CHAPTER 11

The ultrasound diagnosis of the polycystic ovary

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INTRODUCTION

Historically the detection of the polycystic ovary required visualization of the ovaries at laparotomy and histologic confirmation following biopsy[1]. As further studies identified the association of certain endocrine abnormalities in women with histologic evidence of polycystic ovaries, biochemical criteria became the mainstay for diagnosis. Well recognized clinical presentations included menstrual cycle disturbances (oligo/amenorrhea), obesity, and hyperandrogenism manifesting as hirsutism, acne, or androgen-dependent alopecia. Clinical features, however, vary considerably between women, and indeed some women with polycystic ovaries do not appear to display any of the common symptoms[2,3]. Likewise, the biochemical features associated with PCOS are not consistent in all women[4,5]. There is considerable heterogeneity of symptoms and signs amongst women with PCOS and for an individual these may change over time[5,6].

It has been considered necessary to redefine the polycystic ovary syndrome (PCOS) and include within it an appropriate definition of the polycystic ovary[7,8]. At the joint ASRM/ESHRE consensus meeting on PCOS held in Rotterdam, 2003, a refined definition of the PCOS was agreed[9], which, for the first time, includes a description of the morphology of the polycystic ovary (Table 11.1). The new definition requires the presence of two out of the following three criteria:

(1) Oligo- and/or anovulation;

(2) Hyperandrogenism (clinical and/or biochemical);

(3) Polycystic ovaries, with the exclusion of other etiologies[9].

Transabdominal ultrasound

Transabdominal and/or transvaginal ultrasound have now become the most commonly used diagnostic methods for the identification of polycystic ovaries. The characteristic features are accepted as being an increase in the size (volume) of the ovary due to a greater number of follicles and volume of stroma as compared with normal ovaries. Swanson et al.[10] were the first to use high-resolution real-time ultrasound (static B-scanner 3.5 MHz, transabdominal) to describe polycystic ovaries. The follicles were noted to be 2–6 mm in diameter, but the number of follicles was neither recorded nor defined. Stromal characteristics were not described. The

Table 11.1 The Ultrasound Assessment of the Polycystic Ovary: International Consensus Definitions[21]

1. The polycystic ovary should have at least one of the following: either 12 or more follicles measuring 2–9 mm in diameter or increased ovarian volume (>10 cm^3). If there is evidence of a dominant follicle (>10 mm) or a corpus luteum, the scan should be repeated the next cycle.
2. The subjective appearance of polycystic ovaries should not be substituted for this definition. The follicle distribution should be omitted as well as the increase in stromal echogenicity and/or volume. Although the latter is specific to PCO, it has been shown that the measurement of the ovarian volume is a good surrogate for the quantification of the stroma in clinical practice.
3. Only one ovary fitting this definition or a single occurrence of one of the above criteria is sufficient to define the PCO. If there is evidence of a dominant follicle (> 10 mm) or corpus luteum, the scan should be repeated next cycle. The presence of an abnormal cyst or ovarian asymmetry, which may suggest a homogeneous cyst, necessitates further investigation.
4. This definition does not apply to women taking the oral contraceptive pill, as ovarian size is reduced, even though the 'polycystic' appearance may persist.
5. A woman having PCO in the absence of an ovulation disorder or hyperandrogenism ('asymptomatic PCO') should not be considered as having PCOS, until more is known about this situation.
6. In addition to its role in the definition of PCO, ultrasound is helpful to predict fertility outcome in patients with PCOS (response to clomiphene citrate, risk for ovarian hyperstimulation syndrome (OHSS), decision for in-vitro maturation of oocytes). It is recognized that the appearance of polycystic ovaries may be seen in women undergoing ovarian stimulation for IVF in the absence of overt signs of the polycystic ovary syndrome. Ultrasound also provides the opportunity to screen for endometrial hyperplasia.
7. The following technical recommendations should be respected:
   - State-of-the-art equipment is required and should be operated by appropriately trained personnel.
   - Whenever possible, the transvaginal approach should be preferred, particularly in obese patients.
   - Regularly menstruating women should be scanned in the early follicular phase (days 3–5). Oligo/amenorrhoeic women should be scanned either at random or between days 3–5 after a progestogen-induced bleed.
   - If there is evidence of a dominant follicle (>10 mm) or a corpus luteum, the scan should be repeated the next cycle.
   - Calculation of ovarian volume is performed using the simplified formula for a prolate ellipsoid (0.5 × length × width × thickness).
   - Follicle number should be estimated both in longitudinal and antero-posterior cross-sections of the ovaries. Follicle size should be expressed as the mean of the diameters measured in the two sections.

