

BODY FAT DISTRIBUTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract

Background and Aims. Most women with Polycystic Ovary Syndrome (PCOS) are thought to have an abdominal body fat distribution, regardless of body mass index (BMI). The objective of our research was to compare body fat distribution between PCOS cases and BMI/age matched healthy control women. **Materials and Methods.** We compared 102 women with PCOS and 120 healthy female patients matched for age and BMI (retrospective review of the medical records). Visceral fat area (VFA) was measured by bioelectric impedance. **Results.** No significant differences were noted between the PCOS group and controls regarding total cholesterol, LDL-cholesterol and triglycerides levels. Mean HDL-cholesterol concentration was significantly lower in the PCOS group ($p=0.03$). Mean fasting serum insulin and calculated HOMA-IR were higher in the PCOS group (14.2 ± 7.2 vs. $9.1\pm 4.1\mu\text{U/mL}$, $p<0.001$, and 3.1 ± 1.8 vs. 2.3 ± 1.1 , $p=0.01$ respectively). VFA was similar in patients with PCOS and in the control group. **Conclusions.** Obese women with PCOS have no preponderant accumulation of visceral fat, compared with weight/age-matched controls. Our data suggest that the distribution of fat to visceral depots is unlikely to be the entire explanation for the metabolic abnormalities observed in women with PCOS.

key words: polycystic ovary syndrome, visceral fat area, bioelectric impedance

Background and Aims

Polycystic ovary syndrome (PCOS) is a common female endocrinopathy characterized by reproductive, hyperandrogenic, and metabolic features. It is considered the most

frequent and the most important anovulatory pathology involved in couple infertility. The prevalence of PCOS is traditionally estimated between 4% to 8% [1,2] Recently, March et al. reported a prevalence of 18% in a

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community-based study, using the Rotterdam criteria [3].

PCOS is associated with several features of the metabolic syndrome, such as obesity, abdominal obesity [4] and insulin resistance (IR) [5,6]. Most women with PCOS are thought to have an abdominal body fat distribution, regardless of body mass index (BMI) [7]. Despite the increasing number of studies evaluating body fat distribution in women with PCOS, it still remains under debate whether the adiposity-related predisposition to PCOS reflects an overall adiposity, as that reflected by the body mass index, or is more closely related to the regional accumulation of visceral/abdominal fat (android obesity), leading to abnormalities of body fat distribution [5,8-10].

The aim of the present study was to compare body fat distribution using bioelectric impedance between PCOS cases and BMI/age matched healthy control women. Additionally we aimed to assess the relationship between visceral fat, body fat mass and metabolic indicators.

Materials and Methods

Study Design and Study Subjects

A retrospective review of the medical records of female patients addressing for a consultation in a healthcare network in Cluj-Napoca was performed. From 140 patients identified with PCOS, 38 were excluded due to lack of data regarding body composition or metabolic parameters (fasting glucose, fasting insulin, total cholesterol, total triglycerides and HDL-cholesterol). The remaining 102 patients with complete data and without previous treatment were included in the PCOS group. PCOS was diagnosed using the Rotterdam criteria for PCOS (presence of two out of the following three: oligo-anovulation,

clinical and/or biochemical signs of hyperandrogenism or polycystic ovaries, and exclusion of other etiologies [11]).

Healthy female patients matched for age and body mass index (BMI) but without PCOS were included in the control group. Overall, 120 healthy women with completed medical records regarding body composition and metabolic profile were identified.

Evaluation of body composition

Visceral fat area (VFA) and body fat mass (BFM) were measured by bioelectric impedance, using InBody 720 (Biospace, Korea). This is a multifrequency impedance plethysmograph body composition analyzer, which takes readings from the body using an eight-point tactile electrode method, measuring resistance at five specific frequencies (1 kHz, 50 kHz, 250 kHz, 500 kHz, and 1 MHz) and reactance at three specific frequencies (5 kHz, 50 kHz, and 250 kHz). These frequencies were pre-set by the manufacturer to assess extracellular fluid and total body water and introduced into the body in ascending order of frequency. In accordance with the manufacturer's guidelines, participants wiped the bottom of their feet with a proprietary electrolyte tissue before standing on the electrodes embedded in the scale platform of the respective analyzers. The participants were instructed to stand upright and to grasp the handles of the analyzer, thereby providing contact with a total of 8 electrodes (2 for each foot and hand). VFA and BFM were automatically determined when the patient stood on the electrodes embedded within the scale platform of each octapolar analyzer; the weight was also recorded. The % body fat (BF) was computed through the proprietary algorithms, displayed on the analyzer's control panel, and

recorded. For subsequent analyses, the average %BF from the InBody 720 (% BF720) was used [12].

