*Jarosław Kozakowski, Michał Rabijewski, Wojciech Zgliczyński

Association between abdominal and gynoid fat mass, metabolism markers and serum androgens in obese women with polycystic ovary syndrome**

Zależność między masą tłuszczu brzusznego i gynoidalnego a wskaźnikami metabolicznymi i stężeniem androgenów u otyłych kobiet z PCOS

Department of Endocrinology, Medical Center of Postgraduate Education, Warsaw
Head of Department: prof. Wojciech Zgliczyński, MD, PhD

S u m m a r y

Aim. To evaluate associations between abdominal and gynoid fat, glucose and lipid metabolism markers and serum androgens in obese women with polycystic ovary syndrome (PCOS).

Material and methods. In 20 women with PCOS aged 19-49 years with body mass index (BMI) 27.3-53.8 kg/m^2 anthropometric measurements were performed. Fasting serum glucose, lipids, insulin, leptin, LH, FSH, estradiol, androgens, SHBG, fT4 and TSH were estimated. Body composition was measured by DEXA scan.

Results. All of the subjects had increased abdominal fat and were hyperandrogenic, seven of them had elevated fasting serum insulin levels, and fifteen were insulin resistant. BMI, abdominal fat and waist circumference (WC) positively correlated with triglycerides ($r = 0.45$, $p < 0.05$; $r = 0.45$, $p < 0.05$; $r = 0.56$, $p < 0.01$, respectively), insulin ($r = 0.79$, $p < 0.001$; $r = 0.61$, $p < 0.01$; $r = 0.71$, $p < 0.01$, respectively), and systolic blood pressure ($r = 0.68$, $p < 0.001$; $r = 0.59$, $p < 0.01$; $r = 0.58$, $p < 0.01$, respectively). We found a correlation between leptin levels and body weight ($r = 0.68$, $p < 0.05$), BMI ($r = 0.67$, $p < 0.05$), total fat ($r = 0.62$, $p < 0.05$) and WC ($r = 0.83$, $p < 0.01$). No direct correlation between fat mass indices and sex hormones were found. We observed a correlation between androgens and TSH: androstendione ($r = 0.61$, $p = 0.0065$) and DHEA-S ($r = 0.64$, $p = 0.01$).

Conclusions. DEXA is a valuable method of body composition assessment in women with PCOS. Studied subjects had abdominal type of obesity. There was a positive correlation between abdominal obesity and cardiovascular risk factors: triglyceride and insulin levels and blood pressure. We did not prove any direct association between fatness and serum androgens but correlation between androgens and TSH was found.

Key words: polycystic ovary syndrome, body composition, obesity, hyperandrogenism, insulin resistance

S t r e s z c z e n i e

Cel pracy. Ocena zależności między masą tłuszczu brzusznego i gynoidalnego a wskaźnikami metabolizmu węglowodanów i lipidów oraz androgenami w surowicy u otyłych kobiet z zespołem policystycznych jajników (PCOS).

Materiał i metody. U 20 kobiet z PCOS w wieku 19-49 lat, z BMI 27,3-53,8 kg/m^2 dokonano pomiarów antropometrycznych oraz określono na czczo stężenie glukozy, lipidów, insuliny, leptyny, LH, FSH, estradiolu, androgenów, SHBG, fT4 i TSH. Skład ciała oceniono metodą DEXA.

