

Normo- and hyperandrogenic women with polycystic ovary syndrome exhibit an adverse metabolic profile through life

Pekka Pinola, Ph.D.,^{a,b} Katri Puukka, Ph.D.,^{b,c} Terhi T. Piltonen, Ph.D.,^{a,b} Johanna Puurunen, Ph.D.,^{a,b} Eszter Vanky, Ph.D.,^{d,e} Inger Sundström-Poromaa, Ph.D.,^f Elisabet Stener-Victorin, Ph.D.,^g Angelica Lindén Hirschberg, Ph.D.,^h Pernille Ravn, Ph.D.,ⁱ Marianne Skovsager Andersen, Ph.D.,^j Dorte Glintborg, Ph.D.,^j Jan Roar Mellembakken, Ph.D.,^k Aimo Ruokonen, Ph.D.,^{b,c} Juha S. Tapanainen, Ph.D.,^{b,l} and Laure C. Morin-Papunen, Ph.D.^{a,b}

^a Department of Obstetrics and Gynecology, Oulu University Hospital, Oulu, Finland; ^b University of Oulu and Medical Research Center Oulu, Oulu, Finland; ^c Nordlab Oulu, Oulu University Hospital and Department of Clinical Chemistry, University of Oulu, Oulu, Finland; ^d Institute of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway; ^e Department of Obstetrics and Gynecology, St. Olav's University Hospital Trondheim, Trondheim, Norway; ^f Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; ^g Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; ^h Department of Obstetrics and Gynecology, Karolinska University Hospital, Stockholm, Sweden; ⁱ Department of Gynecology and Obstetrics, and ^j Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark; ^k Section of Reproductive Medicine, Department of Gynecology, Women's Division, Oslo University Hospital, Oslo, Norway; and ^l Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Objective: To compare the metabolic profiles of normo- and hyperandrogenic women with polycystic ovary syndrome (PCOS) with those of control women at different ages during reproductive life.

Design: Case-control study.

Setting: Not applicable.

Patient(s): In all, 1,550 women with normoandrogenic (n = 686) or hyperandrogenic (n = 842) PCOS and 447 control women were divided into three age groups: <30, 30–39, and >39 years).

Interventions(s): None.

Main Outcome Measure(s): Body mass index (BMI), waist circumference, blood pressure, glucose, insulin, cholesterol, lipoproteins, triglycerides and high-sensitivity C-reactive protein.

Result(s): Both normo- and hyperandrogenic women with PCOS were more obese, especially abdominally. They had increased serum levels of insulin (fasting and in oral glucose tolerance tests), triglycerides, low-density lipoprotein, and total cholesterol, higher blood pressure, and lower high-density lipoprotein levels independently from BMI compared with the control population as early as from young adulthood until menopause. The prevalence of metabolic syndrome was two- to fivefold higher in women with PCOS compared with control women, depending on age and phenotype, and the highest prevalence was observed in hyperandrogenic women with PCOS at late reproductive age.

Conclusion(s): When evaluating metabolic risks in women with PCOS, androgenic status, especially abdominal obesity and age, should be taken into account, which would allow tailored management of the syndrome from early adulthood on. (Fertil Steril® 2016; ■:■–■. ©2016 by American Society for Reproductive Medicine.)

Key Words: PCOS, hyperandrogenism, metabolism, obesity

Discuss: You can discuss this article with its authors and with other ASRM members at <https://www.fertsterdialog.com/users/16110-fertility-and-sterility/posts/14126-22949>

Received August 18, 2016; revised and accepted December 16, 2016.

P.P. has nothing to disclose. K.P. has nothing to disclose. T.T.P. has nothing to disclose. J.P. has nothing to disclose. E.V. has nothing to disclose. I.S.-P. has nothing to disclose. E.S.-V. has nothing to disclose. A.L.H. has nothing to disclose. P.R. has nothing to disclose. M.S.A. has nothing to disclose. D.G. has nothing to disclose. J.R.M. has nothing to disclose. A.R. has nothing to disclose. J.S.T. has nothing to disclose. L.C.M.-P. has nothing to disclose.

Reprint requests: Laure C. Morin-Papunen, M.D., Ph.D., Adjunct Professor, Department of Obstetrics and Gynecology, Oulu University Hospital, PL 23, OYS 90029, Finland (E-mail: Imp@cc.oulu.fi).

Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/\$36.00

Copyright ©2016 American Society for Reproductive Medicine, Published by Elsevier Inc.

<http://dx.doi.org/10.1016/j.fertnstert.2016.12.017>

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting reproductive-age women (incidence 6%–18% depending on the population and the diagnostic criteria used) (1, 2). It is known to have multifaceted unfavorable effects on women's health. In addition to anovulatory infertility, which is typically associated with the syndrome, women with PCOS exhibit numerous metabolic risk factors, such as abdominal obesity, insulin resistance, impaired glucose tolerance, dyslipidemia, and chronic inflammation (3–6). Hyperandrogenism (HA) plays a central role in the syndrome and has been associated with a more severe metabolic profile in some, but not all, studies (7–11). Obesity is common in PCOS and exacerbates the symptoms and promotes negative health consequences by increasing the risks of type 2 diabetes (T2DM) and cardiovascular disease (CVD). However, regarding the interaction between weight, weight gain, and hyperandrogenism, the results of earlier studies have been inconsistent. Some data suggest that the metabolic risks linked to PCOS are mainly related to obesity and insulin resistance, whereas others support the hypothesis that the syndrome *per se*, especially HA, independently from BMI, are the most important cardiovascular risks (12–14). According to the results of some studies, the unfavorable metabolic profile linked to PCOS seems to worsen after the menopausal transition, highlighting the lifelong health burden of the syndrome (3, 15). A recent study, however, could not confirm any association between a history of androgen excess and menstrual irregularity with worsening of metabolic health after menopause (16).

