In the nonobese women, no differences were observed in the distribution of body fat between those with and without PCOS. Thus, if PCOS predisposes to upper body obesity, this occurs only in those having categorical obesity.

Recently, Dumesic *et al.* [30] reported from a study of 6 normal-weight PCOS women that the intra-abdominal fat mass was significantly increased compared with 14 normal-weight non-PCOS women. In contrast, in our study, we found no increase in intraperitoneal fat between the nonobese women with PCOS and the obese women. Thus, it seems unlikely that PCOS-associated visceral obesity could account for a propensity to the metabolic syndrome.

Several studies have found that women with PCOS are insulin resistant [31, 32]. One view holds that insulin resistance contributes to hyperandrogenemia [33]; another possibility is that hyperandrogenemia underlies insulin resistance. To support the former, metformin therapy improves the metabolic parameters in patients with PCOS [34, 35] and reduces androgen levels [36–38]. In contrast, the relation between insulin resistance and hyperandrogenemia could be confounded by the relatively high prevalence of obesity in PCOS women. In the present study, nonobese women with PCOS features, compared with their nonobese women without PCOS, did not exhibit insulin resistance, despite the presence of hyperandrogenemia. In contrast, our obese women with PCOS features had higher HOMA-IR than that of corresponding non-PCOS women; this is consistent with previous reports [31, 32]. However, the substantially higher HOMA-IR in obese women with PCOS compared with their obese counterparts without PCOS was modest.

If insulin resistance is accentuated among obese PCOS women, these women should be at a greater risk of developing type 2 diabetes. Available data support this connection [39, 40]. However, in the DHS, the average glucose levels and percentage of women with fasting glucose levels >100 mg/dL were not increased in PCOS women.

Another metabolic risk factor reported in patients with PCOS is dyslipidemia of several types [41–43]. In DHS, essentially no differences were observed between PCOS women and their controls for any lipid parameter. It is true that obese women, both with and without PCOS, had higher triglyceride levels, higher triglyceride/HDL cholesterol ratios, and higher non-HDL cholesterol levels than those of their nonobese counterparts. We found no evidence that the presence of PCOS features *per se* is associated with dyslipidemia.

In the present study, the liver triglyceride content was moderately higher in the obese women with PCOS features than in those without PCOS. This finding is consistent with the previously observed association between a higher truncal/lower body fat ratio and increased hepatic triglyceride content [28].

Hypertension has been reported to be more common in women with PCOS [23, 44, 45]. These results are in accord with those from the present study. PCOS women had a greater prevalence of elevated blood pressure than did the controls. This finding in PCOS women was reported previously for DHS women [46].

Some investigators have reported increased cigarette smoking in women with PCOS [47]. A similar trend was observed in the present study. Whether hyperandrogenemia predisposes to smoking is uncertain; however, PCOS women who are smokers apparently have a worsening of endocrine and metabolic profiles [48–51]. Moreover, smoking is common among women with PCOS and their partners and contributes to a decrease in fertility treatment success [52].

It has been reported that CRP levels are often elevated in women with PCOS [52, 53]. In the present study, small differences were noted in CRP levels between the obese controls and obese PCOS women. However, the CRP levels were similar among the nonobese PCOS and non-PCOS women. Previous reports have shown that obesity is accompanied by higher CRP levels [54, 55]. These higher levels could reflect a proinflammatory state that might predispose to cardiovascular disease and/or diabetes. However, we found no compelling evidence for an association between elevated CRP and PCOS *per se*.

In conclusion, many investigators have proposed that PCOS predisposes to cardiovascular disease and diabetes. However, the results from the present study provide little or no evidence to support the contention that any such association is strongly mediated by PCOS-induced metabolic syndrome. It is true that most patients with PCOS features were found to be overweight or categorically obese, which could predispose to the metabolic syndrome. There appeared to be a tendency for subcutaneous fat to be redistributed to the upper body, which potentially could worsen the risk factors. This redistribution, however, was not striking. We further found no evidence for greater intraperitoneal (visceral) adipose tissue in PCOS women compared with controls. This condition itself could raise the risk of cardiovascular disease by inducing insulin resistance, worsening dyslipidemia, increasing hypertension, and inducing a proinflammatory state. A redistribution of body fat might account for the somewhat greater insulin resistance and liver fat content found in obese PCOS women compared with non-PCOS obese women. In addition, hypertension appeared to be more common. Still, no worsening of dyslipidemia or marked enhancement of CRP was found in the PCOS women. Any occurrence of metabolic syndrome in PCOS women seemingly can be explained more by the global obesity than to a redistribution of body fat. Finally, it is possible that the hyperandrogenism in PCOS favors upper body obesity, which, in turn, could predispose to metabolic risk factors. However, in our population of PCOS women, a redistribution of body fat was not striking, nor was the presence of metabolic risk factors conspicuously greater.

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