Biochemical evaluation

Serum glycemia, insulinemia, liver enzymes and the lipids levels were collected from patients' files. The blood samples were collected after an overnight fast. Homeostasis model assessment (HOMA-IR) was used to assess insulin resistance. HOMA – IR was calculated using the formula: fasting serum insulin ($\mu\text{U}/\text{mL}$) x fasting plasma glucose (FPG) (mg/dl)/405 [13].

Statistical analysis

Statistical analysis was carried out using SPSS-PC 13.0 (SPSS Inc., Chicago, IL, USA). Distribution of variables was tested with Kolmogorov- Smirnov test. Statistical data is

presented as mean \pm standard deviation (SD) for normally-distributed variables. Student t-test was used to compare variables with normal distribution. The correlations between the body composition measurements and biochemical variables were calculated by the Pearson's coefficient. The level of significance was set at 5% ($p < 0.05$) in all analyses.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee.

Results

The current study evaluates 102 women with PCOS and 120 healthy patients, matched for age and sex (control group). The demographic features and biochemical results of patients with PCOS and healthy controls are displayed in [Table 1](#).

Table 1. Anthropometrics and laboratory results of patients with PCOS and healthy controls.

Parameter	PCOS group (n=102)	Control group (n=120)	p-value
Age (years)	31.6 \pm 8.8	31.2 \pm 8.3	0.84
BMI (kg/m ²)	31.8 \pm 8.7	31.9 \pm 5.4	0.97
Waist circumference (cm)	104.5 \pm 24.0	96.6 \pm 14.1	0.20
FPG (mg/dl)	95.0 \pm 10.4	86.2 \pm 10.8	<0.001
Fasting insulin ($\mu\text{U}/\text{mL}$)	14.2 \pm 7.2	9.1 \pm 4.1	<0.001
Total cholesterol (mg/dl)	181.2 \pm 36.6	176.0 \pm 35.6	0.47
HDL-cholesterol (mg/dl)	46.5 \pm 12.6	52.2 \pm 12.9	0.03
LDL- cholesterol (mg/dl)	114.1 \pm 33.9	104.7 \pm 30.2	0.15
Triglyceride (mg/dl)	102.2 \pm 60.8	119.8 \pm 74.1	0.19
GOT	20.9 \pm 6.7	21.9 \pm 7.6	0.44
GPT	24.9 \pm 12.4	24.5 \pm 13.3	0.85
VFA (cm ²)	111.9 \pm 36.9	112.9 \pm 32.0	0.87
BFM (kg)	35.4 \pm 17.1	36.3 \pm 11.9	0.75
HOMA-IR	3.1 \pm 1.8	2.3 \pm 1.1	0.01

All data above represent mean \pm SD; FPG – fasting plasma glucose; HOMA-IR – homeostatic model assessment; VFA- visceral fat area; BFM – body fat mass; BMI - body mass index; HDL - High-density lipoprotein; LDL – low density lipoprotein; GOT - glutamic-oxaloacetic transaminase; GPT - glutamic-pyruvic transaminase

The two groups were similar with regard to age, BMI and waist circumference. Additionally, no statistically significant differences were noted between the PCOS group and controls regarding total cholesterol, LDL-cholesterol and triglycerides levels. Mean HDL-cholesterol concentration was significantly lower in the PCOS group compared to controls (46.5 ± 12.6 mg/dl vs. 52.2 ± 12.9 mg/dl, $p=0.03$).

Mean fasting serum insulin was higher in the patient group (14.2 ± 7.2 μ U/mL vs. 9.1 ± 4.1 μ U/mL, $p<0.001$). Also, the calculated HOMA-IR was higher in the PCOS group when compared with controls (3.1 ± 1.8 vs. 2.3 ± 1.1 , $p=0.01$).

Visceral fat area averaged 111.9 ± 36.9 cm² in patients with PCOS, a value similar to that recorded in the control group (112.9 ± 32.0 cm², $p=0.87$). Similar results were observed for body fat mass: 35.4 ± 17.1 kg in PCOS group and 36.3 ± 11.9 kg in the control group ($p>0.75$).

