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Ultrasound assessment of the polycystic ovary: international consensus definitions

Adam H.Balen[1,5], Joop S.E.Laven[2], Seang-Lin Tan[3] and Didier Dewailly[4]

[1]Department of Reproductive Medicine, Leeds General Infirmary, Leeds, UK, [2]Department of Reproductive Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands, [3]Department of Obstetrics and Gynecology, McGill University Hospital, Montreal, Canada and [4]Department of Endocrine Gynecology and Reproductive Medicine, Lille, France

[5]To whom correspondence should be addressed at: Department of Reproductive Medicine, Leeds General Infirmary, Leeds, LS2 9NS, UK. E-mail: adam.balen@leedsth.nhs.uk

The polycystic ovary syndrome (PCOS) is a heterogeneous condition, the pathophysiology of which appears to be both multifactorial and polygenic. The definition of the syndrome has been much debated. Key features include menstrual cycle disturbance, hyperandrogenism and obesity. There are many extra-ovarian aspects to the pathophysiology of PCOS, yet ovarian dysfunction is central. At a recent joint ASRM/ESHRE consensus meeting, a refined definition of the PCOS was agreed, encompassing a description of the morphology of the polycystic ovary (PCO). According to the available literature, the criteria fulfilling sufficient specificity and sensitivity to define the PCO 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 a follicle >10 mm in diameter, the scan should be repeated at a time of ovarian quiescence in order to calculate volume and area. The presence of a single PCO is sufficient to provide the diagnosis. The distribution of follicles and a description of the stroma are not required in the diagnosis. Increased stromal echogenicity and/or stromal volume are specific to PCO, but it has been shown that the measurement of ovarian volume (or area) is a good surrogate for quantification of the stroma in clinical practice. 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. Three-dimensional and Doppler ultrasound studies may be useful research tools but are not required in the definition of PCO. This review outlines evidence for the current ultrasound definition of the polycystic ovary and technical specifications.

Key words: consensus definition/PCOS/polycystic ovary/ultrasound

Introduction

Historically, detection of the polycystic ovary required visualization of the ovaries at laparotomy and histological confirmation following biopsy (Stein and Leventhal, 1935). As further studies identified the association of certain endocrine abnormalities in women with histological evidence of polycystic ovaries, biochemical criteria became the mainstay for diagnosis. Raised serum levels of LH, testosterone and androstenedione, in association with low or normal levels of FSH, described an endocrine profile which many believed to be diagnostic of polycystic ovary syndrome (PCOS) (Franks, 1995). Well-recognized clinical presentations included menstrual cycle disturbances (oligo/amenorrhoea), obesity and hyperandrogenism manifesting as hirsutism, acne or androgen-dependent alopecia. These definitions proved inconsistent, however, as clinical features were noted to vary considerably between women, and indeed some women with polycystic ovaries do not appear to display any of the common symptoms (Polson *et al*., 1988; Michelmore *et al*., 1999). Likewise, the biochemical features associated with PCOS were not consistent in all women (Pache *et al*., 1993; Balen *et al*., 1995). There is considerable heterogeneity of symptoms and signs amongst women with PCOS, and for an individual these may change over time (Balen *et al*., 1995; Elting *et al*., 2000). Thus, consensus on a single biochemical or clinical definition for PCOS was thwarted by the heterogeneity of presentation of the disorder.

Presentation of the syndrome is so varied that one, all or any combination of the above features may be present in association with an ultrasound picture of polycystic ovaries—the defining features of PCOS in the UK and much of Europe (Balen, 1999). The 1990 National Institute of Health Conference on PCOS, however, recommended that diagnostic criteria should include evidence of hyperandrogenism and ovulatory dysfunction, in the absence of non-classic adrenal hyperplasia, and that evidence of polycystic ovarian morphology was not essential (Zawadzki and Dunaif, 1992; this reference is in book form only and no longer