The usefulness of 3D ultrasound, Doppler, or MRI for the definition of PCO has not been sufficiently ascertained to date and should be confined to research studies.

early studies were hampered by the limitations of static B-scanners, which were superseded by high-resolution real-time sector scanners in the early 1980s[11,12]. Ultrasound was used to describe the ovarian appearance in women classified as having PCOS (by symptoms and serum endocrinology) rather than to make the diagnosis.

The transabdominal ultrasound criteria of Adams et al.[13] attempted to define a polycystic ovary as one which contains, in one plane, at

least 10 follicles (usually between 2 and 8 mm in diameter) arranged peripherally around a dense core of ovarian stroma or scattered throughout an increased amount of stroma. This was a seminal paper which has been most often quoted in the literature on the PCOS. The Adams' criteria have been adopted by many subsequent studies which have used ultrasound scanning to detect polycystic ovaries[2,5,14–19].

Transvaginal ultrasound

Transabdominal ultrasound has been largely superseded by transvaginal scanning because of greater resolution and in many cases patient preference – as the need for a full bladder is avoided which saves time and may be more comfortable[20]. Whilst this may be the case in the context of infertility clinics, where women are used to having repeated scans, it was found that 20% of women who were undergoing routine screening declined a transvaginal scan after having first had a transabdominal scan[19]. Furthermore, the transabdominal approach is required for adolescent girls who are yet to commence sexual activity. The transvaginal approach may not always be acceptable for research studies; for example, in a population-based survey, Michelmore et al.[3] detected polycystic ovaries by transabdominal ultrasound in 33% of a population of young women.

The transvaginal approach gives a more accurate view of the internal structure of the ovaries, avoiding apparently homogeneous ovaries as described with transabdominal scans, particularly in obese patients. With the transvaginal route, high frequency probes (> 6 MHz) having a better spatial resolution but less examination depth can be used because the ovaries are close to the vagina and/or the uterus and because the presence of fatty tissue is usually less disruptive (except when very abundant). The consensus definition of polycystic ovaries as visualized transvaginally has been recently proposed (Table 11.1)[3].

Three-dimensional ultrasound

The recent innovation of three-dimensional (3D) ultrasound and the use of color and pulsed Doppler ultrasound are techniques which may further enhance the detection of polycystic ovaries, and which may be more commonly employed in time[21,22]. Three-dimensional ultrasound requires longer time for storage and data analysis, increased training, and more expensive equipment. Nardo et al.[23] found good correlations between 2D and 3D ultrasound measurements of ovarian volume and polycystic ovary morphology.

FEATURES OF THE POLYCYSTIC OVARY

Surface area and volume

It is necessary to identify each ovary and measure the maximum diameter in each of three planes (longitudinal, antero-posterior, and transverse). It is recognized that, because of the irregular shape of the ovary, any calculation of the volume of a sphere, or prolate ellipse, is at best an estimate. Modern ultrasound machines can calculate volume once the callipers have been used to measure the ovary and an ellipse is drawn around the outline of the ovary. The ultrasound software for this calculation appears to be accurate.

Calculation of ovarian volume has been traditionally performed using the formula for a prolate ellipsoid ($\pi/6 \times$ maximal longitudinal, antero-posterior, and transverse diameters)[13,24,25]. As $\pi/6 = 0.5233$ a simplified formula for a prolate ellipse is ($0.5 \times$ length $\times$ width $\times$ thickness)[10,26–29]. In practice this formula is easy to use and of practical value.

