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Abdominal Fat Quantity and Distribution in Women with Polycystic Ovary Syndrome and Extent of Its Relation to Insulin Resistance

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Context: Increased abdominal fat has been linked to insulin resistance and increased cardiovascular risk. Because many patients with polycystic ovary syndrome (PCOS) present abdominal obesity, it may be the cause of insulin resistance in this disorder.

Setting: Fat quantity and distribution were evaluated by dual x-ray absorptiometry at the Departments of Clinical Medicine at the University of Palermo and the University of Naples, Italy.

Patients: A total of 110 patients with PCOS and 112 weight-matched controls were studied. Anthropometric data, blood glucose, serum insulin, and testosterone were evaluated. Total, trunk, and central abdominal fat quantity were measured by total-body dual x-ray absorptiometry.

Results: Compared with weight-matched controls, patients with PCOS had similar quantity of total and trunk fat but higher quantity of central abdominal fat. This difference was not observed when comparing obese PCOS and obese controls but depended on differences between overweight and normoweight patients and controls. All obese subjects, independently of having PCOS or not, had increased central abdominal fat. The same parameter was increased in 71% of overweight PCOS, 50% of overweight controls, and 30% of normoweight PCOS patients. PCOS patients with increased central abdominal fat had significantly higher ($P < 0.01$) insulin levels and significantly reduced ($P < 0.01$) insulin sensitivity than controls with similar quantities of central abdominal fat. Overweight PCOS patients with normal abdominal fat had significantly higher ($P < 0.05$) insulin levels and significantly reduced ($P < 0.05$) insulin sensitivity than overweight controls with normal abdominal fat.

Conclusions: Most obese subjects, independent of being affected by PCOS, have an abdominal form of obesity. However, abdominal fat excess may not be the only determinant of insulin resistance in PCOS. **(*J Clin Endocrinol Metab* 92: 2500–2505, 2007)**

OBESITY IS A CLASSIC characteristic of polycystic ovary syndrome (PCOS) (1, 2). Although profound differences, probably depending on environmental causes, exist in the prevalence of obesity in different countries (3) and also in areas, such as southern Italy, where obesity in PCOS is less common than in the United States, 70% of women with PCOS have increased body weight [body mass index (BMI) > 25 kg/m^2] (4).

However, for many years, there has been relatively little attention on the importance of fat excess in determining the reduced insulin sensitivity that is found in most PCOS patients. In fact, it was shown that, in this disorder, insulin resistance is more severe than that expected on the basis of body weight (5–9). In addition, insulin resistance may be found also in 30–50% of PCOS women having normal body weight (5–9). Therefore, it was suggested that insulin resistance and cardiovascular (CV) risk exist in PCOS independently of obesity, although fat excess, when present, worsens insulin resistance, which in turn further enhances CV risk (5, 6).

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Abbreviations: BMI, Body mass index; CV, cardiovascular; DXA, dual x-ray absorptiometry; PCOS, polycystic ovary syndrome; QUICKI, quantitative insulin-sensitivity check index.

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However, these concepts have been challenged by the finding that, in the general population, fat excess in particular body regions may be linked to insulin resistance and CV risk, independently of the total quantity of body fat (10–13). Obese patients with peripheral distribution of fat have a relatively low CV and metabolic risk, whereas patients with prevalently abdominal obesity have higher insulin levels, more severe lipid alteration, and increased production of inflammatory substances. Most of these differences have been attributed to the increase of visceral fat (14, 15), but sc abdominal fat is also metabolically active (15–18) and some data suggest that it may be as important as visceral fat, at least regarding insulin resistance (17) and some early alterations of endothelium (18).

Because most PCOS patients exhibit an abdominal form of obesity (19–21), recently it has been suggested that increased visceral fat may be the cause or the early consequence of their insulin resistance (22).

However, the available data on measurement of visceral or total abdominal fat in women with PCOS do not support the statement that these patients have a larger quantity of visceral or total abdominal fat than weight-matched controls (23–26). In fact, contrasting results have been presented (23–26) and, in addition, in all studies the number of controls was quite low [from a minimum of 15 (25) to a maximum of 30 (23)].

In this study, using total-body dual x-ray absorptiometry (DXA), we assessed several fat quantity parameters in a large number of women with PCOS and an equal number of controls. Because small changes of body weight may determine relatively large modifications in fat mass, particular care was given to weight matching of controls.

