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Metabolic profile in women with polycystic ovary syndrome across adult life

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ABSTRACT

Objective. To assess insulin sensitivity, insulin secretion and metabolic profile in women with polycystic ovary syndrome (PCOS) in different stages of reproductive life.

Materials and methods. In a cross-sectional study, 190 PCOS women (PCOSw) and 99 controls (Cw) aged between 18 and 55 years were included. PCOSw and Cw were distributed into 3 stages of reproductive life: early reproductive age (18–34 years old), late reproductive age (35–40 years old) and perimenopausal period (41–55 years old). Waist circumference (WC), body mass index (BMI) and blood pressure (BP) were recorded. An oral glucose tolerance test (OGTT) with measurement of glucose and insulin was performed. Sex steroids and lipid profile were also determined in the fasting sample. Insulin sensitivity was assessed by HOMA-IR and ISI composite, and insulin secretion by HOMA-β and insulinogenic index. Visceral adiposity index (VAI) and lipid accumulation product (LAP) were also calculated. Metabolic syndrome (MS) was assessed by the IDF and ATPIII criteria.

Results. At early reproductive age, PCOSw showed higher BMI, WC, and VAI and a higher prevalence of MS compared to Cw ($p < 0.05$). In addition, at late reproductive age PCOSw also showed elevated total cholesterol, triglycerides, insulin secretion, LAP and BP. At perimenopausal period, these parameters were not different between Cw and PCOSw. Within the PCOSw group, HOMA-β was lower at late reproductive and perimenopausal periods compared to the early reproductive age. Regarding control women, a deterioration of anthropometric and metabolic parameters was observed in perimenopausal women compared to early and late reproductive women.

Abbreviations: PCOS, polycystic ovary syndrome; IR, insulin resistance; WHR, waist to hip ratio; BP, blood pressure; BMI, body mass index; OGTT, oral glucose tolerance test; WC, waist circumference; HOMA-IR, homeostasis model assessment for insulin resistance; ISI composite, insulin sensitivity index composite; VAI, visceral adiposity index; LAP, lipid accumulation product; MS, metabolic syndrome; IDF, International Diabetes Federation; ATPIII, National Cholesterol Education Program Adult Treatment Panel III; NIH, National Institutes of Health; FAI, free androgen index; ADA, American Diabetes Association; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; AUC, area under the curve; OR, odds ratio.

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Conclusions. Our results suggest that metabolic derangements associated with PCOS are more evident at the early and late reproductive ages. On the other hand, during perimenopause, there is no further deterioration of metabolic parameters. Nevertheless, a disruption in pancreatic β-cell function is evidenced at this stage.

1. Introduction

Polycystic ovary syndrome (PCOS) is a well-recognized endocrine-metabolic disturbance affecting 6% to 20% of women in fertile age, depending on the diagnostic criteria employed [1]. Insulin resistance (IR) is present in about 50–70% of PCOS patients independent of body mass index (BMI) [2,3]. Moreover, metabolic syndrome (MS) components such as abdominal obesity, dyslipidemia, hyperglycemia and hypertension, are highly prevalent in women with PCOS, predisposing them to the development of type 2 diabetes and cardiovascular disease [4,5].

In normal women, the menopausal transition increases the prevalence of components of MS [6]. This has been associated with a decrease in ovarian function, leading to a decrease in estrogen synthesis and a redistribution of fat to the abdominal depot [7].

In PCOS women, metabolic abnormalities begin early in life and are worsened by the presence of hyperandrogenism [8]. However, the evolution of MS components with advanced age has not been thoroughly explored.

Cross-sectional retrospective studies have shown that the risk of developing an adverse metabolic profile in PCOS women increases during the perimenopausal and menopausal periods [9,10]. In contrast, recently, a longitudinal study showed that hyperandrogenic women with menstrual disorders do not increase their rate of MS, stroke or myocardial infarction when they reach the perimenopausal period [11]. We have suggested that PCOS women maintain their ovarian steroidogenic activity during late reproductive age [12]. However, it is not known if these changes have an impact on the MS associated with PCOS. Therefore, the aim of the present study was to evaluate IR and MS components during the perimenopausal period compared to reproductive life.

2. Materials and methods

2.1. Subjects

One hundred ninety PCOS women (PCOSw) and 99 controls (Cw) between 18 and 55 years of age, with a BMI ranging from 20 to 35 kg/m^2, were included in this study. Women were distributed into 3 stages of reproductive life: early reproductive age (18–34 years old), late reproductive age (35–40 years old) and perimenopausal period (41–55 years old). PCOS women were diagnosed in our Research Unit (1990 to 2014) according to the NIH consensus criteria when the patients were in the early reproductive age.

Control women (Cw) were selected from women attending the preventive medical examination at the Department of Obstetrics and Gynecology in our hospital, as previously described (12). Women who had a history of regular 28- to 32-day menstrual cycles, absence of hirsutism and other manifestations of hyperandrogenism, and no history of infertility or pregnancy complications, were included.

More details are shown in the supplementary materials.

2.2. Study protocol

Control and PCOS subjects were studied 3 to 7 days after menstrual bleeding or whenever feasible in women without regular menses. We performed a complete physical examination with anthropometric measurements including: weight, height, waist circumference (WC), waist to hip ratio (WHR), body mass index (BMI) and blood pressure (BP).

Baseline serum concentrations of testosterone, androstenedione, estradiol and sex hormone binding globulin (SHBG) were determined and free androgen index (FAI) was calculated. In all participants, an oral glucose tolerance test (75 g glucose) was performed after a 12-h overnight fast. Glucose tolerance was evaluated by using the criteria of the American Diabetes Association (ADA). A lipid profile was determined in the fasting sample.

2.3. Surrogate measurements: Insulin sensitivity, β-cell function and adiposity

Insulin resistance was estimated by the homeostasis model assessment for IR (HOMA-IR) and by the insulin sensitivity index (ISI) composite. To assess β-cell function, insulinogenic index and HOMA-β were calculated. Total glucose and insulin secretions were determined as the area under the curve. Lipid accumulation product (LAP) and visceral adiposity index (VAI) were estimated.

Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) III definition and according to the International Diabetes Federation (IDF) criteria.

More details are described in the supplementary material section.

2.4. Statistical evaluation

Data are expressed as median and interquartile range because they are not normally distributed according to the Shapiro–Wilk test. For comparisons between two groups, a Mann–Whitney test was performed. Differences between groups were adjusted by ANCOVA using age or BMI. Comparisons along the different age periods were performed by the Kruskal–Wallis test followed by Dunn's test. A chi-square test of independence was used for comparisons of categorical variables. Associations between sex steroids and metabolic variables were determined using the Spearman correlation coefficients test. A generalized linear model (GLM) with gamma distribution and log-link function