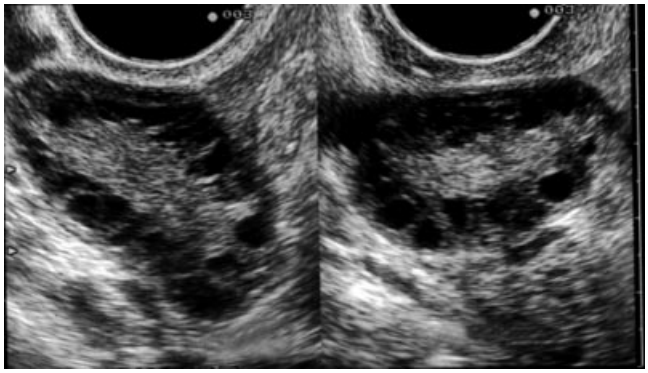

Figure 1. Polcystic ovaries (B mode, transvaginal route). In both left and right ovaries, the ovarian length and width are increased as well as the ovarian area. The follicle number, with a diameter mainly between 2 and 5 mm, is more than 12. The distribution within the ovaries is mainly peripheral. The increased and hyperechoic stroma occupies the centre of the ovaries.

readily available). It has been considered necessary to redefine PCOS and to include within it an appropriate definition of the polycystic ovary (Balen and Michelmore, 2002; Homburg, 2002).

Herein, the literature on ultrasound characteristics of the polycystic ovary has been reviewed. A Medline search was performed of all reports of polycystic ovaries and PCOS published since 1970. Papers were included which attempted to correlate features of the PCOS with specific quantifiable measurements of the ovary in order to best define the polycystic ovary. The present report was first presented at the joint ASRM/ESHRE consensus meeting on PCOS held in Rotterdam, May 1–3, 2003. At this meeting, a refined definition of the PCOS was agreed (Fauser *et al*., 2004) which, for the first time, included a description of the morphology of the polycystic ovary (see Table III and Figure 1). The new definition required the presence of two from the following three criteria: (i) oligo- and/or anovulation; (ii) hyperandrogenism (clinical and/or biochemical); and (iii) polycystic ovaries, with the exclusion of other aetiologies (Fauser *et al*., 2003).

Historical overview of polycystic ovary imaging: technical breakthroughs

Appearance and histology of the polycystic ovary

Numerous descriptions have been made of the morphology of the polycystic ovary, and these have been refined over time, alongside advances in imaging technology. It has been suggested that the first description of the anatomy and pathology of the polycystic ovary and features of the condition was made during the 18th century (Vallisneri, 1721). In more recent times, Stein and Leventhal described the features of seven hirsute, amenorrhoeic women based on the characteristic ovarian morphology from histological specimens taken at wedge resection of the ovaries. The histology of the polycystic ovary was of an ovary with prominent theca, fibrotic thickening of the tunica albuginea and multiple cystic follicles (Stein and Leventhal, 1935). The number of antral follicles (2–6 mm in diameter) was described as 'excessive' (Goldzieher and Green, 1962), but not quantified.

For many years, wedge resection was the only treatment for PCOS, and histological assessment of the ovaries was therefore routine practice. Wedge resection is, however, an outdated operation, and so histological specimens of polycystic ovaries are no longer readily available.

The histopathological criteria have been defined as the observation of: atretic follicles and/or degenerating granulosa cells; hypertrophy and luteinization of the inner theca cell layer; and thickened ovarian tunica. A good correlation has been shown between ultrasound diagnoses of polycystic morphology and the histopathological criteria for polycystic ovaries by studies examining ovarian tissue obtained at hysterectomy or after wedge resection (Saxton *et al*., 1990; Takahashi *et al*., 1994). The literature on correlations between ultrasound and histology is sparse, as histological assessment of the ovary became obsolete before ultrasound became common practice.

The histological data of Hughesdon (Hughesdon, 1982) indicated a 2- to 3-fold increase of follicle number in the polycystic ovary, from the stage of primary follicles up to tertiary follicles, and identified the cystic structures as follicles as opposed to pathological cysts.

Transabdominal ultrasound

In recent years, transabdominal and/or transvaginal ultrasound have become the most commonly used diagnostic methods for the identification of polycystic ovaries. Although the ultrasound criteria for the diagnosis of polycystic ovaries have never been universally agreed, 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.

One group (Swanson *et al*., 1981) were among the first to use high-resolution real-time ultrasound (static B-scanner, 3.5 MHz, transabdominal) to describe polycystic ovaries. Prior to this, it was thought that the tiny cysts/follicles of the polycystic ovary could not be detected by ultrasound. The follicles were noted to be 2–6 mm in diameter, but their number was neither recorded nor defined, nor were stromal characteristics described.

These early studies were hampered by the limitations of static B-scanners, but these were superseded in the early 1980s by high-resolution, real-time sector scanners (Campbell *et al*., 1982; Orsini *et al*., 1983). 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 another group (Adams *et al*., 1985) 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 PCOS.