The objectives of the study were to determine whether total and/or abdominal fat quantity is larger in PCOS than weight-matched controls and to assess whether PCOS patients and controls with similar total or abdominal fat quantity present similar circulating insulin levels and similar insulin sensitivity.

Patients and Methods

Patients and control subjects

One hundred ten consecutive women of reproductive age with PCOS, all referred because of androgen excess to our Endocrine Units, were included in the present study. The diagnosis of PCOS was based on the presence of clinical or biological hyperandrogenism and chronic anovulation and the exclusion of adrenal enzymatic deficiency (by measurement of serum 17-hydroxyprogesterone), Cushing's syndrome, or androgen-secreting tumors (27).

Clinical hyperandrogenism was defined as the presence of hirsutism, acne, or androgenic alopecia. Hirsutism was assessed by Ferriman-Gallwey-Lorenzo scores (28) (patients with scores ≥ 6 were considered hirsute), whereas acne was graded by a scoring system from 0 to 3 (29), and alopecia was evaluated by the Ludwig scoring system (30).

Biochemical hyperandrogenism was defined as serum testosterone greater than 60 ng/dl (>2.08 nmol/liter) and/or free testosterone 3 pg/ml or greater (≥10.34 pmol/liter) and/or serum dehydroepiandrosterone sulfate 3000 μg/liter or greater (≥7.8 μmol/liter). These values of hyperandrogenism have been previously calculated in our population with the same assays (31).

Anovulation was defined as serum P less than 3 ng/ml (<9.54 nmol/liter). In patients with normal menses, at least two consecutive menstrual cycles were studied, and low levels of serum P (<3 ng/ml) in both cycles indicated the presence of chronic anovulation. Therefore, the studied patients presented the classic, more severe form of PCOS (32).

The project design included a medical examination, biochemical analyses, and DXA determination of fat quantity and distribution. The adopted procedures were in agreement with the Helsinki Declaration of 1975 as revised in 1983, and the study was approved by the local ethics council. All subjects gave their informed consent to participate in the study. At admission all subjects underwent a medical examination and also answered a questionnaire on personal and medical items, including age, past medical history, and use of medications. Exclusion criteria included the presence of renal or hepatic diseases. No patient had type 2 diabetes, and no patient had taken medications for at least 3 months.

Height, weight, and waist circumference (measured at the midpoint between the lateral iliac crest and the lowest rib margin at the end of normal expiration) were recorded and BMI was calculated as kilograms per square meter.

As controls, we selected a group of 112 healthy female subjects, matched for age and body weight, with the same exclusion criteria described above. They were recruited from family members of hospital coworkers. Controls were women with regular menses, no clinical or biological hyperandrogenism, and normal (>7 ng/ml in d 22 of the cycle) serum progesterone levels.

A main objective of the study design was to match patients and controls by not only total mean body weight but also body weight distribution to have a similar number of controls and PCOS women and a similar mean body weight inside the subgroups of normoweight (BMI 20–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI 30–40 kg/m^2) subjects. Because in our PCOS population the three different weight subgroups are equally represented (4), we intended to study about 40 patients and 40 controls for each weight subgroup. Therefore, consecutively studied PCOS patients were included in three different subgroups according to their BMI (normal, overweight, and obese), and in each subgroup, every 20 PCOS patients and 20 body weight-matched controls were selected and studied. The final number was slightly lower than 40 patients for weight subgroup because some patients did not complete the endocrine evaluation and were excluded from the study.

No patient or control had a BMI higher than 40 kg/m^2.

In all women with PCOS and normal controls, during the follicular phase (d 5–8), a fasting blood sample was obtained between 0800 and 0900 h for measurements of insulin, glucose, and testosterone.

Assays

Plasma glucose levels were determined by the glucose oxidase technique. Insulin was determined with a double antibody method using reagents obtained from Linco Research, Inc. (St. Charles, MO). Insulin resistance was calculated by the quantitative insulin-sensitivity check index (QUICKI) (9, 33, 34). Testosterone was determined by a RIA method after extraction and chromatography (35).

In all hormonal assays, the intraassay coefficient of variation was less than 6%, and the interassay coefficient of variation was less than 15%.

