The Role of Ultrasound in Poly Cystic Ovaries Assessment

Rana Bakkar [1], Yusuf Bakkar [2]

(1) Consultant Radiologist in PHCC, Qatar, Al Thumama HC Primary Health Care
(2) Specialist in Diagnostic Radiology, Gulf laboratory and x-ray, Qatar

Corresponding author:
Rana Bakkar
Consultant Radiologist in PHCC – Qatar,
Al Thumama HC Primary Health Care
Email: rana82sara@gmail.com

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Abstract

Current knowledge of polycystic ovarian syndrome is reviewed, with emphasis on diagnostic criteria, the role of imaging, and pertinent imaging parameters.
Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality in women of reproductive age and carries with it significant health risks, including infertility, endometrial hyperplasia, diabetes, and cardiovascular disease. The workup of PCOS has evolved to include the use of pelvic ultrasonography (US). Ovarian imaging is crucial in the evaluation of patients with suspected PCOS. Although findings of polycystic ovaries are commonly seen at routine US and are frequently not associated with PCOS, awareness of the criteria and definitions used in the diagnosis of PCOS is important, especially in patients who are being evaluated for ovulatory dysfunction or hyperandrogenism. The imaging report should be specific and should include ovarian volumes and antral follicle counts, in addition to other pertinent findings (eg, the presence of a dominant follicle or corpus luteum). Because patients are frequently referred for radiologic imaging as a part of clinical workup, and polycystic ovaries are a common incidental finding in women undergoing US for other gynecologic complaints, radiologists should be aware of the current diagnostic criteria for PCOS, the role of imaging in workup for this abnormality, and the pertinent reporting parameters for pelvic US.

Keywords: Poly Cystic ovaries assessment, Ultrasound

Introduction

Assessment of the ovarian morphology is one of the most commonly performed ultrasound examinations. Polycystic ovarian syndrome (PCOS) is a multifactorial, multifaceted, polygenic disorder with varying phenotypes. It defines a labyrinthine symptomatology including menstrual cycle irregularities, hormonal imbalance, and metabolic disturbance. Historically, this syndrome has been diagnosed clinically with supportive lab parameters. However, the role of ultrasound has mutated from identifying, to mis-defining and finally to re-classifying PCOS[1-4]. At present it seems that the ultrasound identification of the 'string of pearls' has cemented this disease with a misleading name. A supposed increase in the detection of polycystic ovarian morphology on ultrasound has been accredited to advances in technology allowing better visualization of the ovaries/stroma/follicles by higher frequency probes with the possibility of endovaginal imaging. Nevertheless, there is a disparity in what the ultrasound shows, how the clinician interprets the report, and what the patient understands about her diagnosis. Identification of the multifollicular ovary is still quite frequently ascribed to PCOS, while ovarian ultrasound remains ambiguous to the different phenotype of PCOS. Whether morphological disparities represent a normal variation in ovarian anatomy or true precursors of PCOS remains debatable. The absence of definition of a 'normal' ovary with respect to volume and follicular number, makes the diagnosis of PCOS more challenging (5,6).

Over time, ovarian volume remains the most reliable, reproducible and sensitive method for identification of PCOS. However, it has a lower diagnostic accuracy due to considerable overlap with normal women. Confusion prevails in the setting of pelvic infection, hormonal treatment, and ethnic variability. In the setting of poor image resolution, whether due to use of lower frequency probes or patient habitus, volume remains the best usable criterion (3,6). While endorsing the Rotterdam criteria, the recent 2018 International Evidence-Based Guidelines also acknowledged the fact that ultrasound criteria are evolving, and new thresholds need to be established. This development is accredited to both accelerated development in technology, as well as increased availability of ultrasound in widespread populations. However, it should be mentioned that technical skill varies widely, and as such it's important to realize that it is not only the development of 'defined criteria', but also distribution of skill and expertise among practitioners, which will determine the diagnosis of PCOS at a community level (4).

Technical considerations in Pelvic ultrasound examination

Ultrasound examination was performed between cycle days 2 and 7 with a 7 MHz transvaginal transducer (25). This prevents any growing follicle from hiding smaller ones or modifying ovarian volume. In case of oligo or amenorrhoeic women, scanning may be performed at random, or 2-5 days after progesterone-induced bleeding (4) .