Wyniki. U wszystkich badanych stwierdzono zwiększoną masę tłuszczu brzusznego oraz hiperandrogenizm, u siedmiu hiperinsulinemię, a u piętnastu oporność insulinową. Wykazano dodatnią korelację między BMI, masą tłuszczu brzusznego i obwodem talii (WC) a stężeniem triglicerydów (odpowiednio: $r = 0,45$, $p < 0,05$; $r = 0,45$, $p < 0,05$; $r = 0,56$, $p < 0,01$), insuliny (odpowiednio: $r = 0,79$, $p < 0,001$; $r = 0,61$, $p < 0,01$; $r = 0,71$, $p < 0,01$) i skurczowym ciśnieniem tętniczym (odpowiednio: $r = 0,68$, $p < 0,001$; $r = 0,59$, $p < 0,01$; $r = 0,58$, $p < 0,01$). Stężenie leptyny korelowało z ciężarem ciała ($r = 0,68$, $p < 0,05$), BMI ($r = 0,67$, $p < 0,05$), masą tłuszczu całkowitą ($r = 0,62$, $p < 0,05$), i WC ($r = 0,83$, $p < 0,01$). Nie stwierdzono bezpośredniej korelacji między wskaźnikami otyłości a stężeniem hormonów płciowych. Wykazano korelację między stężeniem androgenów: androstendionu i DHEA-S a TSH (odpowiednio: $r = 0,61$, $p = 0,0065$ i $r = 0,64$, $p = 0,01$).

Wnioski. DEXA jest wartościową metodą oceny składu ciała u kobiet z PCOS. Z jej zastosowaniem u badanych stwierdzono zwiększoną masę tłuszczu brzusznego. Wykazano dodatnią korelację między masą tłuszczu w jamie brzusznej a

**This study was supported by a grant of the Medical Center of Postgraduate Education, Warsaw, Poland; Nº: 501-2-1-07-22/09.

stężeniem trglicerydów i insuliny w surowicy oraz ciśnieniem tętniczym krwi. Nie stwierdzono bezpośredniej korelacji między wskaźnikami otyłości a stężeniem hormonów płciowych, natomiast wykazano zależność między stężeniem hormonów androgenowych i TSH.

Słowa kluczowe: zespół policystycznych jajników, skład ciała, otyłość, hiperandrogenizm, insulinoodporność

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most frequent endocrine disorder in women in the reproductive age and is present in 5-10% of them (1). Criteria for diagnose this syndrome were worked out by the international consensus conference in Rotterdam in 2003 (2). Women with PCOS present clinical heterogeneity, although insulin resistance, disturbed ovarian and adrenal steroidogenesis with menstrual irregularity and polycystic ovarian morphology are most frequent features (3-5).

Obesity, that influences the phenotypic expression of PCOS in approximately 50% of patients (6) is known to be metabolically active, and leads to insulin resistance, subsequent hyperinsulinemia, increased lipolysis and release of free fatty acids from fat cells. However, insulin resistance was found also in lean women with PCOS (7). Abdominal fat secrets several metabolic factors, with proinflammatory cytokines among them. Also androgen excess and fertility disorders may be associated with obesity in these women (8).

A number of different methods to investigate body composition have been worked out. Anthropometric noninvasive measures are widely use because of their simplicity and convenience. Techniques of direct measure of adiposity (e.g. computed tomography, total body water, total body potassium) have important limitations: exposure to ionizing radiations, high cost and methodological complexity. In our study we used dual-energy x-ray absorptiometry (DEXA), that allows to measure accurately both total and regional fat with marginal exposure to radiation.

AIM OF STUDY

The aim of our study was to evaluate associations between abdominal and gynoid fat, glucose and lipid metabolism markers, blood pressure and serum androgen levels in overweight and obese women with polycystic ovary syndrome.

MATERIAL AND METHODS

20 women with PCOS, aged 19-49 years, mean 30.3 ± 8.6 (x ± SD) with BMI 27.3-53.8 kg/m^2, mean 38.02 ± 6.5 were included into the study. All of the women were obese except one that was overweight. The diagnosis of PCOS was based on criteria of the Rotterdam consensus: at least two of the following features: 1) oligomenorrhea or amenorrhea, 2) clinical and/or biochemical evidence of hyperandrogenemia and 3) polycystic ovaries in ultrasound imaging.

Biochemical hyperandrogenemia was defined as serum testosterone levels greater than 0.9 ng/ml, androstendione levels greater than 310 ng/dl and dehydroepiandrosterone-sulfate levels greater than 2000-4100 ng/ml, depending on age. Ovary in USG were defined as polycystic when they included either 10 or more follicles measuring 2-9 mm in diameter or their volume was greater than 10 cm^3.