Fat determination

In both departments of Clinical Medicine, fat quantity was determined by total body DXA using a similar Instrument (QDR Discovery; Hologic, Bedford, MA). Total fat quantity and quantity of fat in trunk area were measured. Quantity of fat was determined also in central abdominal area (R1 area), an area of 50 cm^2 around the central point of the midline between the lateral iliac crests and the lowest rib margins at the end of normal expiration (the same midline used for waist circumference). The central point of R1 area generally but not always corresponded to the umbilicus. To assess fat distribution, percent of total fat in trunk and R1 area were also calculated.

Statistical analysis

Statistical analyses were performed using Statview 4.5 (Abacus Concepts Inc., Berkeley, CA) and SPSS 9.0 for PC (SPSS Inc., Chicago, IL). Univariate analyses were performed using Student's unpaired *t* test for the numeric variables, whereas the differences in the prevalences for the nominal variables were analyzed by χ^2 test. Analysis of covariance was used to assess the differences in fat quantity and distribution and biochemical parameters between subgroups of patients and controls. Correlation analyses were performed using the Spearman rank correlation method. All data are expressed as mean ± SD.

Results

Patients with PCOS and matched controls had similar age (25.1 ± 4.9 *vs.* 24.9 ± 3 yr), whereas testosterone (80.7 ± 29 *vs.* 41 ± 9 ng/dl) and insulin (14.8 ± 5 *vs.* 11.3 ± 5.1 μU/ml) were significantly higher ($P < 0.01$) in PCOS than controls. QUICKI was significantly lower (0.324 ± 0.02 *vs.* 0.351 ± 0.02, $P < 0.01$) in PCOS than matched controls.

As shown in Table 1, BMI, total fat, and trunk fat quantity were similar in PCOS and weight-matched controls. However, waist circumference, R1 fat quantity, percent trunk fat,

TABLE 1. Fat parameters by total-body DXA in PCOS and controls

	PCOS (n = 110)	Controls (n = 112)
BMI	28.0 ± 5.5	28.0 ± 5.6
Waist circumference (cm)	92.4 ± 15.1[a]	88.2 ± 12.8
Total fat (g)	27,307 ± 10,182	27,020 ± 10,143
Trunk fat (g)	11,830 ± 5,772	10,981 ± 5,320
Trunk fat *vs.* total fat (%)	41.4 ± 6.1[a]	38.9 ± 6.3
R1 fat (g)	785 ± 387[a]	679 ± 363
R1 fat *vs.* total fat (%)	2.78 ± 0.50[a]	2.46 ± 0.49

[a] $P < 0.01$.

and percent R1 fat were significantly higher in PCOS than weight-matched controls.

Fat parameters in patients and controls divided by body weight

Thirty-five PCOS patients (31.8%) and 36 controls (32.1%) were obese (BMI $\geq$ 30 kg/m^2). As shown in Table 2, all fat parameters were similar in obese PCOS and obese controls.

Thirty-five PCOS patients (31.8%) and 36 controls (32.1%) were overweight (BMI $<$ 30 but $\geq$ 25 kg/m^2). As shown in Table 2, BMI, total fat, trunk fat, and percent trunk fat were similar in overweight PCOS and controls, whereas waist circumference, R1 fat, and percent R1 fat were higher in overweight PCOS, compared with overweight controls.

Forty PCOS patients (36.4%) and 40 controls (35.8%) had normal body weight (BMI between 19 and 24.9 kg/m^2). As shown in Table 2, BMI, total fat, and trunk fat were similar in the two groups of subjects. However, waist circumference, R1 fat, percent trunk fat, and percent R1 fat were significantly higher in normoweight PCOS, compared with normoweight controls.

Correlations between anthropometric measures and fat parameters

In total group (PCOS + controls), body weight (expressed as BMI) strongly correlated ($P < 0.01$) with total fat (r = 0.94), trunk fat (r = 0.93), and central abdominal fat (R1: r = 0.89). BMI also correlated with fat distribution but r values, although statistically significant, were lower (with percent trunk fat 0.69, $P < 0.01$; with percent R1 fat 0.41, $P < 0.05$).

Waist circumference exhibited similar correlations (with total fat 0.90, trunk fat 0.91, R1 fat 0.91, percent trunk fat 0.69, with percent R1 fat 0.47). When separately evaluating PCOS and controls, similar correlations were found.

When evaluating only obese subjects, the same correlations were observed. However, in overweight and normoweight subjects, no correlation between R1 fat and percent R1 fat with BMI or waist circumference was found.