Scanning should be done with an 'optimally' filled bladder, avoiding extremes in transabdominal sonography (TAS), and empty bladder in transvaginal sonography. Identify the ovaries in relation to iliac vessels. Entire ovary should be scanned in two orthogonal planes. Measurement of ovarian volume (length x width x thickness) should be done precisely, ensuring adequate visualization of the ovarian contour. If possible, a follicular count should be obtained with careful meticulous sweeping of both ovaries individually. This count may not help in the diagnosis of a particular patient, but will help long-term to allow us to redefine criteria. If the setting allows, estimation of stromal area should be done offline. Additionally, it should be ensured to assess the liver and pancreatic fat grade, and have a look on the adrenal areas(4).

Ultrasound measurements were taken in real time, according to a standardized protocol. The highest possible magnification was used to examine the ovaries. After the longest medial axis of the ovary had been determined, the length and thickness were measured and the area was calculated using a manual or automatic ellipse to outline the ovary as described previously (26). Several follicles were measured in two planes of the ovary in order to estimate the size and their position. All follicles of 2 mm, were counted. The diameter of several follicles was measured from the mean of two diameters (longitudinal and anteroposterior), then the number of follicles measuring >5 mm or 80 pg/ml, were also excluded from the study so as not to confound the data with the presence of a dominant follicle (25).

Polycystic Ovarian Morphology

Number and Size of Ovarian Follicles

Assessment of the number of follicles has been upheld to be one of the specific features of PCOS. The concept is to sweep through the entire ovarian volume and count the number of follicles in each ovary in totality, keeping in mind not to measure sonolucencies <2 mm, as they do not represent actual follicles. Grid systems, tagging, and marking have been used in post-processing to accurately measure the follicular number per ovary (FNPO) in order to improve reliability and reproducibility. However, these methods are time-consuming and not widespread. Though there have been documented ethnic variations, generally PCOS patients are seen to have a higher number of follicles per ovary. The FNPO has been found to be the best describing feature in cases of unilateral PCOS. The distribution of follicles has also been proposed to help identify 'classic PCOS', though its accuracy remains in doubt. Disordered follicular growth and recruitment has been identified using ultrasound as well. Transvaginal ultrasound allows a superior assessment of follicles to transabdominal ultrasound, and should be utilized whenever possible. However, in circumstances involving cultural or personal barriers, transabdominal remains the only modality widely accepted (3,4,6-11).

The most common ultrasound definition of a polycystic ovary image, which is included in the Rotterdam criteria, is based on the results obtained by, among others, Jonard et al. who have determined the diagnostic threshold of the number of ovarian follicles using the ROC curve analysis (27). In order to specify ultrasonographic criteria concerning the number of ovarian follicles in PCOS, Jonard et al. compared 112 healthy controls with a group of 214 patients with PCOS. All patients were examined with a transvaginal probe using the two-dimensional technique. The number of follicles measuring 2–9 mm was assessed between the 2nd and 7th day of the cycle. The study revealed a significantly higher mean number of ovarian follicles in PCOS patients compared with the controls (15.5 and 6.0, respectively). The ROC curve analysis demonstrated that the number of 12 follicles measuring 2–9 mm was the best border that differentiated the features of PCOS with the sensitivity of 99% and specificity of 75%. Furthermore, the number of ovarian follicles was also assessed in relation to their diameter in both groups. In this case, no significant differences were found between the groups when analyzing follicles measuring 6–9 mm. However, patients with PCOS presented significantly more follicles with a diameter of 2–5 mm (27). Dewailly et al. (2011) and Lujan et al. (2013) compared the ovarian structure in patients with PCOS and in controls, and specified diagnostic thresholds for follicle count at ≥19 and ≥26, respectively(28, 29). The conflicting results of both studies can result from the selection of controls. In the study of Dewailly et al., women with sonographic features of PCO but without diagnosed PCOS were excluded from the control group, whereas Lujan et al. did not use this exclusion criterion.

Size of an ovary in the assessment of its polycystic morphology

The available studies indicate that ovarian volume does not change much between the age of 20 and 39 (29, 30). The results presented prove that there are natural, age-related changes in ovarian volume, which should be taken into account when diagnosing PCO in adolescents and women older than 40 years of age.