Correlation of VFA and BFM with metabolic parameters in women with PCOS

Pearson's correlation coefficients were calculated in order to assess the relationship between visceral adipose tissue, body fat mass and metabolic parameters: fasting plasma glucose, fasting insulin, HOMA-IR, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides. As shown in [Table 2](#) and [Figure 1](#), VFA was positively correlated with fasting plasma glucose, fasting insulin, HOMA-IR and fasting triglycerides levels ($p<0.05$, for all). Also, positive correlation was found between BFM and fasting plasma glucose, fasting insulin, HOMA-IR and fasting triglycerides levels ($p<0.05$, for all) ([Table 2](#), [Figure 2](#)). No significant correlations were found between VFA and BFM with total cholesterol, HDL-cholesterol and LDL-cholesterol ($p>0.05$ for all).

Table 2. Pearson correlation coefficients for the association between VFA, BFM and metabolic variables.

	VFA		BFM	
	R	p value	R	p value
FPG	0.42	0.003	0.39	0.007
Fasting insulin	0.57	<0.001	0.62	<0.001
HOMA-IR	0.62	<0.001	0.66	<0.001
Total cholesterol (mg/dl)	0.23	0.12	0.01	0.99
HDL-cholesterol (mg/dl)	-0.18	0.25	-0.29	0.06
LDL- cholesterol (mg/dl)	0.23	0.13	-0.07	0.66
Triglyceride (mg/dl)	0.33	0.02	0.36	0.04

Discussions

The present study provided no evidence regarding a difference in body fat distribution between the groups with and without PCOS. Women with PCOS had significantly higher

plasma glucose and insulin concentrations, as well as higher HOMA-IR levels and lower HDL cholesterol. Within the PCOS group, correlations were found between visceral fat area and metabolic parameters: fasting plasma

glucose, fasting insulin, HOMA-IR and triglycerides. Correlation was also found

between body fat mass and the metabolic parameters.