Correlation between fat and biochemical parameters

When evaluating all patients and controls together, serum insulin correlated with all fat parameters. The best correlations were with percent R1 fat (r = 0.58, $P < 0.01$) and R1 fat (r = 0.41, $P < 0.01$). QUICKI negatively correlated with all fat parameters. The best correlations were with R1 fat (r = -0.56, $P < 0.01$) and percent R1 fat (r = -0.49, $P < 0.01$). When separately evaluating PCOS and controls, similar findings were observed, but the correlations were much stronger. In PCOS patients, the stronger correlations were between serum insulin and R1 fat (r = 0.65, $P < 0.01$) and between R1 fat and QUICKI (r = -0.73, $P < 0.001$).

When dividing patients and controls by BMI, similar correlations were found. In the group of PCOS patients, central abdominal fat showed stronger correlations with insulin and QUICKI in overweight (with insulin: r = 0.81, $P < 0.01$; QUICKI: r = -0.76, $P < 0.01$) and normoweight (with insulin r = 0.69, $P < 0.01$; QUICKI: r = -0.66, $P < 0.01$) than obese (with insulin: r = 0.34, $P < 0.05$; QUICKI: r = -0.49, $P < 0.01$) PCOS patients.

No correlations were found between serum testosterone and fat parameters.

Assessment of normal and pathological values of fat parameters

The mean + 2 SD values of normoweight controls were used to determine the upper normal ranges of fat parameters. Therefore, the following values were considered higher than normal values: total fat, 23,400 g; trunk fat, 8,800 g; R1 fat, 560 g.

Total fat was increased in all obese patients and controls and normal in all normoweight patients and controls. Total fat was increased in 20 overweight PCOS patients (57%) and in 22 overweight controls (61%).

Trunk fat was increased in all obese subjects (both PCOS patients and controls) but also in 71% of overweight PCOS patients and 72% of overweight controls. All normoweight controls had normal trunk fat, whereas five normoweight PCOS patients (12.5%) had increased trunk fat.

Central abdominal fat was increased in all obese subjects (both PCOS and controls) and also 71% of overweight PCOS and 50% of overweight women. Central abdominal fat was normal in all normoweight controls but was increased in 12 normoweight PCOS patients (30%).

Biochemical parameters in PCOS patients and controls with increased central abdominal fat

Insulin, QUICKI, and testosterone levels were compared in patients and subjects divided according to excess or not of central abdominal fat. Because central abdominal fat was increased in all obese subjects, the entire groups of obese PCOS and controls were compared. In obese PCOS, serum insulin was significantly higher ($P < 0.01$) (17.8 $\pm$ 4.5 μU/ml)

TABLE 2. Fat parameters by total-body DXA in PCOS patients and controls, divided according to body weight

	Obese PCOS (n = 35)	Overweight PCOS (n = 35)	Normoweight PCOS (n = 40)	Obese controls (n = 36)	Overweight controls (n = 36)	Normoweight controls
BMI (kg/m^2)	34.4 $\pm$ 3.8	27.8 $\pm$ 1.1	22.4 $\pm$ 1	34.5 $\pm$ 3.8	27.8 $\pm$ 1.8	22.4 $\pm$ 1.5
Waist circumference (cm)	108 $\pm$ 16	89.7 $\pm$ 5.5[a]	79.9 $\pm$ 4.8[b]	102 $\pm$ 12.3	85.8 $\pm$ 5.6	77.6 $\pm$ 3.3
Total fat (g)	39,101 $\pm$ 3,193	26,628 $\pm$ 5,515	17,304 $\pm$ 2,393	38,334 $\pm$ 6,347	25,782 $\pm$ 4,804	17,492 $\pm$ 2,934
Trunk fat (g)	18,630 $\pm$ 3,094	11,101 $\pm$ 3,300	6,366 $\pm$ 1,443	17,485 $\pm$ 2,632	10,219 $\pm$ 2,315	5,813 $\pm$ 1,486
Trunk fat *vs.* total fat (%)	46.9 $\pm$ 4.1	41.2 $\pm$ 5.2	36.6 $\pm$ 5.1[a]	44.9 $\pm$ 4.3	39.7 $\pm$ 4.1	32.8 $\pm$ 3.3
R1 fat (g)	1,223 $\pm$ 294	719 $\pm$ 219[a]	451 $\pm$ 103[a]	1,119 $\pm$ 215	586 $\pm$ 119	344 $\pm$ 107
R1 fat *vs.* total fat (%)	3.14 $\pm$ 0.57	2.64 $\pm$ 0.35[a]	2.60 $\pm$ 0.37[a]	2.89 $\pm$ 0.49	2.27 $\pm$ 0.28	2.22 $\pm$ 0.37