The Adams' criteria have been adopted by many subsequent studies which have used ultrasound scanning to detect polycystic ovaries (Polson *et al*., 1988; Conway *et al*., 1989; Kiddy *et al*., 1990; Fox *et al*., 1991; Abdel Gadir *et al*., 1992; Clayton *et al*., 1992; Farquhar *et al*., 1994; Balen *et al*., 1995). In common with many authors, one of these groups (Abdel Gadir *et al*., 1992) found that the visualization of polycystic ovaries supported the diagnosis

of the syndrome in women with signs and symptoms, rather than being key in making the diagnosis.

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 (Goldstein, 1990). 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 those undergoing routine screening declined a transvaginal scan after first having had a transabdominal scan (Farquhar *et al*., 1994).

The transvaginal approach provides 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), which have 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).

Three-dimensional ultrasound and magnetic resonance imaging

The recent innovation of three-dimensional (3-D) ultrasound, as well as colour- and pulsed-Doppler ultrasound, may further enhance the detection of polycystic ovaries, and may be more commonly employed in time (Zaidi *et al*., 1995a; Kyei-Mensah *et al*., 1996a). Although 3-D ultrasound requires a longer time for storage and data analysis, increased training and more expensive equipment, good correlations were found between 2-D and 3-D ultrasound measurements of ovarian volume and polycystic ovary morphology (Nardo *et al*., 2003) (Table I).

The use of magnetic resonance imaging (MRI) to visualize the structure of pelvic organs has been claimed to have even greater sensitivity than ultrasound for the detection of polycystic ovaries (Mitchell *et al*., 1986; Faure *et al*., 1989). However, the substantial cost and practical problems involved with this imaging technique may limit its use as an easily accessible diagnostic tool in general clinical practice. The early reports of MRI were also made at a time when high-resolution transvaginal ultrasound was emerging as a valuable tool, and time has confirmed the place of the latter and limited further interest in MRI.

Examination of the polycystic ovary: technical aspects and normative data

External features of the polycystic ovary

Surface area and volume

Technical aspects: It is necessary to identify each ovary and measure the maximum diameter in each of three planes (longitudinal, anteroposterior 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. The left ovary may be more difficult to measure because of the overlying sigmoid colon, particularly if there is distension with flatus in the bowel. 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.

Table I. Correlation of ultrasound formulaic methods with 3-D ultrasound volume measurements (Nardo *et al.*, 2003)

Method	Correlation coefficient
$\pi/6$ tv × ap × long	0.70
$\pi/6$ $(tv)^3$	0.55
$\pi/6$ $(ap)^3$	0.61
$\pi/6$ $(long)^3$	0.10
$\pi/6$ $[(tv + ap)/2]^3$	0.72
$\pi/6$ $[(long + ap)/2]^3$	0.49
$\pi/6$ $[(tv + long)/2]^3$	0.61
$\pi/6$ $[(tv + ap + long)/3])^3$	0.73
$\pi/6$ $(tv)^2(ap)$	0.67
$\pi/6$ $(ap)^2(tv)$	0.73
$\pi/6$ $(tv)^2(long)$	0.61
$\pi/6$ $(ap)^2(long)$	0.51
$\pi/6$ $(long)^2(tv)$	0.49
$\pi/6$ $(long)^2(ap)$	0.30

ap = anteroposterior diameter; long = longitudinal diameter; tv = transverse diameter.

Traditionally, the calculation of ovarian volume has been performed using the formula for a prolate ellipsoid ($\pi/6$ × maximal longitudinal, anteroposterior and transverse diameters) (Sample *et al*., 1977; Adams *et al*., 1985; Orsini *et al*., 1985). As $\pi/6 = 0.5233$, a simplified formula for a prolate ellipse is (0.5 × length × width × thickness) (Swanson *et al*., 1981; Hann *et al*., 1984; Saxton *et al*., 1990; Pache *et al*., 1991; Fulghesu *et al*., 2001). In practice, this formula is both 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 ($\pi/6$ × anteroposterior diameter^2 × transverse diameter) was found to correlate well with ovarian volume as assessed by 3-D ultrasound (Nardo *et al*., 2003). A similar correlation was found with the spherical volume method $\{[\pi/6$ × (transverse diameter + anteroposterior diameter + longitudinal diameter)/3]$\}^3$. However, as polycystic ovaries appear to be more spherical than ovoid, it was suggested that the formula should be modified (Nardo *et al*., 2003).