A large number of different ultrasound formulae with different weightings for the different diameters were used to calculate ovarian volume and the prolate spheroid formula ($\pi/6 \times$

antero-posterior diameter^2 × transverse diameter) was found to correlate well with ovarian volume as assessed by 3D ultrasound[23]. A similar correlation was found with the spherical volume method ($\pi/6 \times$ [(transverse diameter + antero-posterior diameter + longitudinal diameter)/3])^3. As polycystic ovaries appear to be more spherical than ovoid it was suggested that the formula should be modified[23].

In the first study to assess ovarian volume, the simplified formula for a prolate ellipse was used for the calculation and found on average to be 12.5 cm^3 (range 6–30 cm^3)[10]. This formula was also used by Hann et al.[26] who reported considerable variety in ultrasound characteristics in women with polycystic ovary syndrome. They took the upper limit of ovarian volume to be 5.7 cm^3 based on data from Sample et al.[24]. In that study ovarian volume was calculated using the more accurate formula for a prolate ellipsoid (0.5233 × maximal longitudinal, antero-posterior, and transverse diameters)[24]. Women with PCOS were compared with normal controls and were found to have significantly greater ovarian volume (14.04 ± 7.36 cm^3 vs. 7.94 ± 2.34 cm^3) and smaller uterine volume. There was no record of timing of the scan in relation to the menstrual cycle in either PCOS or control subjects.

In the paper of Adams et al.[13] polycystic ovaries were found to have a higher volume (14.6 ± 1.1 cm^3) than both multicystic (8.0 ± 0.8 cm^3) and normal ovaries (6.4 ± 0.4 cm^3). Uterine cross-sectional area was also greater in women with PCOS than in those with multicystic or normal ovaries (26.0 ± 1.4 vs. 13.1 ± 0.9 vs. 22.4 ± 1.0 cm^2), which is a reflection of the degree of estrogenization.

A large study of 80 oligo/amenorrheic women with PCOS was compared with a control group of 30 using a 6.5 MHz transvaginal probe[29]. Based on mean ± 2 SD data from the control group, the cut-off values were calculated for ovarian volume (13.21 cm^3), ovarian total area (7.00 cm^2), ovarian stromal area (1.95 cm^2), and stromal/area ratio (0.34). The sensitivity of these parameters for the diagnosis of PCOS was 21%, 4%, 62%, and 100%, respectively, suggesting that a stromal/area ratio > 0.34 is diagnostic of PCOS[29]. Whilst these data may be useful in a research setting, the measurement of ovarian stromal area is not easily achieved in routine daily practice.

Thus the consensus definition for a polycystic ovary includes an ovarian volume of greater than 10 cm^3. It is recognized that not all polycystic ovaries will be enlarged to this size or greater and that the consensus is based on the synthesis of evidence from many studies that have reported a greater mean ovarian volume for polycystic ovaries combined with a consistent finding of a smaller mean volume than 10 cm^3 for normal ovaries. The consensus view is that until more data are collected and validated the volume of the polycystic ovary should be calculated using the more widely accepted criterion of a prolate ellipsoid[30].

Uterine size and relationship to ovarian size

The size of the uterus is often enlarged in women with PCOS because of the increased degree of estrogenization[5,13]. It had been suggested that the ratio of ovarian:uterine volume is never higher than 1.0 in women with polycystic ovaries[31]. Orsini et al.[25], however, found a wide range of ovarian:uterine volumes and this diagnostic criterion was subsequently abandoned.

Follicles: size and number

We now know that it is oocyte-containing follicles that we are observing when describing the polycystic ovary, rather than pathologic or atretic cystic structures. The early literature often refers to 'cysts' rather than follicles and as the latter are indeed small cysts – that is a 'sac containing fluid' – the terminology poly*cystic* ovary syndrome has remained.

Sample et al.[24] described the follicles as < 8 mm whilst Swanson et al.[10] noted the folli-

cles to be 2–6 mm in diameter, but a prerequisite number was neither recorded or defined. Orsini et al.[25] described ovaries as either being predominantly solid if fewer than four small (< 9 mm) cystic structures were detected in the ovary or predominantly cystic if multiple small (neither quantified) cystic structures or at least one large (> 10 mm) cyst were present. Patients with PCOS usually had follicles of between 4 and 10 mm, but occasionally follicles of 15 mm – presumably indicative of follicular recruitment. The seminal paper of Adams et al.[13] described the polycystic ovary as having, in one plane, at least 10 follicles (usually between 2 and 8 mm in diameter), usually arranged peripherally – although when scattered through the stroma it was suggested that the follicles were usually 2–4 mm in diameter[13]. Others claimed that the transvaginal definition of a polycystic ovary should require the presence of at least 15 follicles (2–10 mm in diameter) in a single plane[16].