In women without PCOS, an impaired metabolic profile is associated with obesity and weight gain. Especially during the menopausal transition, weight gain has been shown to have an adverse effect on glucose metabolism (17). Furthermore, circulating levels of ovarian and adrenal androgens do not seem to have a significant impact on chronic inflammation markers or lipid profile in women in the general population, whereas a low serum level of SHBG is an independent predictor of an increased risk of CVD (18, 19).

Given the lack of data regarding age-related metabolic changes in women with PCOS, the aim of the present study was to explore and compare metabolic profiles in women with PCOS and in control women throughout their reproductive life spans in a cross-sectional dataset. We also aimed to identify specific metabolic risk factors and the impact of hyperandrogenism in PCOS during early adulthood.

MATERIALS AND METHODS

Study Population

Women taking part in eight Nordic PCOS studies contributed to the present investigation. Two centers in Finland, three in Sweden, two in Norway, and one in Denmark were involved, and there were totals of 1,550 women with PCOS (age range 14–59 years) and 447 control women without the syndrome (age range 18–62 years) (6,20–27). The women with PCOS were recruited both from hospital gynecology or infertility clinics and from the community with advertisements in local newspapers and the healthy control women from the

community by advertisements in local newspapers. Circulating levels of androgens in a subpopulation of this Nordic PCOS cohort population have been recently published (28).

Diagnoses of PCOS were made according to the Rotterdam criteria (29). Diagnosis of PCOS in peri- and postmenopausal women was based on the presence of oligo-amenorrhea combined with hyperandrogenism (either biochemical or clinical) reported at reproductive age. Thus, retrospectively, all of the women met the Rotterdam criteria. Ovarian morphology was examined by means of transvaginal ultrasonography in all participants. Biochemical hyperandrogenism was defined in relation to the upper limits used in the respective laboratories, depending on the method used, and clinical hyperandrogenism was diagnosed when a subject had a Ferriman–Gallwey score of >7. The Ferriman–Gallwey scoring was performed by a physician in all studies. The PCOS population was further divided into two groups: hyperandrogenic women with PCOS (HA-PCOS, including biochemical and/or clinical hyperandrogenism) and normoandrogenic women with PCOS (NA-PCOS, including women with both oligo-amenorrhea and polycystic ovaries observed in ultrasonography). The control population consisted of women with normal ovaries (according to ultrasonography) and absence of PCOS-related symptoms, e.g., oligo- or anovulation and/or hirsutism and/or elevated serum T levels. The PCOS and control groups were grouped according to age as follows: <30 years, 30–39 years, and >39 years. Women using hormonal preparations, medication affecting androgen levels and glucose metabolism, as well as statins or antihypertensive drugs were excluded from the study. Alternatively, a 2-month washout period for hormonal preparations or medication affecting androgen levels was required before entering the study. Furthermore, none of the women had T2DM, because having the diagnosis of preexisting diabetes was an exclusion criterion in all studies.

BMI was calculated as kg/m^2 . Waist circumference was assessed according to a generally accepted method. Both systolic and diastolic blood pressures (BPs) were measured in a sitting position after 15 minutes of resting.

A diagnosis of metabolic syndrome (MetS) was made according to the Rotterdam consensus (28), requiring three out of the following five criteria: waist circumference >88 cm and/or BMI $\geq 30 \text{ kg/m}^2$, triglycerides $\geq 150 \text{ mg/dL}$ (1.70 mmol/L), high-density lipoprotein (HDL) $\leq 50 \text{ mg/dL}$ (1.30 mmol/L), systolic BP $\geq 130 \text{ mm Hg}$ and/or diastolic BP $\geq 85 \text{ mm Hg}$, and fasting glucose ≥ 110 –126 mg/dL (6.11–6.99 mmol/L) and/or 2-hour oral glucose tolerance test (OGTT) glucose ≥ 140 –199 mg/dL (7.78–11.04 mmol/L).

Laboratory Methods

The metabolic variables (glucose, insulin, cholesterol, lipoproteins, triglycerides, and high-sensitivity C-reactive protein) were assayed by means of the routine methods used in the laboratories of the different study centers (6,19–26). According to the Nordic Reference Interval Project 2000 (30) the reference ranges for the serum lipid levels were similar in all subpopulations of the study.

In five study populations (20–25), assays of T were performed by means of liquid chromatography–mass

Download English Version:

<https://daneshyari.com/en/article/5690054>

Download Persian Version:

<https://daneshyari.com/article/5690054>

[Daneshyari.com](https://daneshyari.com)