Three means have been proposed for calculating ovarian area:

1. Using the formula for an ellipse (length × width × $\pi/4$). As $\pi/4 = 0.78$, a simplified formula for an ellipse is (0.8 × length × width).
2. Fitting an ellipse to the ovary, the area of which is calculated by the ultrasound machine.
3. Outlining by hand the ovary with automatic calculation of the outlined area.

This last technique is preferred in cases of non-ellipsoid ovaries, as may sometimes be observed.

Normative data: 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) (Swanson *et al*., 1981). This formula was also used by others (Hann *et al*., 1984), who reported considerable variety in ultrasound characteristics in women with PCOS. These authors took the upper limit of

ovarian volume to be 5.7 cm^3 based on data from another group (Sample *et al.*, 1977). In the latter study, ovarian volume was calculated using the more accurate formula for a prolate ellipsoid (0.5233 × maximal longitudinal, anteroposterior and transverse diameters). Women with PCOS were compared with normal controls and found to have significantly greater ovarian volume (14.04 ± 7.36 versus 7.94 ± 2.34 cm^3) and smaller uterine volumes. However, no record was made of the timing of the scan in relation to the menstrual cycle in either the PCOS or control subjects.

In another report (Adams *et al.*, 1985), 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 versus 13.1 ± 0.9 versus 22.4 ± 1.0 cm^2), which is a reflection of the degree of estrogenization.

A large study of 80 oligo-/amenorrhoeic women with PCOS was compared with a control group of 30 using a 6.5 MHz transvaginal probe (Fulghesu *et al.*, 2001). 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 (Fulghesu *et al.*, 2001). 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 >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 which 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.

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 (Adams *et al.*, 1985; Balen *et al.*, 1995). The ratio of ovarian:uterine volume had been suggested as never being higher than 1.0 in women with polycystic ovaries (Parisi *et al.*, 1982). However, others (Orsini *et al.*, 1985) reported a wide range of ovarian:uterine volumes, and this diagnostic criterion was subsequently abandoned.

Internal features of the polycystic ovary

Follicles: size and number

Technical aspects: It is now known that it is oocyte-containing follicles that were observed when describing the polycystic ovary, rather than pathological 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.

Each ovary should be scanned in longitudinal cross-section from the inner to outer margins in order to count the total number of cysts/follicles. Follicle number should be estimated in two planes of the ovary in order to estimate their size and their position. The diameter of follicles is measured as the mean of three diameters (longitudinal, transverse and antero-posterior).

Normative data: One group (Sample *et al.*, 1977) described the follicles as being <8 mm in size, whilst others (Swanson *et al.*, 1981) noted the follicles to be 2–6 mm in diameter, though a prerequisite number was neither recorded nor defined. Ovaries were also described 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 (Orsini *et al.*, 1985). Patients with PCOS usually had follicles of between 4 and 10 mm, but occasionally follicles of 15 mm were identified, presumably indicative of follicular recruitment. A seminal paper (Adams *et al.*, 1985) 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 (Adams *et al.*, 1985). 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 (Fox *et al.*, 1991).

In a study of 214 women with PCOS (oligo-/amenorrhoea, elevated serum LH and/or testosterone, and/or ovarian area >5.5 cm^2) and 112 with normal ovaries, the aim was to determine the importance of follicle number per ovary (FNPO) (Jonard *et al.*, 2003). These authors performed a 7 MHz transvaginal ultrasound scan, and three different categories of follicle size were analysed separately (2–5, 6–9 and 2–9 mm). The size range of follicles has been considered important by some authors, with polycystic ovaries tending to have smaller follicles than normal or multicystic ovaries (Hughesdon, 1982; Pache *et al.*, 1993). 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%) (Jonard *et al.*, 2003) (Table II). These authors suggested that intra-ovarian 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. This should help to discriminate PCO from the other causes of multifollicular ovaries.