Jonard et al.[32] studied 214 women with PCOS (oligo/amenorrhea, elevated serum LH and/or testosterone, and/or ovarian area > 5.5 cm^2) and 112 with normal ovaries to determine the importance of follicle number per ovary (FNPO). A 7 MHz transvaginal ultrasound scan was performed and three different categories of follicle size analyzed separately (2–5, 6–9, and 2–9 mm). The size range of the follicles has been considered important by some, with polycystic ovaries tending to have smaller follicles than normal or multicystic ovaries[4,33]. The mean FNPO was similar between normal and polycystic ovaries in the 6–9 mm range, but significantly higher in the polycystic ovaries in both the 2–5 and 2–9 mm ranges. A FNPO of ≥ 12 follicles of 2–9 mm gave the best threshold for the diagnosis of PCOS (sensitivity 75%, specificity 99%)[32] (Table 11.2). The authors suggest that intraovarian hyperandrogenism promotes excessive early follicular growth up to 2–5 mm, with more follicles able to enter the growing cohort which then become arrested at the 6–9 mm size. Thus the consensus definition for a polycystic ovary is one that contains 12 or more follicles of 2–9 mm diameter[30].

Multi-cystic and polycystic ovaries

The multi-cystic ovary is one in which there are multiple (≥ 6) follicles, usually 4–10 mm in diameter with normal stromal echogenicity[13]. Again, the terminology might be better annotated as multi-follicular rather than multicystic. The multi-follicular appearance is characteristically seen during puberty and in women recovering from hypothalamic amenorrhea – both situations being associated with

Table 11.2 Receiver operating characteristic (ROC) curve data for the assessment of polycystic ovaries[32]

FNPO	*Area under the ROC curve*	*Threshold*	*Sensitivity (%)*	*Specificity (%)*
2–5 mm	0.924	10	65	97
		12	57	99
		15	42	100
6–9 mm	0.502	3	42	69
		4	32.5	80
		5	24	89
2–9 mm	0.937	10	86	90
		12	75	99
		15	58	100

follicular growth without consistent recruitment of a dominant follicle[34,35]. It is therefore necessary to make careful consideration of the clinical picture and endocrinology.

Stromal echogenicity

The increased echodensity of the polycystic ovary is a key histologic feature[33], but is a subjective assessment that may vary depending upon the setting of the ultrasound machine and the patient's body habitus. In a study by Ardaens et al.[36], subjectively increased stromal hyperechogenicity assessed transvaginally appeared exclusively to be associated with PCOS.

Normal stromal echogenicity is said to be less than that of the myometrium, which is a simple guide that will take into account the setting of the ultrasound machine. Stromal echogenicity has been described in a semi-quantitative manner with a score for normal (= 1), moderately increased (= 2), or frankly increased (= 3)[28]. In this study the total follicle number of both ovaries combined correlated significantly with stromal echogenicity. Follicle number also correlated significantly with free androgen index. A further study comparing women with PCOS with controls found that the sensitivity and specificity of ovarian stromal echogenicity in the diagnosis of polycystic ovaries were 94% and 90%, respectively[37].

Echogenicity has been quantified by Al-Took et al.[38] as the sum of the product of each intensity level (ranging from 0 to 63 on the scanner) and the number of pixels for that intensity level divided by the total number of pixels in the measured area: Mean = $(\Sigma\, x_i f_i)/n$, where n = total number of pixels in the measured area, x = intensity level (from 0 to 63), and f = number of pixels corresponding with the level. The stromal index was calculated by dividing the mean stromal echogenicity by the mean echogenicity of the entire ovary in order to correct for cases in which the gain was adjusted to optimize image definition[38]. Using these measurements the stromal index did not predict responsiveness to clomiphene citrate and neither did the stromal index differ after ovarian drilling[38].