Three-dimensional ultrasound is a recognized diagnostic modality to assess ovarian volume. The mean volume in patients with PCOS ranges from 10.6 and 16.7 ml whereas healthy women present values ranging from 5.2 and 8.7(31, 32). The comparison of ovarian volume measured in two- and three-dimensional images has been the subject of numerous studies. However, the presented outcomes indicate conflicting results(33, 31, 34). This could be caused by non-uniform technical standardization of examinations and different interpretation by different ultrasonographers.

It is believed that the assessment of ovarian volume belongs to the diagnostic criteria of PCO. However, it is characterized by a lower sensitivity compared with the assessment of ovarian follicles. The usage of such assessment is then recommended particularly when the visualization of the ovaries is difficult or it is not possible to conduct an examination with a transvaginal probe(2).

Other parameters used in the assessment of PCO

Vascularization and Morphology Of Ovarian Stroma

Three-dimensional sonography enables the assessment of the volume of the ovary and ovarian follicles. Using the difference between these two parameters, the volume of the ovarian stroma can be assessed. Fulghesu et al. demonstrate the usage of stromal volume to ovarian volume ratio as a diagnostic feature of PCOS that correlates with androgen concentration(30). However, stromal volume is a variable that is strictly correlated with the volume of the entire ovary. That is why its assessment is of little use in clinical practice.

Increased ovarian volume not only correlates with increased stromal volume, but also with its increased vascularization.

However, studies that compare the intensity of vascularization using two- and three-dimensional imaging techniques among patients with features of PCOS and healthy women indicate contradicting results (29, 35). Such discrepancies can result from the lack of the standardization of measurement methods and examinations conducted in small and diversified populations. Currently, because of non-uniform results and the lack of differentiating limit values, the assessment of stromal vascularization is not clinically used in the diagnosis of PCOS.

Bright, echogenic stroma has been subjectively accredited to PCOS. There have been many efforts to correlate qualitative indexes of stromal echogenicity with PCOS; however, it has been found that the intrinsic echogenicity of the ovarian stroma is no different in PCOS than in the normal ovary. 'Feature analysis' objectively measures the brightness, or echogenicity, of the ovarian stroma. This is done by measuring the intensity level of the ultrasound pixels within the stroma displayed on an ultrasonic image. The mean echogenicity of a given area can then be calculated. In a study by Buckett et al.,(12) it was found that even though the stromal index was significantly elevated in polycystic ovaries, the mean stromal echogenicity was not different. The subjective 'bright' stromal echotexture in polycystic ovaries is attributed to a synergistic effect of increase in ovarian stromal volume, and hence a relative lower mean echogenicity of the entire ovary (6,12). The stromal/total area ratio has also been found to have high sensitivity and specificity, albeit with poor reproducibility. With the improvement in ultrasound software, the brightness or echogenicity of the ovarian stroma can be determined much more objectively, and therefore, the quantification of ovarian stroma by computerised reading of ultrasound images has revealed that stromal hypertrophy is a frequent and specific feature in ovarian androgenic dysfunction, with some studies demonstrating that increased stromal volume correlates positively with serum androgen level (6,15). However, no standardised method exists for determining stromal volume. Because overall ovarian volume correlates well with stromal volume in polycystic ovaries, and is more easily measured in clinical practice, the determination of overall ovarian volume is a reliable surrogate for ovarian stromal assessment (6,13,14).

Elevation of impedance indices of the uterine arteries has been described in patients with PCOS, though it seems a multitude of factors contribute to this finding, including co-existence of obesity. A higher pulsatility Index and systolic/diastolic ratio has also been described. Since most of these studies were performed on patients primarily concerned with infertility, it is not known where exactly these findings fit into the pathophysiology of PCOS (1,16-19).