Multicystic and polycystic ovaries: The multicystic ovary is one in which there are multiple (⩾6) follicles, usually 4–10 mm in diameter, with normal stromal echogenicity (Adams *et al.*, 1985). Almost no histological data about multicystic ovaries are available. Again, the terminology might be better annotated as multi-follicular rather than multi-cystic. The multi-follicular appearance is characteristically seen during puberty and in women recovering from hypothalamic amenorrhoea—both situations being associated with follicular growth without consistent recruitment of a dominant follicle (Venturoli *et al.*, 1983; Stanhope *et al.*, 1985). There may be confusion among inexperienced ultrasonographers,

Table II. Receiver operating characteristic (ROC) curve data for the assessment of polycystic ovaries (Jonard *et al.*, 2003)

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

FNPO = follicle number per ovary.

Table III. Ultrasound assessment of the polycystic ovary (PCO): international consensus definitions

Definition
1. The PCO 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 during the next cycle.
2. The subjective appearance of PCOs 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 polycystic ovary, it has been shown that 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 PCOs may be seen in women undergoing ovarian stimulation for IVF in the absence of overt signs of PCOS. 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 (>10mm) 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, transverse and antero-posterior cross-sections of the ovaries. Follicle size should be expressed as the mean of the diameters measured in the three sections.
The usefulness of 3-D ultrasound, Doppler or MRI for the definition of PCO has not been sufficiently ascertained to date, and should be confined to research studies.

radiologists and gynaecologists; hence the need for careful consideration of the clinical picture and endocrinology.

Stroma: volume and echogenicity

Stromal echogenicity: The increased echodensity of the polycystic ovary is a key histological feature (Hughesdon, 1982), but is a subjective assessment that may vary depending upon the setting of the ultrasound machine and the patient's body habitus. In one study (Ardaens *et al.*, 1991), subjectively increased stromal hyperechogenicity, when 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) (Pache *et al.*, 1991). In the latter study, the total follicle number of both ovaries combined correlated significantly with stromal echogenicity, and 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 (Pache *et al.*, 1992).

Echogenicity has been quantified by one group (Al-Took *et al.*, 1999) 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 = (Σ $x_i.f_i$)/n, where n = total number of pixels in the measured area, x = intensity level (0–63), 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 (Al-Took *et al*., 1999). When using these measurements, the stromal index did not predict responsiveness to clomiphene citrate, and neither did the stromal index differ after ovarian drilling (Al-Took *et al*., 1999).

Another approach used a 7.5 MHz transvaginal probe with histogram measurement of echogenicity (Buckett *et al*., 1999). The mean echogenicity was defined as the sum of the product of each intensity level (0–63) using the same formula as others (Al-Took *et al*., 1999; see above). Women with PCOS had greater total ovarian 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 entire ovary) was higher in PCOS, due to the finding of a reduced mean echogenicity of the entire ovary (Buckett *et al*., 1999). The conclusion was that the subjective impression of increased stromal echogenicity was due both to increased stromal volume alongside reduced echogenicity of the multiple follicles.

Stromal area or volume: One group (Dewailly *et al*., 1994) 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 amenorrhoea. Transvaginal ultrasound (5 MHz) was used and polycystic ovaries were 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)' (Ardaens *et al*., 1991; Dewailly *et al*., 1994). The computerized technique for reading the scans involved a longitudinal section in the middle part of the ovary and a calculation of stromal area and the area of the follicles. Of 57 women with hyperandrogenism, 65% had an 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 levels of androstenedione and 17-hydroxy-progesterone, but not of testosterone, LH or insulin; follicle area did not correlate with endocrine parameters (Dewailly *et al*., 1994). Thus, it was suggested that in women with polycystic ovaries an analysis of ovarian stromal area is better than quantification of the follicles.

Three-dimensional ultrasound has been shown to be a good tool for the accurate measurement of ovarian volume, and to be more precise than 2-D ultrasound (Kyei-Mensah *et al*., 1996b). Three groups of patients were defined: (1) those with normal ovaries; (2) those with asymptomatic polycystic ovaries; and (3) those with PCOS (Kyei-Mensah *et al*., 1998). The ovarian and stromal volumes were similar in groups 2 and 3, and both were greater than the volumes in group 1. Stromal volume was positively correlated with serum androstenedione concentrations in group 3 only (Kyei-Mensah *et al*., 1998). 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 or quantitative assessment of the ovarian stroma is required.

Blood flow

The combination of transvaginal ultrasound with colour 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 (Zaidi *et al*., 1995b, 1996a). Blood flow through the uterine and ovarian arteries has been extensively investigated in spontaneous and stimulated cycles (Tan *et al*., 1996). Colour (or 'power') Doppler also allows assessment of the vascular network within the ovarian stroma. Intra-ovarian 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 (Zaidi *et al*., 1996b; Engmann *et al*., 1999).

