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Background: The knowledge of the polycystic ovary syndrome (PCOS) natural history and its long-term health consequences is limited, mainly because of a paucity of longitudinal cohort studies with participants diagnosed with PCOS.

Objective: The aim of the study was the evaluation of the metabolic disturbances, the changes of clinical, hormonal and ovarian sonographic PCOS features and the assessment of fertility in a group of young women originally diagnosed with PCOS according to the Rotterdam criteria between 2003 and 2009. Additionally, our objective was to explore associations between anthropometric and biochemical parameters estimated at the baseline and final development of abnormal glucose tolerance in the women with PCOS and identify parameters which impact the PCOS course.

Methods: Thirty-one Caucasian women with a previous diagnosis of PCOS participated in the re-evaluation. Clinical history, examination, anthropometric measurements, transvaginal ultrasound scans, an oral glucose tolerance test (OGTT) with the estimations of serum glucose and plasma insulin concentrations, lipids, sex hormone binding globulin (SHBG) and sex hormones assessments were performed at the beginning and at the end of the follow-up in all the participants. Median follow-up lasted 120.9 months (IQr = 107.17-127.38). At the first examination insulin sensitivity was estimated with the euglycaemic hyperinsulinaemic clamp technique in all the women.

Results: At the final assessment participants were 35 years old (IQr = 31.2-39.8). Final body mass index (BMI), Matsuda index, mean concentrations of glucose and insulin were correlated with previously assessed BMI, SHBG and glucose utilisation estimated using glucose clamp technique (all p<0.01). At the end of the follow-up, all concentrations of serum glucose increased significantly in OGTT, whereas concentrations of plasma insulin 0' and 30'

decreased. Indirect indices of insulin resistance did not change during the observation. The annualised incidence rate for conversion from normoglycaemia to prediabetes totalled 4.5% in the studied cohort. Baseline BMI, free androgen index (FAI), fasting plasma glucose concentrations and glucose utilisation were the most important predictors of prediabetes in the young women with PCOS (respectively, OR=1.17, OR=1.42, OR=1.2, OR=0.73, all p<0.05).

Menstrual cycles became regular and morphology of ovaries normalised in 55% and 49% of the participants, respectively (all p<0.001), during the observation. At the final examination, 55% of the women no longer met the criteria for PCOS (p=0.0001). Age, serum concentrations of follicle stimulating hormone (FSH) and E-selectin assessed at the beginning of the observation were the most important predictors of the PCOS persistence into later years (respectively, OR=0.84, OR=0.39, OR=1.08, all p<0.05). 86% of the patients, who had ever been trying to conceive, gave birth to at least one child. Every third women, who had ever been pregnant, reported at least one pregnancy loss. It was observed that the number of miscarriages, in women with a history of PCOS, was correlated with ovarian volume, serum concentrations of 17-hydroxyprogesterone, androstendione and luteinizing hormone (LH), all assessed at the final examination (respectively, R=0.46; R=0.49; R=0.54; R=0.59, all p<0.05) and additionally, with the metabolic parameters assessed at the baseline study, such as BMI, waist circumference, fat mass (%) and insulin sensitivity assessed with euglycaemic hyperinsulinaemic clamp (respectively, R=-0.66, R=-0.61; R=-0.72; R=0.63, all p<0.01).

Conclusions: The obtained results confirm the hypothesis that β -cell function in PCOS deteriorates with time. Furthermore, a high rate of adverse change in glucose metabolism in young women with PCOS was observed. Anthropometric and biochemical parameters assessed at the beginning and at the end of the observation were significantly correlated, which emphasises the role of early intervention in order to prevent disturbances of glucose metabolism in young patients with PCOS. Progression from the third to the fourth decade of life is

associated with a reduction of PCOS diagnostic features. Serum concentrations of FSH and E-selectin determined at the initial PCOS diagnosis impact on the disappearance of the syndrome years after. It seems that lean women with polycystic ovaries morphology in ultrasonography scans, adrenal hyperandrogenism and high concentration of LH should be considered at a particular high risk of miscarriages.