Anti-Müllerian hormone as a marker of polycystic ovaries

Anti-Müllerian hormone (AMH) is produced in granular cells in the follicular phase and participates in the early follicle recruitment process. AMH secretion is continued until follicles grow to a diameter of 8 mm. The secretion is negligible in larger follicles (36). There is then a good correlation between AMH levels and the number of small follicles as well as ovarian volume. The results of published studies indicate that the level of AMH is higher in patients with PCOS, which can be helpful in the diagnosis in this syndrome (2, 36, 37). Moreover, it has also been shown that there is a correlation between higher AMH concentration, rare menstruation and hyperandrogenism(38). However, due to the usage of various methods to analyze plasma AMH levels, it is difficult to compare previous studies and specify diagnostic norms that would be characterized by high sensitivity and specificity for patients with the features of PCO (2, 38).

Role of sonographic assessment of polycystic ovaries
Currently, the sonographic assessment of ovaries is one of the obligatory criteria in the diagnosis of PCOS according to the Rotterdam consensus (2003) and Androgen Excess & PCOS Society (2006)(39–40). However, because of the presence of ultrasound features of PCO in healthy women, the inclusion of this sign to the diagnostic criteria of polycystic ovary syndrome is still questioned (28). On the other hand, the available publications prove that PCO can be hereditary (41). It has also been confirmed that the coexistence of polycystic ovaries with PCOS is common (over 90% of cases) irrespective of ethnic factors or race(42, 2). The excess of ovarian follicles in this syndrome is strictly associated with hyperandrogenism, which has been demonstrated by Dewailly et al.(42). The authors of this publication also prove that there is a correlation between the presence of PCO features, increased AMH levels and ovulation disorders in patients with PCOS. That is why, the assessment of the features of PCO and increased AMH levels can be useful in the diagnosis of oligoovulation in PCOS patients(43, 44).

The sonographic features of PCO, as included in the Rotterdam criteria, are currently identified in 50% of the general population of women(2). Considering the results of studies, it has been shown that the presence of PCO features in healthy women of child-bearing age is not associated with significant metabolic disturbances, but a slight increase in AMH and androgen levels, compared with women with the normal ovarian structure, can be observed(43). The presence of PCO in the population of adolescent patients frequently coexists with menstrual disorders and acne. However, these symptoms are not sufficient to diagnose PCOS. However, the polycystic ovarian structure in this age group can be indicative of PCOS in further life. These patients should therefore be monitored clinically and sonographically, and the AMH levels should be controlled. The available studies on the commonness of sonographic signs of PCO have yielded conflicting results. On the one hand, they attest to the heterogeneity of phenotypes in completely healthy and normally ovulating women and in those with mild occult PCOS (44). On the other hand, they reveal the homogeneity of the female population with PCO features as a mild form of polycystic ovary syndrome (45).

Role of MRI in Assessing Polycystic Ovaries

The imaging of ovaries on magnetic resonance is a new and exciting frontier. Ovarian volume on MRI has been shown to be quite sensitive for diagnosis, with high reproducibility. Peripheral follicular distribution and FNPO>28 is supportive, but not as reproducible. Though the advantages of MRI in obese patients with poor quality scans is obvious, MRI cannot be extrapolated to the entire ‘PCOS eligible’ population due to sheer number and cost (6,22). Artificial intelligence and convolutional neural networks form another exciting area which, however, may not translate to clinical practice soon or enough (23).

Conclusion

Three-dimensional ultrasonography (3D USG) allows accurate measurement of the stromal volume, follicular number, and ovarian volume. Accuracy is comparable to 2-dimensional USG, with ample agreement of the Rotterdam criteria. Although promising, 3D USG is relatively expensive, and not widely available (20,21).
To conclude, it must be emphasized that the influence of the development of new technologies in the sonographic assessment of PCO features is undoubtedly noticeable. This process has caused an increase in the percentage of diagnoses of PCO and PCOS since the Rotterdam criteria were published. It is therefore needed to prepare new commonly accepted diagnostic norms concerning the number of ovarian follicles and the standardization of the technique in which they are counted. However, the application of new examination techniques does not entail the need for the modification of diagnostic norms concerning ovarian volume, which are characterized by lower sensitivity compared with ovarian follicle count. Attention is paid to the need of determining diagnostic norms depending on patients’ age and ethnic origin in individual populations of women. The assessment of AMH levels as an equivalent of ultrasound features of PCO is a promising method. However, analytic methods have to be standardized in order to establish commonly accepted diagnostic norms. That is why further studies, conducted on appropriately selected populations of women, are needed to investigate this non-uniform disease entity.

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