[a] $P < 0.01$ *vs.* controls of similar body weight.
[b] $P < 0.05$ *vs.* controls of similar body weight.

and QUICKI was significantly lower (0.309 ± 0.01) than in obese controls (insulin 13 ± 3 μU/ml; QUICKI 0.333 ± 0.01).

As shown in Figs. 1 and 2, overweight PCOS patients with increased central abdominal fat had significantly higher ($P < 0.01$) values of serum insulin and significantly lower ($P < 0.01$) QUICKI than overweight PCOS patients with normal central abdominal fat and overweight controls with increased or normal central abdominal fat. PCOS patients with normal central abdominal fat had similar values of insulin and QUICKI than overweight controls with central abdominal fat, and both subgroups had significantly higher ($P < 0.05$) insulin and lower QUICKI values than overweight controls with normal central abdominal fat. No differences in serum testosterone among the different subgroups of overweight PCOS patients were observed.

Serum insulin and insulin resistance calculated by QUICKI were significantly higher ($P < 0.01$) in normoweight PCOS patients with increased central abdominal fat than normoweight PCOS patients with normal central abdominal fat and normoweight controls (Figs. 3 and 4). No differences in insulin levels and insulin resistance between these two subgroups of subjects were observed. No differences in serum testosterone between normoweight PCOS with normal or increased abdominal fat were found.

Discussion

Although women with PCOS present anthropometric evidence of abdominal obesity (19–21), in these patients previous measurements of abdominal fat quantity have given contrasting results (24–26). In fact, whereas some studies showed increased abdominal fat (23, 24) or increased trunk to extremity fat ratio (25), in other studies no differences in total or trunk fat quantity between patients and weight-matched controls were found (26).

The different results probably depend on the small number of studied patients and controls but may also depend on the method used. In fact, one small study assessed visceral fat by ultrasonography (23), whereas in other studies total trunk fat was measured by DXA (24–26).

Different methods may be used to assess fat quantity and distribution, each presenting advantages and disadvantages. In a small group of subjects, multislice computed tomography or magnetic resonance imaging scanning is the best

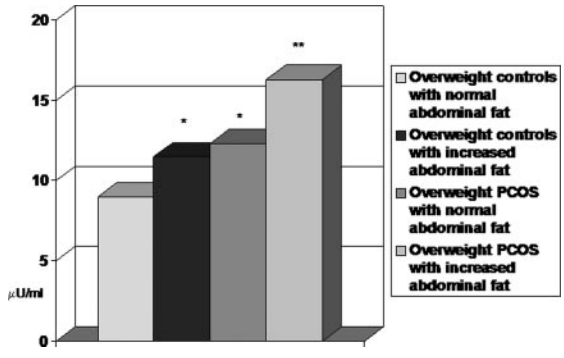

FIG. 1. Serum insulin in overweight PCOS patients and controls. To convert to picomoles per liter, multiply by 7.18. *, $P < 0.05$ *vs.* overweight controls with normal abdominal fat; **, $P < 0.01$ *vs.* overweight controls with normal abdominal fat.

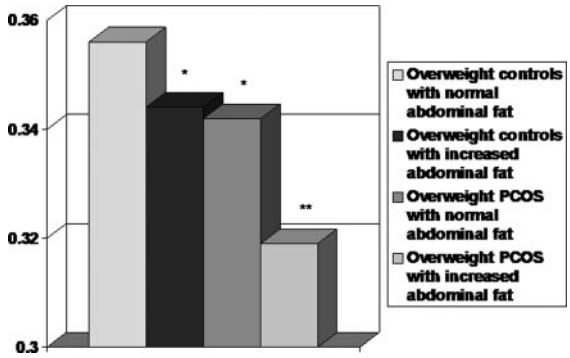

FIG. 2. Insulin sensitivity (calculated by QUICKI) in PCOS patients and controls. *, $P < 0.05$ *vs.* overweight controls with normal abdominal fat; **, $P < 0.01$ *vs.* overweight controls with normal abdominal fat.

method because it allows one to distinguish and measure the different compartments of sc fat and the visceral abdominal fat (14, 17). However, these methods may be used only in a small group of particularly selected patients but not in screening studies of large populations. Ultrasound evaluation of sc and visceral abdominal fat has also been used (14, 35), but this method, although simple and feasible in large populations, is largely operator dependent and has reduced sensitivity in normoweight or slightly overweight patients (35).