Another approach used a 7.5 MHz transvaginal probe with histogram measurement of echogenicity[39]. The mean echogenicity was defined as the sum of the product of each intensity level (from 0 to 63) using the same formula as Al-Took et al.[38]. The ovaries from women with PCOS had greater total volume, stromal volume, and peak stromal blood flow compared with normal ovaries, yet mean stromal echogenicity was similar. The stromal index (mean stromal echogenicity: mean echogenicity of the entire ovary) was higher in PCOS, due to the finding of a reduced mean echogenicity of the entire ovary[39]. The conclusion is that the subjective impression of increased stromal echogenicity is due both to increased stromal volume alongside reduced echogenicity of the multiple follicles.

Stromal area or volume

Dewailly et al.[40] designed a computer-assisted method for standardizing the assessment of stromal hypertrophy. Patients with hyperandrogenism, of whom 68% had menstrual cycle disturbances, were compared with a control group and a group with hypothalamic amenorrhea. Transvaginal ultrasound (5 MHz) was used and polycystic ovaries defined as the presence of 'abnormal ovarian stroma and/or the presence of at least 10 round areas of reduced echogenicity < 8 mm in size on a single ovarian section and/or an increased cross-sectional ovarian area (>10 cm^2)'[36,40]. The computerized technique for reading the scans involved a longitudinal section in the middle part of the ovary and calculation of the stromal area and the area of the follicles. Of 57 women with hyperandrogenism, 65% had polycystic ovaries visualized on ultrasound and elevated serum testosterone and LH concentrations were found in 50% and 45%, respectively. There was no correlation between LH and androstenedione

concentrations. Stromal area, however, correlated significantly with androstenedione and 17 hydroxyprogesterone (17OHP), but not testosterone, LH, or insulin concentrations; follicle area did not correlate with endocrine parameters[40]. Thus it was suggested that the analysis of ovarian stromal area is better than quantification of the follicles in polycystic ovaries.

Three-dimensional ultrasound has been shown to be a good tool for the accurate measurement of ovarian volume, and more precise than 2D ultrasound[21]. Three groups of patients were defined:

(1) Those with normal ovaries,

(2) Those with asymptomatic polycystic ovaries, and

(3) Those with polycystic ovary syndrome[41].

The ovarian and stromal volumes were similar in groups 2 and 3, and both were greater than group 1. Stromal volume was positively correlated with serum androstenedione concentrations in group 3 only[41]. The mean total volume of the follicles was similar in all groups, indicating that increased stromal volume is the main cause of ovarian enlargement in polycystic ovaries.

In summary, ovarian volume correlates well with ovarian function and is both more easily and reliably measured in routine practice than ovarian stroma. Thus in order to define the polycystic ovary neither qualitative nor quantitative assessment of the ovarian stroma is required.

Blood flow

The combination of transvaginal ultrasound with color Doppler measurements is beginning to provide a detailed picture of follicular events around the time of ovulation and also allows assessment of the uterine blood flow to predict endometrial receptivity[42,43]. Blood flow through the uterine and ovarian arteries has been extensively investigated in spontaneous and stimulated cycles[44]. Color (or 'power') Doppler also allows assessment of the vascular network within the ovarian stroma. Intraovarian stromal blood flow is significantly higher in polycystic ovaries than normal ovaries and its measurement, either in the early follicular phase or following pituitary suppression, has been found to be predictive of follicular response to ovarian stimulation for IVF[45,46].

A number of studies of color Doppler measurement of uterine and ovarian vessel blood flow have demonstrated a low resistance index in the stroma of polycystic ovaries (i.e. increased flow) and correlations with endocrine changes[47–49]. Battaglia et al.[50] reported a good correlation between serum androstenedione concentrations and the LH:FSH ratio with the number of small follicles, and the LH:FSH ratio also correlated well with the stromal artery pulsatility index. In another study, the blood flow was more frequently visualized in PCOS (88%) than in normal patients (50%) in the early follicular phase and seemed to be increased[51].