A number of studies of colour 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 (Battaglia *et al*., 1995; Loverro *et al*., 2001; Pan *et al*., 2002). One of these groups (Battaglia *et al*., 1999) reported a good correlation between serum androstenedione concentrations and LH:FSH ratio with the number of small follicles; the LH:FSH ratio also correlated well with the stromal artery pulsatility index (PI). In another study, the blood flow was more frequently visualized in PCOS (88%) than in normal patients (50%) in the early follicular phase and also appeared to be increased (Battaglia *et al*., 1996).

Both the resistance index (RI) and PI have been found to be significantly lower in PCOS than in normal patients, and the peak systolic velocity (PSV) greater (Aleem and Predanic, 1996). No correlation was found with the number of follicles and the ovarian volume, but there was a positive correlation between LH levels and increased PSV. One group (Zaidi *et al*., 1995a) found no significant difference in PI values between the normal and PCOS groups, while the ovarian flow—as reflected by the PSV—was increased in the former.

Recent data have indicated that assessment of Doppler blood flow may have some value in predicting the risk for ovarian hyperstimulation during gonadotrophin therapy (Agrawal *et al*., 1998). Increased stromal blood flow has also been suggested as a more relevant predictor of ovarian response to hormonal stimulation (Buckett *et al*., 1999; Engmann *et al*., 1999) than parameters such as ovarian or stromal volume. However, 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 polycystic ovary.

Definition of PCO

With all imaging systems, the ovarian size (i.e. volume) and number of pre-antral follicles are, when in combination, the key

and consistent features of polycystic ovaries. In routine clinical practice it is transabdominal or transvaginal ultrasound alone that suffices in assessment of the ovary.

Previously proposed definitions

During the early 1990s, a series of studies was performed to distinguish between normal and polycystic ovaries and to determine the key features of the polycystic ovary (Pache *et al*., 1991; 1992, 1993). First, PCOS was defined (on the basis of elevated serum testosterone or LH) and transvaginal ultrasound (5 MHz) then used to compare those women with the syndrome to a control group (Pache *et al*., 1992). Women with amenorrhoea had similar ultrasound features to those with oligomenorrhoea. Control ovaries never had a volume of more than 8.0 cm^3, or contained more than 11 follicles. The mean number of follicles was 10 in polycystic ovaries and five in normal ovaries. Median values for mean ovarian volume were 5.9 cm^3 in controls and 9.8 cm^3 in PCOS ($P < 0.001$), while mean follicular size and number were 5.1 versus 3.8 cm^3 and 5.0 versus 9.8 for control and PCOS women respectively. Stromal echogenicity was also significantly increased in the PCOS patients, based on a semi-quantitative assessment (see below) (Pache *et al*., 1992). 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 normogonadotrophic oligomenorrhoea or amenorrhoea (Van Santbrink *et al*., 1997). In the normal ovaries the mean number of follicles per ovary was 7.0 ± 1.7, and none of the women had more than nine follicles or an ovarian volume >10.7 ml. Polycystic ovaries were therefore considered to have ⩾10 follicles and a volume ⩾10.8 ml.

Based on their findings, one group (Jonard *et al*., 2003) proposed a new definition of the polycystic ovary as being an 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).

Proposition for a consensus definition

Based on the literature review and on discussions held at the joint ASRM/ESHRE consensus meeting on PCOS held in Rotterdam, May 1–3, 2003, a consensus definition may be provided (Table III).

Sensitivity and specificity

A recent study set out to assess variability in the detection of polycystic and normal ovaries with four experienced practitioners, who independently reviewed recordings of 27 pairs of ovaries, and demonstrated intra-observer agreement of 69.4% and inter-observer agreement of 51% (Amer *et al*., 2002). Polycystic ovaries were defined as the presence of ⩾10 follicles (2–8 mm diameter), ovarian volume ⩾12 cm^3 and bright echogenic stroma. Thus, there was significant intra-observer and inter-observer variability using these criteria. This suggests either that these criteria are too subjective, or that their measurement is too insensitive. It was concluded (Amer *et al*., 2002) that the use of 3-D ultrasound might provide a more reliable and reproducible diagnostic tool, although a similar evaluation of observer variability was not carried out.