In this study we used total-body DXA to assess fat quantity and distribution (36). The main advantage of the DXA method is the possibility to measure directly the quantity of fat in different body regions, giving numerical data that are independent of the operator. It is a simple method that may be used in large populations. The main disadvantage is the impossibility to differentiate sc from visceral abdominal fat. However, because sc abdominal fat is also metabolically active and linked to insulin resistance (17) and vascular early alterations (18), assessment of abdominal fat by DXA is a good indicator of metabolic and cardiovascular consequences of obesity (17, 36) and may be a better indicator than simple visceral fat determination (16).

DXA software assesses body composition in the trunk, an area that includes not only the abdomen but also the thorax.

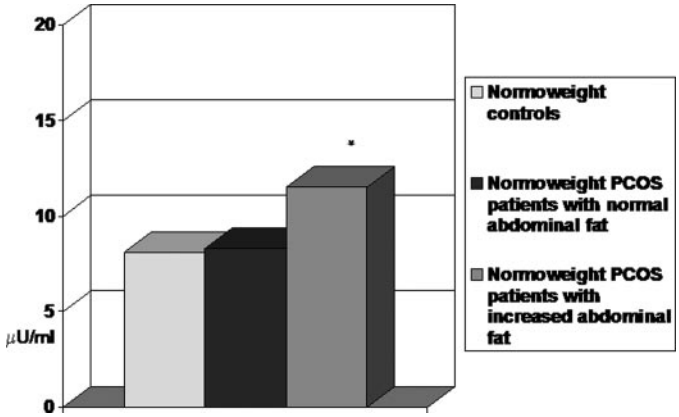

FIG. 3. Serum insulin in normoweight PCOS patients and controls. To convert to picomoles per liter, multiply by 7.18. *, $P < 0.05$ *vs.* normoweight controls.

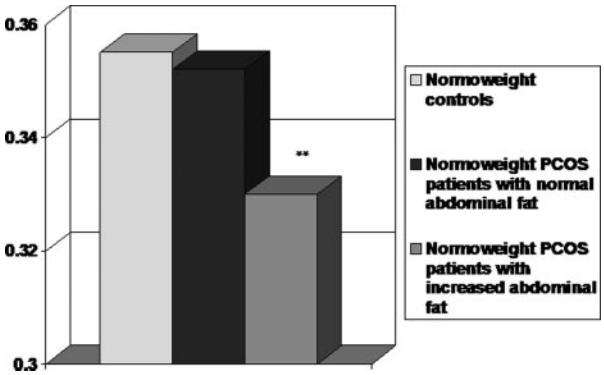

FIG. 4. Insulin sensitivity in normoweight PCOS patients and controls. **, $P < 0.01$ *vs.* normoweight controls.

Because of this, to improve the sensitivity of the method, some authors measured the fat quantity in the area between the first and fourth lumbar vertebra (36). We preferred to assess fat quantity in the central abdominal region, evaluating an area of 50 cm^2 around the midpoint of the midline between the lateral iliac crests and the lowest rib margins at the end of normal expiration. This method presents the advantage of measuring abdominal fat in the same area that is used for assessing waist circumference and abdominal sagittal diameter. In fact, it has been shown that these two parameters are better correlates of abdominal visceral adipose tissue accumulation and cardiovascular disease risk factors than other measures of body weight or fat distribution (37).

By evaluating a large population of PCOS patients and carefully weight-matched controls (a total of 222 subjects), we found that, despite the difference in the simple measurement of waist circumference, PCOS patients and controls have similar quantities of not only total fat but also trunk fat. Only percent trunk fat was significantly increased in PCOS patients, confirming the data reported by Puder *et al.* (25). However, central abdominal fat was significantly increased in PCOS patients, indicating that, by improving the sensitivity of the method, it is possible to demonstrate that PCOS patients have increased fat in abdominal region.