The exclusion criteria included hypothyroidism, hyperprolactinemia, Cushing's syndrome, nonclassical congenital adrenal hyperplasia and current or previous (within the last 3 months) use of oral contraceptives and other hormonal, antidiabetic and antiobesity drugs.

A screening consisted of full physical examination, laboratory tests and imaging. Patients were examined after an overnight fast. Waist circumference, body height and weight were assessed, and then body mass index (BMI) was calculated. Blood was collected at about 8.00 h for glucose, lipids (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglicerydes), insulin, leptin, LH, FSH, estradiol, testosterone, androstendione, dehydroepiandrosterone-sulfate, sex hormone-binging globulin (SHBG), free tyroxine and TSH through an iv catheter placed in the forearm. HOMA index was calculated by the formula: fasting plasma insulin (microinternational units per milliliter) x fasting plasma glucose (millimoles per liter)/22.4. Usually the other day all of the subjects underwent transvaginal ultrasonography (TV-USG) and USG of abdomen (to exclude adrenal pathology). Body composition was determined by DEXA. The same two operators performed all TV-USG and DEXA measurements, respectively.

ASSAYS

Insulin was measured by immunoradiometric method (Insulin IRMA – Immunotech SA, France); sensitivity was 2.0 mIU/ml. Leptin was measured by RIA (Linco Res. Inc, USA), using rabbits antibodies against human leptin. The sensitivity for this assay was 0.5 ng/ml. LH, FSH and TSH were measured by immunochemiluminescence method with IMMULITE 2000 (Siemens Healthcare Diagnostics, Inc). Estradiol was measured with the same IMMULITE 2000 analyzer; sensitivity was 15 pg/ml. Total testosterone was measured by RIA-CT method (Immunotech SA, France); sensitivity of this method was 0.025 ng/ml. Androstendione was measured by direct RIA-CT (DSL, USA). Dehydroepiandrosterone-sulfate was measured by RIA-CT method (Spectria, Orion Diagnostica, Finland); sensitivity of this method was 10 ng/ml. Prolactin was measured by IMMULITE 2000 (Siemens Healthcare Diagnostics, Inc) sensitivity of the method was 0.01 μg/mL.

Body mass index was calculated as a body weight (kg)/height (m^2). To perform measurements of body

composition by DEXA we used a region of interest (ROI) program. In this method abdominal fat is estimated in region between the upper part of the pelvis with the upper margin 96 mm superior to the lower part of this region. The lateral part of this region is defined by the lateral part of the thorax. The upper part of the gynoid fat region is defined by the superior part of trochanter major, with the lower margin 96 mm inferior to the upper part of the trochanter major. The lateral part of this region is defined by the subcutaneous tissue on the hip, which can be visualized using the Image Values option (fig. 1). We used Lunar Prodigy (GE Lunar, Madison, WI, USA) equipment, which was calibrated each day with a standardized phantom and serviced regularly. The coefficient of variation for measurements of body composition with this method is about 2%.