Definition of PCO in particular circumstances

There are circumstances where the above definition does not fit, until more data are collected:

1. In women taking the combined oral contraceptive pill, the ovarian volume is suppressed but the appearance may still be polycystic (Franks *et al*., 1985).
2. Polycystic ovaries can also be detected in post-menopausal women and whilst, not surprisingly, smaller than in pre-menopausal women with polycystic ovaries, they are still larger (6.4 versus 3.7 cm^3) with more follicles (9.0 versus 1.7) than normal post-menopausal ovaries (Birdsall and Farquhar, 1996). However, no threshold is available.
3. Criteria to discriminate polycystic ovaries from multi-cystic ovaries in adolescent girls have not been established (Herter *et al*., 1996). Indeed, it appears that PCOS manifests for the first time during the adolescent years, which are critical for future ovarian and metabolic function (Gulekli *et al*., 1993; Balen and Dunger, 1995).

Use of ultrasonography in the diagnostic strategy for PCOS

Making the diagnosis of PCOS has been a matter of great debate, and in particular the use of ultrasound as a universal standard has been disputed. The PCOS phenotype can be structured into three components: anovulation, hyperandrogenism, and obesity (with associated hyperinsulinaemia) (Dewailly, 1997). However, these components are neither constantly, necessarily nor equally associated, thus explaining the great variability in the clinical presentation of PCOS (Balen *et al*., 1995; Dewailly, 1997). In some cases, only one or two components are present (e.g. 'ovulatory PCOS' or 'non-hirsute anovulatory PCOS')—hence the new consensus definition of the *syndrome* which requires the presence of two out of the following three criteria: (i) oligo- and/or anovulation; (ii) hyperandrogenism (clinical and/or biochemical); and (iii) polycystic ovaries, with the exclusion of other aetiologies (Fauser et al., 2004).

It is important to assess the ultrasound features of the ovary in all clinical presentations, alongside appropriate endocrine, biochemical and metabolic tests as indicated by the presentation. For example, in patients who might be considered to have 'obvious PCOS' when being referred for treatment of anovulatory infertility, it is also important to remember that abnormalities of basal serum prolactin or FSH levels may indicate a coexistent hypothalamic–pituitary disorder or incipient ovarian failure. Ultrasound assessment of the ovaries will help in the prediction of response to stimulation.

In cases of an isolated menstrual disorder or so-called 'idiopathic hirsutism' (i.e. with ovulatory menstrual cycles), PCOS is the most likely diagnosis. The clinical picture may not clearly provide the diagnosis without appropriate hormonal assays together with ultrasound. However, the finding of polycystic ovaries at ultrasound does not exclude other diagnoses as polycystic ovaries may be coincidentally associated with other conditions.

The incidental discovery of polycystic ovaries at ultrasound is common in women undergoing investigation for any gynaecological 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

Table IV. The ultrasound scan report

Name and age of patient
Identifying unique hospital record number
Date of scan
Relation to menstrual cycle
Relevant treatment (COCP, GnRHa, etc.)
Type of scan (transabdominal/transvaginal, etc.)
Ovarian morphology: each ovary recorded separately
Volume (and area – optional)
No. and size/range of cysts
Stromal echogenicity (if local grading system exists)
Doppler studies (if performed)
Uterine morphology, cross-sectional area and endometrial thickness
Other features
Hard copy and/or electronic copy
Grade and signature of person performing scan
Grade and signature of person verifying scan (if relevant)

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 as they could indicate risks for long-term health.

Conclusion

Although by its sensitivity (providing that sufficient specificity is guaranteed), ultrasonography has widened the clinical spectrum of PCOS, this has led to a reduction in the numbers of cases diagnosed with 'idiopathic hirsutism' and 'idiopathic anovulation'. Establishing the diagnosis of PCOS is, and will always be, a matter of good clinical sense.

The international consensus definitions for the ultrasound assessment of the polycystic ovary are proposed in Table III.

Appendix 1: Practical considerations for ultrasound assessment of ovaries in PCOS

Timing of the ultrasound scan

Few studies that describe the morphology and endocrinology of PCOS make reference to timing of the menstrual cycle. The baseline ultrasound scan of the pelvis is best performed in the early follicular phase (days 1–3), when the ovaries are relatively quiescent. This is the optimal approach in order to obtain consistency in the measurement of ovarian volume and area. It is recognized that in routine clinical practice it is not always possible to schedule the scan to coincide with the first 3 days of the menstrual cycle. It is important to be as precise as possible when performing scans for research studies, in which consistency is more relevant than the pragmatic approach that is often taken in day-to-day practice.