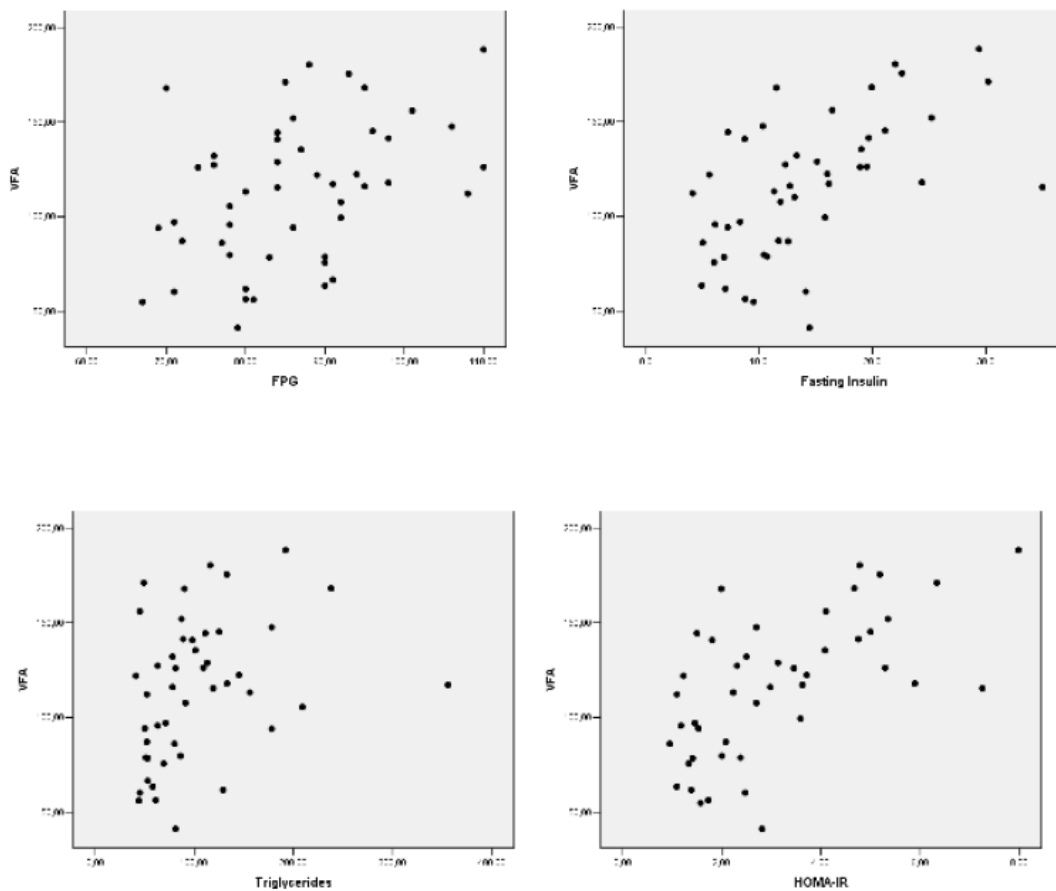


Figure 1. Scatter plots diagrams of correlation between VFA and metabolic parameters. Correlation coefficients are shown in [Table 2](#).

Our data are in accordance with the results of Barber et al [14] and Mannerås-Holm et al [15]. Both studies investigated fat distribution, assessed with magnetic resonance imaging (MRI), in women with PCOS and controls, matched for BMI and revealed no difference in fat accumulation in visceral, abdominal subcutaneous and gluteofemoral depots, despite significant differences in insulin resistance. Our findings are also supported by the study of Penaforte et al [16], using bioelectrical impedance analysis suggesting that there are no differences regarding the VFA between the PCOS and control groups.

Also Marsden et al. [17] showed that lean women with PCOS are as insulin resistant as obese women with PCOS. Moreover, a study performed by Dolfing et al demonstrated that the content of visceral deposited fat was lower in lean PCOS cases compared with matched controls [18]. However, the findings noted above differ from those of some other previous studies [4,19-22], where it was suggested that women with PCOS have preferential fat accumulation in the upper body compared to controls matched for weight and age.