The resistance index (RI) and pulsatility index (PI) have been found to be significantly lower in PCOS than in normal patients and the peak systolic velocity (PVS) greater[52]. No correlation was found with the number of follicles and the ovarian volume, but there was a positive correlation between LH levels and increased PVS. Zaidi et al.[22] found no significant difference in PI values between the normal and PCOS groups, while the ovarian flow, as reflected by the PVS, was increased in the former.

The assessment of Doppler blood flow may have some value in predicting the risk for ovarian hyperstimulation during gonadotropin therapy[53]. Increased stromal blood flow has also been suggested as a more relevant predictor of ovarian response to hormonal stimulation[39,46] than parameters such as ovarian or stromal volume. The measurement of Doppler blood flow requires specific expertise and machinery and at the present time is not necessary as part of the diagnostic criteria for the polycystic ovary.

DEFINING THE POLYCYSTIC OVARY

With all imaging systems, the ovarian size (i.e. volume) together with the number of preantral follicles are the key and consistent features of polycystic ovaries. Pache and colleagues performed a series of studies to distinguish between normal and polycystic ovaries and to determine the key features of the polycystic ovary[4,28,37]. First PCOS was defined (on the basis of elevated testosterone or LH) and transvaginal ultrasound (5 MHz) was used to compare those with the syndrome to a control group[37]. Women with amenorrhea had similar ultrasound features to those with oligomenorrhea. Control ovaries never had a volume of more than 8.0 cm^3 or more than 11 follicles. The mean number of follicles was 10 in polycystic ovaries and 5 in normal ovaries. Median values for mean ovarian volume were 5.9 cm^3 in controls and 9.8 cm^3 in PCOS ($p < 0.001$); mean follicular size and number were 5.1 vs. 3.8 and 5.0 vs. 9.8 for controls and PCOS, respectively. Stromal echogenicity was also significantly increased in the PCOS patients, based on a semi-quantitative assessment[37]. The greatest power of discrimination between normal and polycystic ovaries was provided by a combined measurement of follicular size and ovarian volume (sensitivity 92%, specificity 97%).

A later study from the same group defined normal ovarian morphology in a control group of 48 normally cycling women and compared both ultrasound and endocrine parameters with those in patients with normogonadotropic oligomenorrhea or amenorrhea[54]. In the normal ovaries the mean number of follicles per ovary was 7.0 ± 1.7 and none had more than 9 follicles or an ovarian volume of greater than 10.7 ml. Polycystic ovaries were therefore considered to have ≥ 10 follicles and a volume of ≥ 10.8 ml.

From their data, Jonard et al.[32] proposed a new definition of the polycystic ovary: increased ovarian area (> 5.5 cm^2) or volume (> 11 cm^3) and/or the presence of ≥ 12 follicles of 2–9 mm diameter (as a mean of both ovaries). According to the literature review and to the discussion at the joint ASRM/ESHRE consensus meeting on PCOS held in Rotterdam in 2003 a consensus definition was decided (Table 11.1)[30]. There are circumstances where the above definition does not fit, until more data are collected:

- In women taking the combined oral contraceptive pill, the ovarian volume is suppressed but the appearance may still be polycystic[55].
- Polycystic ovaries can also be detected in postmenopausal women and whilst, not surprisingly, smaller than in premenopausal women with polycystic ovaries, they are still larger (6.4 cm^3 vs. 3.7 cm^3) with more follicles (9.0 vs 1.7) than normal postmenopausal ovaries[56]. However, no threshold is available.
- Criteria to discriminate polycystic ovaries in adolescent girls from multi-cystic ovaries have not been established[57]. Indeed it appears that PCOS manifests for the first time during the adolescent years, which are critical for future ovarian and metabolic function[58].

The incidental discovery of polycystic ovaries at ultrasound is common in women undergoing investigation for any gynecological complaint, such as pelvic pain, unexplained bleeding, or infertility. If polycystic ovaries are observed in ovulatory infertile women (in whom PCOS is not the cause of infertility), the information is very important when designing a 'superovulation' protocol because there is an increased risk of OHSS. Also, it may be useful to look for a family history of PCOS, as some siblings may have symptomatic, yet undiagnosed, PCOS. In addition, metabolic features of hyperinsulinism may be present and deserve careful evaluation since they could indicate risks for long-term health.

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