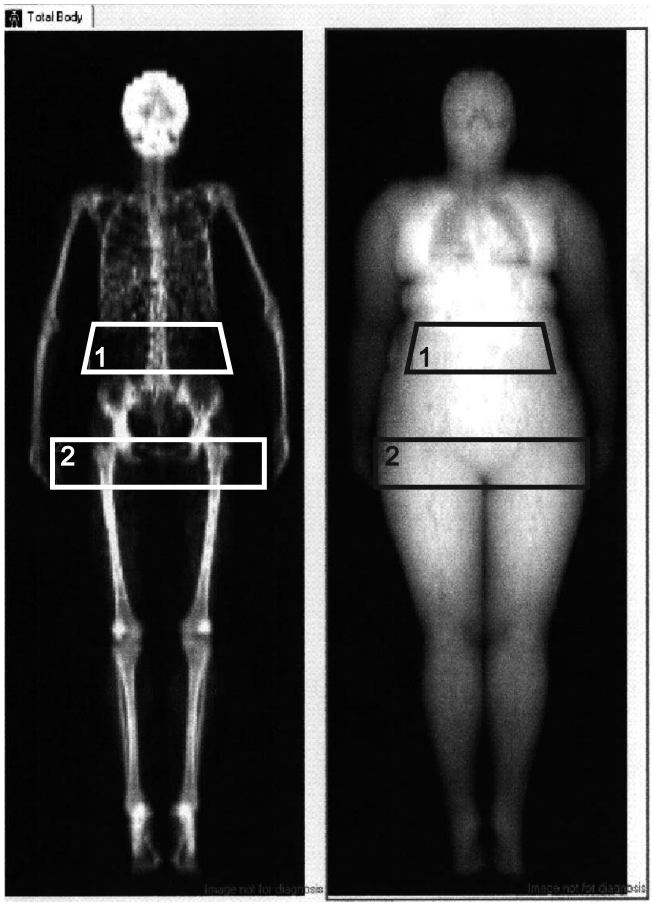

Fig. 1. Example of the regions of interest (ROI) delimiting abdominal (1) and gynoid (2) fat in one of our studied obese woman with polycystic ovary syndrome.

STATISTICAL ANALYSIS

All the data are presented as the mean ± SD. The normality of the distribution of variables was verified with a Kolmogorov-Smirnov and Lilieforse tests. To examine bivariate relationships between data Pearson correlation or Spearman rank analyses were used. Comparisons between groups with normal distribution of the data were performed by unpaired Student's t-test, in other cases comparisons were performed by Kolmogorov-Smirnov test for two samples. For all analysis, a two-tailed $P \leq 0.05$ was considered to indicate statistic significance.

RESULTS

Twenty women participated in the study. Their mean age was 30.25 ± 8.6 years. Table 1 shows anthropometric data, body composition, biochemical estimations and blood pressure of the studied subjects. Cohort represented a relatively broad range of age. One patient was overweight, eleven were obese and eight (40%) were considered as morbidly obese. All of the subjects had increased abdominal fat. Two women were hypertensive. They didn't take any hypotensive drugs until recent diagnose. In eight hypercholesterolemia and in ten hypertriglycerydemia were found.

Table 1. Anthropometric characteristics, blood pressure and biochemical results in the women with polycystic ovary syndrome.

No		N	Mean ± SD	Range
1	Age (yr)	20	30.25 ± 8.6	19.0-49.0
2	Height (m)	20	1.6 ± 0.06	1.5-1.7
3	Weight (kg)	20	103.2 ± 22.2	70.0-163.0
4	BMI (kg/m^2)	20	38.02 ± 6.5	27.3-53.8
5	WC (cm)	18	110.2 ± 14.3	85.5-137.0
6	Total FM (kg)	19	49.3 ± 13.4	27.0-78.1
7	Abdominal FM (kg)	19	3.36 ± 1	1.37-4.91
8	Gnyoid FM (kg)	19	5.91 ± 1.3	3.76-7.93
9	Systolic BP (mmHg)	20	125.2 ± 11.5	105-150
10	Diastolic BP (mmHg)	20	80.7 ± 10.4	60-100
11	Total cholesterol (mmol/l)	20	5.13 ± 0.9	3.60-7.89
12	LDL cholesterol (mmol/l)	19	3.06 ± 0.7	1.90-5.51
13	HDL cholesterol (mmol/l)	20	1.15 ± 0.2	0.77-1.60

BMI – body mass index; WC – waist circumference; FM – fat mass; BP – blood pressure; LDL – low density lipoprotein cholesterol; HDL – high density lipoprotein cholesterol.

In table 2 hormonal results from studied women are shown. All patients were hyperandrogenic and all except one were euthyrotic (one woman met hormonal criteria of subclinical hyperthyroidism). Seven had elevated fasting serum insulin levels, and fifteen were considered as insulin resistant according to HOMA index.