By dividing the patients in subgroups according to body weight, we observed that this difference is mainly dependent on differences in abdominal fat accumulation in overweight and normoweight PCOS patients, compared with controls of similar body weight. In fact, when comparing obese PCOS and obese controls, all fat parameters were similar. Probably when obesity is present, most subjects, independently of having PCOS or not, have an abdominal obesity. One hundred percent of our obese controls (and 100% of our obese PCOS patients) showed increased quantity of trunk and central abdominal fat. On the other hand, it has been reported that at least 80% of obese subjects are affected by abdominal obesity (11, 12).

On the contrary, when compared with controls with similar body weight, overweight and normoweight PCOS patients had an increased quantity of central abdominal fat. Interestingly, in these patients, anthropometric measures (BMI or waist circumference) did not permit us to predict the presence of central abdominal fat excess, and this suggests that DXA evaluation of fat quantity and distribution may be particularly useful in such PCOS patients.

Because abdominal fat is strongly correlated with insulin and insulin resistance (as confirmed by our own data), the presence of increased abdominal fat in a large proportion of nonobese PCOS may indicate that the finding of hyperinsulinemia and insulin resistance in PCOS, compared with weight-matched controls, is just the consequence of abdominal obesity in a larger proportion of subjects. However, our study suggests that the increase in abdominal fat is not the only determinant of hyperinsulinemia and insulin resistance in PCOS. Comparing patients and controls with similarly increased quantities of central abdominal fat, we found that PCOS patients had higher insulin levels and reduced insulin sensitivity.

In fact, obese PCOS patients, despite presenting similar abdominal quantity of fat than obese controls, had higher insulin and more severe insulin resistance than obese controls. In addition, overweight PCOS patients with increased abdominal fat had higher insulin and lower QUICKI than overweight controls with similarly increased abdominal fat. Finally, overweight PCOS patients with normal central abdominal fat had higher insulin levels and lower insulin sensitivity than overweight controls with a similar quantity of abdominal adipose tissue.

These data suggest that factors different from abdominal fat may be involved in the increase of insulin levels and insulin resistance of PCOS patients.

A similar evaluation between normoweight PCOS and controls was not possible because all normoweight controls exhibited normal abdominal fat. However, normoweight PCOS with normal central abdominal fat did not show any evidence of hyperinsulinemia and insulin resistance. These patients are relatively common in our population and, in this study, 28 PCOS patients (25% of studied PCOS women) had normal body weight and normal central abdominal fat.

It is difficult to reconcile the differences in results between obese and overweight PCOS who present higher insulin and reduced insulin sensitivity than controls with similar abdominal fat and normoweight PCOS with normal abdominal fat who have similar insulin and insulin sensitivity, compared with their own controls.

Maybe normoweight controls with normal fat quantity and distribution represent a subgroup of PCOS in whom insulin resistance does not have a role in the pathogenesis of the disorder. In fact, insulin resistance may influence fat distribution, and it is probable that the differences in fat distribution that we observed in PCOS patients are the consequence of reduced insulin sensitivity.

In this study we did not measure visceral fat but measured only sc and visceral central abdominal adipose tissue. Multislice computed tomography scanning determination of different compartments of abdominal fat, followed by comparison of populations of PCOS women and control women with similar quantities of visceral fat, may be needed to better understand the relationships between fat distribution and insulin sensitivity in PCOS. However, it is unlikely that patients and controls with similar quantities of total, trunk, and central abdominal fat have substantial differences in quantity of visceral fat. In fact, patients with a higher quantity of

visceral fat should have a lower quantity of abdominal sc fat. On the other hand, it has been shown that the profound component of sc abdominal fat is probably more important than visceral fat in determining insulin resistance (17), whereas visceral fat seems to be more related to increased inflammatory activity of adipose tissue.

In conclusion, we have shown that not only obese PCOS patients but also a large proportion of overweight PCOS patients and a minority of normoweight PCOS patients have increased abdominal fat. Although this alteration may contribute to hyperinsulinemia and reduced insulin sensitivity, it is unlikely to be the only determinant of insulin resistance of PCOS. In fact, when comparing obese and overweight patients and controls with similar quantities of abdominal fat, PCOS patients still have higher insulin levels and reduced insulin sensitivity. As a partial exception, normoweight PCOS patients with normal abdominal fat presented similar insulin levels and insulin sensitivity than normoweight controls. Further studies are needed to understand better the relationships between fat distribution and insulin sensitivity in PCOS.

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