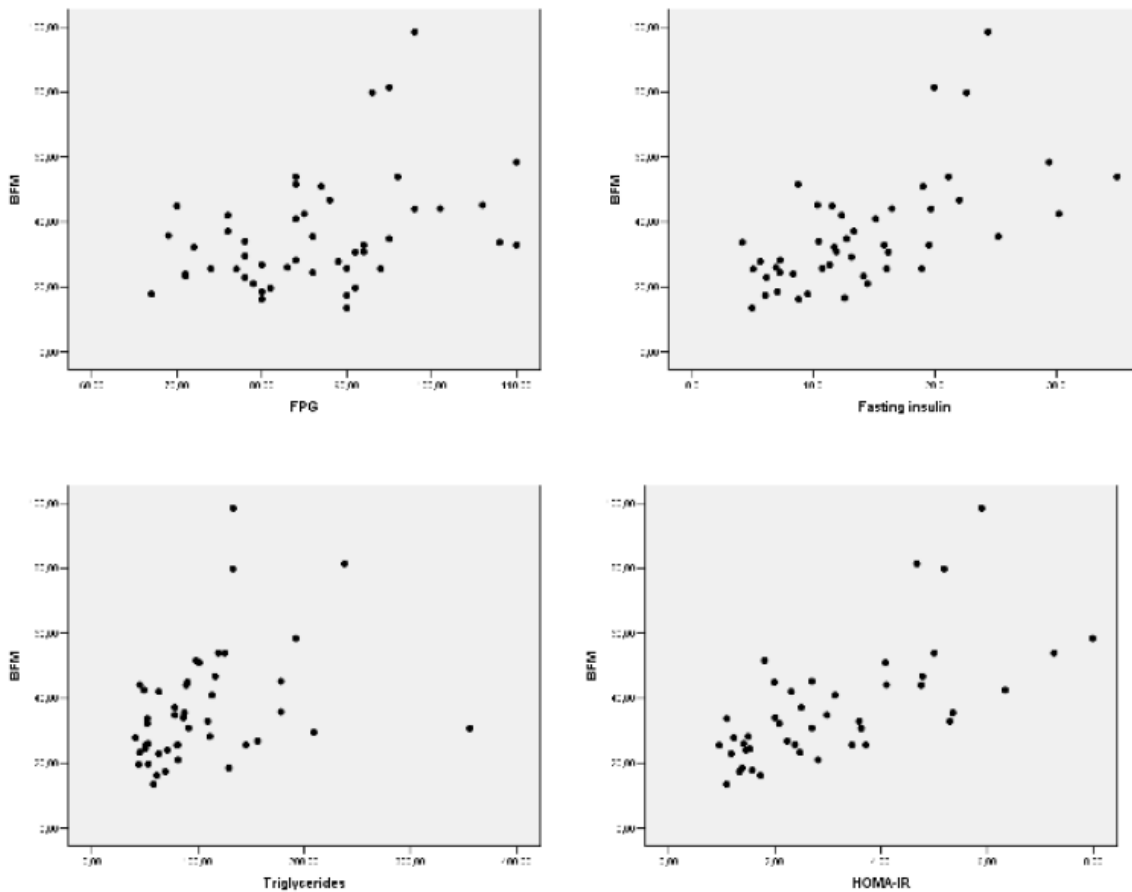


Figure 2. Scatter plots diagrams of correlation between BFM and metabolic parameters. Correlation coefficients are shown in [Table 2](#).

Despite the similarity in fat distribution, including VFA between the PCOS cases and BMI/age-matched controls, we also observed significant differences in insulin concentrations and insulin sensitivity between these groups, result concordant with previous descriptions [5,14,23]. These data suggest that the metabolic abnormalities of PCOS are not as closely linked to increased abdominal adiposity. A possible explanation for the differences observed between the PCOS and control groups is that women with PCOS have abnormal ectopic fat deposition (e.g. in liver and muscle) [24]. Differences in ectopic fat deposition between PCOS cases and controls, including differences in intrahepatic fat

content, would not have been detected by our approach. In PCOS, insulin resistance (IR) is more than a biomarker of the disease, but is rather an active contributor to its pathogenesis [25]. The molecular basis of IR in PCOS is related to a variety of defects, including postbinding receptor failure [26] and insulin signaling defect at the level of glucose transport in skeletal muscle [27]. Specifically, the cause of IR in skeletal muscle might be due to low levels of Insulin receptor substrate 1 (IRS-1) expression, impaired IRS-1 phosphorylation, reduced activity of the serine / threonine kinase AKT2 and altered glucose transporter GLUT4 translocation to the plasma membrane [28]. Also, current evidence

indicates that women with PCOS are genetically predisposed to the development of IR [29] and an increased VFA could emphasize this predisposition by being more strongly associated with various metabolic changes. However, some studies have shown that muscular IR in PCOS results from both intrinsic factors (genetically determined defects in insulin signalling) and extrinsic conditions pertinent to environmental exposures (obesity, ovarian dysfunction) [28].

Dyslipidaemia is common in PCOS compared to weight matched controls, with higher triglycerides and lower HDL cholesterol [30].

The correlations that we found between VFA and metabolic parameters in women with PCOS are in line with the results of other studies showing that the association of visceral adipose tissue in PCOS with hyperinsulinism is explained in part by the occurrence of insulin resistance and compensatory hyperinsulinism in women with abdominal adiposity, overweight and obesity, and by the fact that systemic hyperinsulinism plays a major role in the development of the hyperandrogenism which is characteristic of PCOS [6,31]. A study performed by Lord et al [32] also showed that visceral fat is the most significant variable correlating with metabolic dysfunction in women with PCOS, although they did find also correlations with subcutaneous fat, weight and BMI. The relationships between VFA and metabolic disorders have been well described in the general population, suggesting that our population of women with PCOS have similar metabolic trends [33,34].

Limitations

The most important limitation of our study is its retrospective design. The use of bioelectrical impedance analysis (BIA) for the measurement of VFA and BFM instead of MRI could be another limitation of our study. BIA is an accessible, safe and cost-efficient method that avoids exposure to radiation and has been widely used to measure body composition in clinical populations [35]. However, BIA lacks specificity and accuracy because it is based on differences in resistance when an electrical current is conducted through fat and lean components of the body [36]. Recent attempts to assess the amount of abdominal subcutaneous and visceral fat by BIA indicated significant correlations when compared with precise imaging techniques such as CT [37]. A recent statement of the American Heart Association support the use of BIA as a useful method in classifying adipose tissue distribution for the initial diagnosis of abdominal obesity for individuals, and for general application in epidemiological studies [38].

Conclusion

This study confirms recent findings showing that obese women with PCOS have no preponderant accumulation of visceral fat, compared with weight/age-matched controls. The presented data suggest that although women with PCOS frequently manifest abdominal obesity, the distribution of fat to visceral depots is unlikely to represent the entire explanation for the metabolic abnormalities observed in PCOS.

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