Correlation of blood lipids, glucose metabolism markers, blood pressure and estimates of fatness in studied subjects are presented in table 3. Body mass index, abdominal fat and waist circumference positively significantly correlated with triglycerides, insulin and systolic blood pressure.

Table 4 presents correlation between estimates of adiposity and serum hormones. We found significant positive correlation between fat estimates and leptin levels. No such correlation between fat mass indices and sex hormones were found.

Table 2. Hormonal results of studied women with polycystic ovary syndrome.

No	Hormone	n	Mean ± SD	Range
1	Insulin (μIU/mL)	19	18.7 ± 9.0	2.0-33.0
2	HOMA	19	4.40 ± 2.39	0.35-9.86
3	Leptin (μg/mL)	11	49.7 ± 23.0	13.6-86.0
4	Testosterone (ng/mL)	20	1.04 ± 0.45	0.20-2.10
5	DHEA-S (ng/mL)	17	2849.3 ± 1156.5	518.0-4496.0
6	Androstendione (ng/dL)	20	306.6 ± 163.2	104.0-835.0
7	LH/FSH	19	1.57 ± 2.39	0.09-11.10
8	Estradiol (pg/mL)	19	74.8 ± 42.9	40.0-238.0
9	Prolactin (μg/mL)	20	12.9 ± 8.1	4.0-41.0
10	TSH (μIU/mL)	18	1.16 ± 0.6	0.012-2.01

HOMA – homeostatic model assessment; DHEA-S – dehydroepiandrosterone-sulfate; LH – luteinizing hormone; FSH – follicle stimulating hormone; TSH – thyroid stimulating hormone.

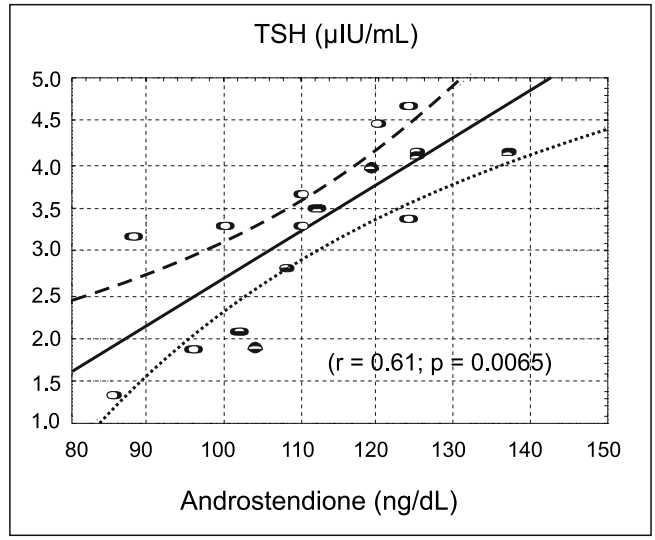

Fig. 2. Positive correlation between TSH and androstendione in women with polycystic ovary syndrome (r = 0.61; p = 0.0065).

We found a positive correlation between TSH and serum androgens: androstendione (r = 0.61; p = 0.0065; fig. 2), DHEA-S (r = 0.64; p = 0.01; fig. 3) and nearly significant relationship between TSH and total testosterone (r = 0.41; p = 0.09).

DISCUSSION

Polycystic ovary syndrome is the most common reproductive endocrinopaty and affects 5-10% of women. Etiology of PCOS is still unknown and theories of impact of genetic, intrauterine and environmental factors, such as diet and lifestyle patterns are the matter of debate. It was previously demonstrated that approximately 50% of the women with PCOS are overweight or obese. It is believed that patients with this syndrome exhibited rather central type of obesity, however estimations of the body composition have gave in fact

Table 3. Correlation between serum lipids, systolic and diastolic blood pressure, serum glucose and insulin levels and different estimates of fatness in our studied women with polycystic ovary syndrome. In the table Pearson's correlation coefficients (r_{xy}) are shown.

