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POLYCYSTIC OVARIAN SYNDROME AND MENOPAUSE

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Abstract: Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies, which occurs in 4–21% of women during reproductive age and is the most common form of hyperandrogenism [1, 2]. The clinical manifestations of PCOS are diverse, and most of them accompany a woman throughout her life, varying depending on age, ethnicity, constitutional and other factors. Due to the increase in average life expectancy, modern women spend quite a long period in peri- and postmenopause, which determines the need to monitor the clinical manifestations of PCOS, its long-term complications, as well as the features of the onset and course of age-associated diseases in this endocrinopathy [3–6].

Key words: syndrome, ovaries, menopause, postmenopause, endocrinopathies, polycystic disease, uterus.

In reproductive age, the diagnosis of PCOS is based on the assessment of menstrual and ovulatory function, registration of clinical and laboratory hyperandrogenism, as well as ultrasonographic signs of polycystic ovary syndrome. According to the US National Institutes of Health criteria, the diagnosis of PCOS requires the presence of oligoanovulation, hyperandrogenemia and/or hirsutism. This approach makes it possible to diagnose the so-called “classic” PCOS [7].

Currently, to make a diagnosis of PCOS, it is preferable to use the consensus criteria of the American Society for Reproductive Medicine/European Society of Human Reproduction and Embryology (2003), which assume the presence of any two of three signs: oligoanovulation, hyperandrogenemia and/or hirsutism, polycystic ovarian morphology on ultrasound [8]. Modern approaches to diagnosis also include determining the clinical phenotype of PCOS in each specific case, which significantly influences the patient’s management tactics and the prognosis of complications [9].

In 2013, an expert committee of the Endocrine Society formulated proposals for defining postmenopausal PCOS [1] (Table). The Endocrine Society's recommendations are based primarily on a history of menstrual dysfunction and the presence of hyperandrogenism during reproductive age. Polycystic ovarian structure

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is considered as an additional sign, but its use is unlikely due to age-related changes in ovarian morphology.

A necessary condition for the diagnostic process is the exclusion of all diseases and conditions that have similar symptoms [1]. International evidence-based guidelines for PCOS published in 2018 consider polycystic ovarian morphology, along with menstrual irregularities and hyperandrogenism, as a possible criterion for postmenopausal PCOS, but also only in a historical context [2].

In general, it should be noted that diagnosing PCOS in peri- and postmenopausal women is difficult. On the one hand, many patients with PCOS with age experience a normalization of the menstrual cycle, a decrease in the volume of the ovaries and the number of follicles in them [5]. At the same time, despite the general age-related trend towards a decrease in the levels of circulating androgens, in women with PCOS during peri- and postmenopause their levels may remain elevated relative to those of their peers without PCOS [6].

In clinical practice, the diagnosis of hyperandrogenemia in older women is difficult due to the lack of data on normal androgen levels during the menopausal transition [1]. The most informative is the increase in free testosterone levels. Dehydroepiandrosterone sulfate and androstenedione are auxiliary markers of biochemical hyperandrogenism in PCOS. The optimal method is to study the concentration of total testosterone using liquid chromatography with mass spectrometry (LC–MS), gas chromatography with mass spectrometry (GC–MS), as well as radioimmunoassay with extraction with organic solvents followed by chromatography [8].

Along with the use of anamnesis data indicating the presence of previous oligomenorrhea and hyperandrogenism, it is recommended to take into account information about infertility and the results of histological examination obtained during a diagnostic examination or surgical treatment [5]. Some experts suggest using an indicator of insulin resistance, the HOMA (Homeostatic Model Assessment) index, as an additional criterion for diagnosing PCOS after menopause, along with a history of ovarian dysfunction and hyperandrogenism [2].

The need to assess the clinical phenotype of PCOS was emphasized at the US National Institutes of Health expert panel meeting in December 2012 [1]. However, in peri- and postmenopausal women, correct determination of the clinical phenotype is

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not always possible. Thus, it has been shown that the clinical manifestations of the classic PCOS phenotype are leveled out with the onset of menopause [2]. A significant limitation of the use of universal clinical criteria for PCOS for peri-/postmenopausal women is the lack of differentiated diagnostic approaches taking into account the race and ethnicity of patients.

The onset of menopause with PCOS has its own characteristics, although many aspects of this process have not been sufficiently studied. Due to chronic oligoanovulation and frequent use of hormonal contraception for therapeutic purposes in patients with PCOS, it is difficult to determine the stage of aging of the reproductive system in accordance with modern criteria (STRAW) [3].

The average age of natural menopause in women in economically developed countries is 48–52 years. Epidemiological data regarding the age of menopause in PCOS are contradictory: a number of authors provide information that women with PCOS experience menopause on average 2–5 years later than in population, and in other studies, on the contrary, earlier menopause is noted in PCOS. There is also data on the ethnic characteristics of menopause in general and in PCOS in particular [8].

The most common menopausal manifestations are vasomotor symptoms, which affect most women and significantly affect quality of life. It is known that the frequency and severity of hot flashes in women with PCOS is significantly less than in the general female population of the same age [6]. On the other hand, with PCOS there are all the conditions for the development of menopausal metabolic syndrome and the risk of cardiovascular diseases is increased. Abdominal obesity, which is often observed in PCOS already in reproductive age, becomes an important marker of metabolic syndrome and is associated with insulin resistance, hypertension, dyslipidemia and cardiovascular diseases [2].

With the onset of menopause in women, androgen secretion decreases; however, PCOS is characterized by a slow decrease in the production of both ovarian and adrenal androgens [4]. At the same time, epidemiological data indicate an association of hyperandrogenism and ovulatory dysfunction with an increased risk of cardiovascular diseases [7]. In addition, even at a young age, women with PCOS develop endothelial dysfunction, which is especially significant in insulin resistance and abdominal obesity, which is an important mechanism for the risk of cardiovascular diseases in older age [9].

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At the same time, the frequency of fatal cardiovascular events in these postmenopausal patients is not increased. Research suggests that, despite the increased risk of cardiovascular disease, cardiovascular disease-related mortality in postmenopausal women with PCOS is comparable to that in the non-PCOS cohort [40]. Nevertheless, prediction and prevention of long-term complications of PCOS are an integral part of the modern strategy for managing such postmenopausal patients.

CONCLUSION:

Diagnosis of polycystic ovary syndrome (PCOS) in peri-/postmenopause is based on a history of menstrual dysfunction, the presence of hyperandrogenism during reproductive age and its persistence in peri-/postmenopause. The polycystic structure of the ovaries is considered as an additional diagnostic sign, but its value is low due to age-related changes in ovarian morphology.

Diagnosis and monitoring of hyperandrogenism in postmenopause requires the use of modern laboratory methods and developed age standards taking into account the ethnicity of patients. With manifestations of hyperandrogenism that first appeared in postmenopause, severe or progressive hyperandrogenism, it is necessary to exclude androgen-producing tumors or ovarian hyperthecosis.

Patients with PCOS have an increased risk of menopausal metabolic syndrome and long-term cardiovascular complications, which determines the need for careful monitoring and timely correction of identified disorders.

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