In the survey by Cussons et al (1), endocrinologists were most likely to select menstrual irregularity (70%) with either clinical or biochemical androgenization as essential for the diagnosis of PCOS. About 47% of the gynaecologists believed that menstrual irregularity was an essential diagnostic criterion (P< 0·001). Gynaecologists were less likely to include androgenization as a diagnostic criterion, although when this was selected the majority also believed that either clinical or biochemical androgenization was adequate for diagnosis. Sixty-one percent of the gynaecology group compared with 14% of the endocrinology group felt that polycystic ovaries on ultrasound were essential for the diagnosis of PCOS (P<0·001). The LH/FSH ratio was more likely to be included as essential for diagnosis by gynaecologists (P< 0·001). Only 41% of endocrinologists and 16% of gynaecologists were in line with the more recent Rotterdam consensus criteria (4), with polycystic ovaries on ultrasound added as one of the possible criteria (P< 0·001).

Revolution in Diagnosis of PCOS-Proposed Ultrasonic Measurements and Formulae

Since the advent of ultrasound, numerous parameters have been proposed to morphologically define polycystic ovaries (PCO), but there is still no consensus as to their respective diagnostic value. In his morphological review of the PCO, Hughesdon et al (5) found twice the number of all types of antral follicles, generally <4 mm in diameter, in comparison with control ovaries. Since ultrasound can only detect follicles >2 mm in size, the multifollicular nature of PCO can be confused with the other causes of multifollicular ovaries (MFO) in which only the latest stages of follicular development (>4 mm) are involved. Indeed, MFO are observed by ultrasound in various physiological and pathological situations, such as mid-late normal puberty, central precocious puberty, hypothalamic anovulation, hyperprolactinaemia and, most importantly, the early normal follicular phase in adult women, in only one ovary, before one follicle among the cohort becomes dominant.

This raises the question of which threshold should be accepted if follicle number per ovary (FNPO) is used to diagnose PCO. Therefore, the definition proposed by Adams et al (6) still prevails and is used by the majority of authors today. The presence of ≥10 cysts measuring 2-8 mm in diameter arranged peripherally around a dense core of ovarian stroma or scattered through an increased amount of ovarian stroma is seen in polycystic ovaries (6). It includes the two main histological features of PCO, namely the excessive number of follicles, also termed multifollicularity, and stromal hypertrophy.

In recent years, the ultrasonographic evaluation of polycystic ovaries has received a great deal of attention, focusing on improving its diagnostic performance by evaluating other parameters as subjective or objective assessments of ovarian stroma hypertrophy (7-9). Pelvic ultrasound scans have assumed an increasing importance in the diagnosis and management of ovulatory disorders. Assessment of ovarian morphology by use of ultrasound has become a substitute for histologic examination in diagnosing PCOS (7,8,10).

Various parameters have been studied by ultrasound such as follicle number scoring, stromal echogenicity scoring, ovarian volume, ovarian area, ovarian stromal area and stroma/total area ratio (S/A). Ovarian volume is calculated using the formula ½× anteroposterior diameter × transverse diameter × longitudinal diameter of the ovary. Ovarian area is evaluated by outlining with the caliper the peripheral profile of the stroma, identified by a central area slightly hyperechoic with respect to the other ovarian area (11).

One of the main diagnostic criteria for PCOS is the presence of high number of subcortical atretic follicles; however; the predictive value of this criterion is suboptimal (9), because considerable overlap exists in the size and number of follicles, and ovarian volume between control women and patients with PCOS (10). Furthermore, the search for microcysts may lead to a misleading diagnosis because of similarities between polycystic and multifollicular ovaries (12).

Fulghesu et al (11) evaluated ovarian volume, area, stroma and the stromal/total area (S/A) ratio by adding the sizes of each ovary and then dividing by 2 using Transvaginal Pelvic Ultrasound and assayed serum levels of gonadotrophin, androgen and estradiol during early follicular phase of the menstrual cycle in regularly cycling controls and on a randomly day in amenorrhoeic or oligomenorrhoeic women with PCOS. Patients with

PCOS showed significantly higher ovarian volume, area, stroma and mean S/A ratio when compared to multifollicular and control groups. Cut off values were defined for ovarian volume (13.21 ml), area (7.00 cm^2), stroma (1.95 cm^2) and S/A ratio (0.34). The sensitivity for diagnosis of PCOS was 21%, 4%, 62% and 100% respectively. The S/A ratio showed the most significant correlation with serum androgen levels and poor correlation between LH and Ultrasonographic criteria in contrast to Pache et al (10) who showed that ovarian volume and stromal echogenicity correlated significantly with LH levels. This difference could partly be explained by different method of analysis as Pache et al (10) performed a subjective and semiquantative evaluation of ovarian stroma using a scale ranging from 1 to 4 on the basis of its echogenicity.