	Body Weight	BMI	Total Fat	Abdominal Fat	Gynoid Fat	Waist Circumference
Total cholesterol	0.08	0.05	0.07	0.19	0.12	0.14
Triglycerides	0.44	0.45[a]	0.39	0.46[a]	0.26	0.56[b]
Glucose	0.08	0.10	0.23	0.24	0.15	0.13
Insulin	0.61[b]	0.79[c]	0.70[b]	0.61[b]	0.47	0.71[b]
HOMA	0.52[a]	0.46[a]	0.40	0.40	0.42	0.49[a]
SBP	0.69[c]	0.68[c]	0.71[c]	0.59[b]	0.77[c]	0.58[b]
DBP	0.50[a]	0.48[a]	0.49[a]	0.34	0.50[a]	0.26

BMI – body mass index; HOMA – homeostatic model assessment; SBP – systolic blood pressure; DBP – diastolic blood pressure
[a]P < 0.05
[b]P < 0.01
[c]P < 0.001

Table 4. Correlation between serum hormones and different estimates of fatness in studied women with polycystic ovary syndrome. Table shows correlation coefficients (r_{xy}).

	Body Weight	BMI	Total Fat	Abdominal Fat	Gynoid Fat	Waist Circumference
Leptin	0.68[a]	0.67[a]	0.62[a]	0.39	0.64[a]	0.83[b]
FH/FSH	-0.29	-0.22	-0.21	-0.33	-0.16	-0,14
Estradiol	-0.29	-0.24	-0.26	-0.31	-0.21	-0.23
Testosterone	-0.44	-0.04	-0.03	-0.08	0.14	0.14
Androstendione	-0.28	-0.05	0.04	-0.03	0.19	0.12
DHEA-S	-0.32	-0.38	-0.38	-0.29	0.29	-0.11
TSH	-0.19	-0.18	-0.01	-0.06	0.13	0.17

BMI – body mass index; LH – luteinizing hormone; FSH – follicle stimulating hormone; DHEA-S – dehydroepiandrosterone sulfate; TSH – thyroid stimulating hormone
[a]P < 0.05
[b]P < 0.01

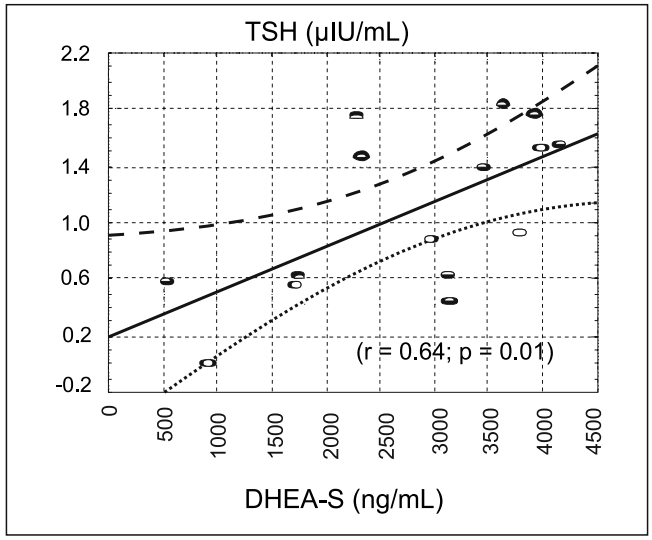

Fig. 3. Positive correlation between TSH and dehydroepiandrosterone-sulfate (r = 0.64; p = 0.01).

contrasting results (9-11). A very well known strong relationship between abdominal obesity and insulin resistance that leads to subsequent disturbances and diseases – type 2 diabetes, dyslipidaemia and hypertension makes important to determine type of obesity in patients with this syndrome. Moreover, in women with PCOS fat excess is also associated with several abnormalities of sex steroid metabolism and is related to menstrual disorders and anovulatory infertility (8).