If the patient is oligo-/amenorrhoeic, the scan should be performed at random. It is recognized that women with PCOS are usually oligo-ovulatory rather than totally anovulatory, and so it is not uncommon to see a recruited follicle when assessing the ovaries. The presence of a follicle $\geqslant$10 mm diameter or a corpus luteum will result in an increased ovarian volume and area, and therefore the scan should be repeated during days 1–3 of the next cycle.

The time of day needs to be recorded only if Doppler studies are being performed, in which diurnal variation has been demonstrated in uterine (Zaidi *et al*., 1995c) and ovarian (Zaidi *et al*., 1996a) blood flow. The V_{max} in the ovary with a dominant follicle rises during the day, while the PI is highest in morning and lowest in afternoon and evening (Zaidi *et al*., 1996a).

Unless there is evidence of a dominant follicle (>10 mm) or a corpus luteum, it is probably not necessary to repeat the scan for validation of the findings as there is evidence of little change if the scan is repeated one or two times over a 9- to 12-day period (Pache *et al*., 1991), although few data are available from other studies on successive ultrasound scans over time.

Transabdominal, transvaginal, or both routes?

The transabdominal route is of course required in girls and women who are virgo intacta or for patients who decline a transvaginal scan. A transabdominal scan offers a panoramic view of the pelvic cavity, and so may be useful if there are associated uterine or ovarian developmental abnormalities, or if the transvaginal scan fails to visualize caudally displaced ovaries. Although a full bladder is required for visualization of the ovaries, one should be cautious that an overfilled bladder can compress the ovaries, yielding a falsely increased length. This emphasizes the need for assessing the ovarian size by measuring the area or the volume (see below) and by repeating the measurement after partial micturition. If not found between the uterus and the iliac vessels, the ovaries must be searched for upward, in the iliac fossa close to the abdominal wall, or downward and backward in the Douglas cul-de-sac.

In one study (Farquhar *et al*., 1994), there was no significant difference in the detection of polycystic ovaries, and the same criteria for the number of follicles was felt to be appropriate for both types of scan. There was only a 78% agreement between transabdomianl and transvaginal ultrasound for polycystic ovaries, though this was 92% for normal ovaries (Farquhar *et al*., 1994). Another group (Ardaens *et al*., 1991) also compared transabdominal (3.5 MHz) with transvaginal (6.5 MHz) ultrasound and reported that the latter was more consistent in achieving the diagnosis of polycystic ovaries in women with PCOS. Increased stromal echogenicity assessed transvaginally appeared exclusively to be associated with PCOS, but this was a subjective appearance rather than quantifiable measurement (Ardaens *et al*., 1991).

It has been argued that transvaginal ultrasound is a more sensitive method for the detection of polycystic ovaries. For example, polycystic ovaries were not detected in 30% of women with PCOS when a 3.5 MHz transabdominal transducer was used; however, a 7.5 MHz transvaginal probe was found to be more reliable (Fox *et al*., 1991).

Appendix 2: Guidelines for ultrasound assessment of ovaries in PCOS

A pelvic ultrasound scan should be performed by appropriately trained personnel, who have obtained the relevant qualifications and continue to participate in continuing professional development and appraisal programmes. Only trained personnel should report

on ultrasound scans. Assessment of inter-observer variation should be performed on a regular (e.g. annual) basis and at the start of scientific studies of ovarian function.

State-of-the-art equipment is required, which should be up to date and serviced regularly. An appropriate selection of transabdominal and transvaginal probes should be available for all body shapes/sizes. In addition to a real-time assessment of ovarian and uterine morphology, images should be recorded as either hard copy or electronically.

The scan should be performed with the patient's consent. She should be accompanied by a relative, friend or her partner if she wishes. Due consideration should be taken for her need for privacy when changing. A chaperone should be present and should sign that the procedure has been witnessed.

The scan should be performed in a systematic fashion. Each ovary should be scanned from the inner to outer margins in order to count the total number of cysts/follicles. Appropriate measurements should then be performed of the ovarian and uterine dimensions (see above). A suggested scheme for the ultrasound report is presented in Table IV.

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