Robert et al (13) showed that computerized assisted analysis of ovarian stroma for diagnosis of PCOS was more specific than visual analysis and avoids false positive results in normal patients. Stromal area was increased using visual analysis in 74% as compared to 61% in computer assisted analysis. Specificity of this sign was 84% and 96% by visual and computerized analysis respectively.

With the introduction of recent advances in ultrasound software, the brightness, or echogenicity, of the ovarian stroma can be determined objectively by measuring the intensity level of the ultrasound pixels of the stroma displayed or an ultrasonic image. Simple evaluation of stromal area by S/A ratio is an easily reproducible diagnostic criterion for the ultrasound analysis of PCOS women.

Real time 2-dimensional ultrasound has been determined to be a relatively accurate and reliable technique to determine ovarian volume and morphology (14). Nardo et al (15) proposed the prolate spheroid volume method, using the anteroposterior diameter as the major axis and the transverse diameter as the minor axis (volume=π/6×anteroposterior diameter^2×transverse diameter), which had a strong correlation with the ovarian volume measured using the 3-dimensional formula ($p<.001$). Also, the spherical volume method, using all the three diameters (volume= π/6×[(transverse diameter+anteroposterior diameter +longitudinal diameter)/3] (3), demonstrated the same positive correlation with the ovarian volume determined by using the 3 dimensional formula. This study was the first to demonstrate that the most accurate formula is the spherical formula.

Are biochemical investigations a diagnostic necessity for Polycystic Ovary Syndrome?

Elevated mean serum concentrations of luteinizing hormone (LH) are common in all reported series of women with PCOS (16). It seems likely, however that abnormal gonadotropin secretion is a result, rather than the cause of ovarian dysfunction (17). Measurement of serum LH levels should not be considered necessary for the clinical diagnosis of PCOS (4). Many women with polycystic ovary syndrome have hypersecretion of luteinizing hormone, although normal serum concentrations of luteinizing hormone do not rule out the diagnosis. No tests of insulin resistance are necessary to make the diagnosis of PCOS, nor are they needed to select treatments (4).

Previously it was thought essential not only to have elevated level of LH, but the LH to FSH ratio was also required to be elevated in order to define PCOS. Initially the ratio was 2:1, then 3:1. However, the idea of both elevated levels of LH and the ratios being essential for diagnosis of PCOS has now been abandoned (4). Similarly elevated levels of androgens are unhelpful in defining the syndrome, as these levels are inconsistently elevated. Other limitations of the biochemical diagnosis of PCOS included the variable and imprecise nature of the assays and the dynamic nature of the hormonal steroidal release from the ovaries.

LH levels could be useful as a secondary parameter (especially in lean women with amenorrhea or in research). Additional research is needed to further clarify the clinical relevance of LH in PCOS and the potential effects of LH suppression with GnRH analogs or its enhancement through LH activity administration at different stages of follicular maturation (4).

Conclusion

The classical definition of PCOS is too restrictive and the other diagnostic criteria such as an increased ovarian stroma or an abnormal steroid response to a GnRH diagnostic challenge test may be more sensitive

to diagnose a functional ovarian hyperandrogenism. However, the use of ultrasonography for diagnosis of hyperandrogenism and ovulatory disorders by clinicians is still reticent because of subjectivity. Analysis of ovarian stroma is purely visual and the specificity of computerized stromal analysis is better than visual analysis as it avoids false positive results. The precise measurement of total ovarian area correlates well to stromal area and a specific parameter, being abnormal when it exceeds 11 cm^2 for both ovaries or 5.5 cm^2 per ovary, using transvaginal ultrasonography.

Polycystic ovaries contain numerous follicles, which are of small size (4 to 5 mm), whereas normal ovaries in follicular phase have fewer but larger follicles. Women with polycystic ovaries, hyperandrogenism and regular menses do not fit into the classical definition of PCOS.

The recent advent of 3D ultrasonography allows accurate detection of uterine and ovarian structures and volume. The third reconstructed plane (coronal plane) can be displayed simultaneously with traditional two dimensional sections (longitudinal and transverse planes). Two new formulas, namely, the prolate spheroid formula and spherical formula for ovarian volume measurement in PCOS have been described in literature. The clinical significance of these formulas is still minimal as the conventional ellipsoid formula has a good correlation with 3D ultrasound measurement and has been a well established measurement tool for ovarian volume.

PCOS can be diagnosed non-invasively by ultrasonography on the basis of increased ovarian size, an excessive number of small follicles and increased or hyperechogenic ovarian stroma. Early detection and diagnosis could help in improvement of menstrual function and increase fecundity of these women.

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