In our study we tested usefulness of dual energy x-ray absorptiometry to estimate abdominal and gynoid fat in women with PCOS. Using this method we found that all of the our studied subjects had abdominal fat mass increased. Although only two of them were hypertensive, eleven had hypercholesterolaemia and/or hypertriglycerydaemia and fifteen were insulin resistant. Moreover, we found significant positive correlation between fasting serum insulin levels and almost all of the estimations of adiposity except one (gynoid fat). Also HOMA index turned out to be highly correlated with obesity measurements. Then our results make confirmation, that in women with PCOS obesity is related to insulin resistance and subsequent hyperinsulinaemia.

We found positive correlation between almost all obesity indices and systolic blood pressure. Data regarding the incidence of hypertension in women with PCOS are controversial. In one study authors suggest that young women with this syndrome generally do not manifest increased blood pressure (12), however another long-term follow up indicates that in these patients hypertension may be developed later in life (13). Our findings confirm that abdominal obesity may be considered as a factor that predispose to hypertension.

We couldn't find any direct correlation between serum androgens and obesity. In this our data are in agreement with results of Carmina et al. (14) who also did not find any association between fat parameters and serum testosterone levels in PCOS patients. On the other hand, Holte et al. demonstrated positive correlation between obesity and testosterone, free androgen index and DHEAS (21). Apparent discrepancy between ours and those findings may be explained partly by differences in age and BMI between studied groups. In other study of Holte et al. in obese women increased total testosterone and/or free testosterone as well as higher free androgen index, but not increased androstendione and DHEA levels were found (16). Authors demonstrated, that dihydrotestosterone (DHT) levels were lower in obese compared with non-obese patients, possibly indicating increased peripheral conversion for testosterone. The lower DHT levels may also reflect the lower SHBG levels, as the DHT has a very high affinity for SHBG. We didn't estimate DHT levels but also in our subjects reduced levels of SHBG was found (mean 29.2 nmol/l, unpublished data). Our data makes up a confirmation of previous results that SHBG suppressed secondary to hyperandrogenaemia is an early finding in obese women with PCOS (17).

Interestingly, we found a correlation between TSH and androgens: androstendione and DHEA-S and nearly significant correlation between TSH and total testosterone. It is known, that thyroid hormones influence women reproductive system on a numerous ways. Thyroid hormones modulate menstrual cycle through impact on prolactin and gonadotropins secretion, an impact on the ovaries function and on SHBG production (18). In only a few studies thyroid function in women with PCOS was studied. In women with PCOS higher prevalence of autoimmune thyroid disease in comparison to normal age-matched controls was found (19). All of our subjects except one were euthyrotic and had normal TSH levels (mean 1.16 μIU/ml), however they all had low androgens and SHBG levels. Hence, it can be speculated that in our studied subject thyroid hormones might possibly no modulate steroid hormone production.

Our study has some limitations. Firstly, it suffers from lack of an adequate control group of healthy women. Secondly, it includes small number of studied patients. Thirdly, it was not possible to differentiate visceral from subcutaneous fat analyzing ROI with DEXA method. In order to do that computed tomography should be used, but limitation of CT is a great exposure to ionizing radiations. On the other hand, it was proved that also subcutaneous abdominal fat, especially its profound component is metabolically active and contribute to insulin resistance and its subsequent metabolic and clinic consequences (20), so it seems that DEXA can be considered as a reliable method to identify and appreciate the risk associated with abdominal obesity.

In conclusion, we demonstrated that DEXA is a valuable method of body composition assessment in women with PCOS. Our patients had abdominal type of obesity. Total body fat and abdominal fat in obese women with PCOS correlated with cardiovascular risk factors: fasting triglycerides and insulin levels, HOMA index of insulin resistance and blood pressure. We did not prove any direct association between fatness and serum androgens but correlation between androgens and TSH was found.

