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## Updating the PCOS diagnosis: does ultrasound matter?

Allison S. Komorowski & Christina E. Boots

At the heart of the debate on diagnosis of polycystic ovary syndrome (PCOS) is the question: what is PCOS? It is a syndrome; a compilation of many symptoms affecting many organs throughout a woman's body that collectively describe the end result of anovulation and hyperandrogenism. As Fritz and Speroff aptly described, "...PCOS is not a discrete or specific endocrine disorder having a unique cause or pathophysiology. Instead, the condition is best viewed as a final common pathway in the chronic anovulatory state."<sup>1</sup>

PCOS is considered a diagnosis of exclusion, and the original Rotterdam criteria for diagnosis included the presence at least two of three factors: oligo or anovulation, clinical or biochemical hyperandrogenism and 12 or more follicles present on a single ovary or ovarian volume >10 cm<sup>3</sup>.<sup>2</sup> The updated PCOS guidelines released in 2018 support and amend the Rotterdam criteria by requiring that sonographic diagnosis identifies 20 or more follicles on at least one ovary. This revision reflects the technologic improvements in sonography.<sup>3</sup>

The etiology for the polycystic ovary syndrome remains evasive likely because PCOS is caused by a combination of genetic and environmental factors that are unlikely to be exactly the same for two different women. And thus, the diagnosis of PCOS also remains evasive. All of the criteria used for diagnosis have some diagnostic uncertainty. For example, there is a wide spectrum spanning from normal, regular 28-day menstrual cycles to chronic anovulation. Some women have long, but regular, menstrual cycles, while others have "regularly irregular" cycles and still others may have decades of irregular cycles followed by new regularity in their later reproductive years. When considering hyperandrogenism, there is the difficulty of ethnic variation in vellus hair growth and cultural norms influencing use of topical treatments and laser hair removal, which may be done to remove hair that is not truly considered hirsutism of a "male pattern". Regarding ultrasonography, there are issues of inter-operator differences among sonographers and in interpretation by physicians (radiologists and gynecologists may interpret scans differently), as well as discrepancies in machine resolution. Finally, the Rotterdam criteria do not include any of the metabolic components of the syndrome, which are increasingly recognized as important contributors to the physiology of PCOS and the long-term health risks of the syndrome.

Kostroun et al. describe the evolution of the diagnostic criteria for this syndrome that is arguably the most common reproductive endocrinopathy.<sup>4</sup> The authors retrospectively analyzed a cohort of women ages 12-50 that were diagnosed with PCOS by ICD code in 2017, and then applied the 2018 PCOS diagnostic criteria to assess how many women retained the PCOS diagnosis. As expected with more stringent criteria, there was a statistically significant reduction in the number of women meeting the diagnosis of PCOS, with 76 percent retaining the diagnosis. The resultant PCOS cohort has a more severe phenotype, including higher body mass index, and higher serum concentrations of anti-Müllerian hormone (AMH), total and free testosterone, total cholesterol and triglycerides.

There are some limitations of the data that are important to consider. Of the 258 women included for analysis, only 123 had ultrasound data available. These women were included because they met PCOS criteria by anovulation and hyperandrogenism. However, the study would be strengthened by information on how many of these women demonstrated polycystic ovaries. Many of the cohort also lacked serum biomarker data, limiting the interpretation of the risk of metabolic syndrome associated with PCOS. Further, several adolescent patients were included, and it is not recommended to utilize sonographic criteria to diagnose an adolescent with PCOS given that polycystic-appearing ovaries are normal in this population.<sup>5</sup> Finally, race and ethnicity data were reported for only 83% of women, and of those, nearly half were Hispanic and only 5% reported Black race, limiting generalizability of the study.

Importantly, Kostroun et al. note that the diagnosis of PCOS in their cohort was most often made by an OB/GYN provider, however several of the women were diagnosed by family medicine, pediatric, or endocrinology providers. This is a critical point when considering the utility of the diagnostic criteria. Providers not trained in gynecology may have less understanding of folliculogenesis and ovarian biology, as well as limited access to or ability interpreting sonographic results. If perhaps sonography is not the answer, is there a simpler proxy for ultrasound that is more readily interpreted? This may be where serum testing for concentration of anti-Müllerian hormone becomes relevant. AMH concentrations increase with an increasing pool of ovarian follicles and/or an increased ovarian volume, and as the authors found in their cohort, AMH concentrations were higher in the cohort meeting the 2018 PCOS criteria.

As Kostroun et al. seek to answer, do the updated criteria improve the diagnosis of PCOS? In order to answer the question, we need to ask how we will use this information. As our Fritz and Speroff write, *"In our view, the primary advantage to having specific diagnostic criteria for PCOS relates to research, because varying criteria cloud the conclusions and questions the generalizability of results from studies involving women with "PCOS". In clinical medicine, simply knowing and understanding the health implications and consequences of chronic anovulation and methods for their effective management are far more important than assigning a specific diagnosis of PCOS..."*<sup>1</sup> Along this line of thought, the updated criteria help to create a more homogenous and more affected cohort in which to study and understand PCOS pathophysiology. However, from a clinical perspective, dwelling on the specifics of the diagnostic criteria does not help anyone. In clinical medicine, our goal is to help women understand their symptoms, to educate them, and then to focus on improving individualized symptoms and prevent negative long-term health sequelae.

With these updated criteria, we have decreased the pool of women meeting PCOS criteria simultaneously increasing the pool of women without a diagnosis. When women do not receive another diagnosis to explain their symptoms, then perhaps we should keep them on the "PCOS spectrum". Whether or not women meet the exact PCOS criteria (regardless of which criteria are being used), we should be providing care to all patients that present with any

concerns about menstrual cycle irregularities or hyperandrogenism. To improve the current and long-term health of patients, we should provide lifestyle counseling to those presenting with any symptoms concerning for PCOS to prevent glucose intolerance/diabetes, cardiovascular disease, and obesity. We should also be screening all patients for mental health disorders, including depression, anxiety, disordered eating and sleep disorders.<sup>5</sup> PCOS is diagnosis of exclusion and then a treatment of inclusion. Our focus should be on helping patients: improving their wellbeing, preventing progression of disease and addressing the specific symptoms affecting their quality of life, whether that includes irregular periods, infertility, hirsutism or depression.

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