BIBLIOGRAPHY

1. Carmina E, Lobo RA: Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with significant morbidity in women. J Clin Endocrinol Metab 1999; 84: 1897-1899.
2. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group 2004 Revised 2003 consensus on diagnostic criteria and long-term health risk related to polycystic ovary syndrome. Fertil Steril 81: 19-25.
3. Dunaif A: Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev 1997; 18: 774-800.
4. DeUgarte CM, Bartolucci AA, Azziz R: Prevalence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. Fertil Steril 2005; 83: 1454-1460.
5. Hoffman LK, Ehrmann DA: Cardiometabolic features of polycystic ovary syndrome. Nat Clin Pract Endocrinol Metab 2008; 4: 215-222.
6. Gambineri A, Pelusi C, Vicennati V et al.: Obesity and the polycystic ovary syndrome. Int J Obes Relat Metab Disord 2002; 26: 883-896.
7. Guzick DS: Cardiovascular risk in PCOS. J Clin Endocrinol Metab 2004; 89: 3694.
8. Pasquali R: Obesity and androgens: facts and perspectives. Fertil Steril 2006; 85: 1319-1340.
9. Yildrim B, Sabir N, Kaleli B: Relation of intra-abdominal fat distribution to metabolic disorders in nonobese patients with polycystic ovary syndrome. Fertil Steril 2003; 79: 1358-1364.
10. Puder JJ, Varga S, Kraenzlin M et al.: Central fat excess in polycystic ovary syndrome: relation to low grade inflammation and insulin resistance. J Clin Endocrinol Metab 2005; 90: 6014-6021.
11. Faloia E, Canibus P, Gatti C et al.: Body composition, fat distribution and metabolic characteristics in lean and obese women with polycystic ovary syndrome. J Endocrinol Invest 2004; 27: 424-429.
12. Zimmermann S, Phillips RA, Dunaif A et al.: Polycystic ovary syndrome: lack of hypertension despite profound insulin resistance. J Clin Endocrinol Metab 1992; 75: 508-513.
13. Holte J, Gennarelli G, Berne C et al.: Elevated ambulatory day-time blood pressure in women with polycystic ovary syndrome: a sign of a pre-hypertensive state? Hum Reprod 1996; 11: 23-28.
14. Carmina E, Bucchieri S, Esposito A et al.: Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extend of its relation to insulin resistance. J Clin Endocrinol Metab 2007; 92: 2500-2505.
15. Holte J, Bergh T, Gennarelli G, Wide L: The independent effects of polycystic ovary syndrome and obesity on serum concentrations of gonadotrophins and sex steroids in premenopausal women. Clin Endocrinol (Oxf) 1994; 41: 473-481.
16. Holte J, Bergh T, Berne C, Lithell H: Serum lipoprotein lipid profile in women with the polycystic ovary syndrome: relation to anthropometric, endocrine and metabolic variables. Clin Endocrinol (Oxf) 1994; 41: 463-471.
17. Silfen ME, Denburg MR, Manibo AM et al.: Early endocrine, metabolic and sonographic characteristics of polycystic ovary syndrome (PCOS): comparison between nonobese and obese adolescents. J Clin Endocrinol Metab 2003; 88: 4682-4688.
18. Poppe K, Velkeniers B, Glinoer D: Thyroid disease and female reproduction. Clin Endocrinol (Oxf) 2007; 66(3): 309-321.
19. Janssen OE, Mehlmauer N, Hahn S et al.: High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol 2004; 150: 363-369.
20. Wajchenberg PL: Subcutaneous and visceral adipose tissue: their relation to metabolic syndrome. Endocr Rev 2000; 21: 697-738.

received/otrzymano: 03.10.2012
accepted/zaakceptowano: 31.10.2012

Address/adres:
*Jarosław Kozakowski
Department of Endocrinology,
Medical Center of Postgraduate Education, Bielański Hospital
ul. Cegłowska 80, 01-809 Warszawa
tel./fax: +48 (22) 834-31-31
e-mail: kyaroslaw@tlen.pl