Polycystic ovary morphology: age-based ultrasound criteria

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Objective: To determine age-based criteria for polycystic ovary morphology.
Design: Cross-sectional, case-control design.
Setting: Outpatient setting.
Subject(s): Women with polycystic ovary syndrome (PCOS) defined by hyperandrogenism and irregular menses (n = 544) and controls with regular menses and no evidence of hyperandrogenism (n = 666) participated. Parameters were tested in a second cohort of women with PCOS (n = 105) and controls (n = 32) meeting the same criteria.
Intervention(s): Subjects underwent a pelvic ultrasound documenting ovarian volume and maximum follicle number in a single plane.
Main Outcome Measure(s): A receiver operating characteristic curve was constructed to determine the ovarian volume and follicle number with the best sensitivity and specificity to define PCOS for age groups at approximately 5-year intervals from age 18 to >44 years.
Result(s): The best sensitivity and specificity were obtained using a threshold volume of 12 mL and 13 follicles for ages ≤24 years, 10 mL and 14 follicles for ages 25–29 years, 9 mL and 10 follicles for ages 30–34 years, 8 mL and 10 follicles for ages 35–39 years, 10 mL and 9 follicles for ages 40–44 years, and 6 mL and 7 follicles for ages >44 years. Data from a second cohort confirmed the need to decrease volume and follicle number with increasing age to diagnose PCOS. Polycystic ovary morphology was most accurate at predicting the PCOS diagnosis for women ages 30–39 years.
Conclusion(s): The ovarian volume and follicle number threshold to define polycystic ovary morphology should be lowered starting at age 30. (Fertil Steril® 2017;108:548–53. ©2017 by American Society for Reproductive Medicine.)
Key Words: Ultrasound, polycystic ovary syndrome, volume, follicle

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Polycystic ovary syndrome (PCOS) is a heterogenous disorder, originally identified by Stein and Leventhal in 1935, based on the abnormal anatomic ovarian morphology (1). Since the 1980s, ultrasonography has allowed for noninvasive assessment of polycystic ovarian morphology (PCOM) (2). In 2003, a group of PCOS investigators redefined the ultrasound criteria for PCOM at a consensus conference in Rotterdam (3). They determined that an ovarian volume >10 mL provided excellent specificity for PCOS in a majority of studies and used 12 or more follicles of 2–9 mm as the follicle number with the best sensitivity and specificity to distinguish PCOS (4). However, with improvement in ultrasound technology it was recognized that the criteria defining PCOM needed to evolve to better distinguish the ovarian morphology in women with PCOS from that in women who do not have irregular menses and hyperandrogenism (5). A more recent review of the literature increased the follicle number threshold to ≥25 follicles to provide better specificity for PCOS but found that the sensitivity of the measurement was compromised (5, 6).

None of the criteria take into account the normal decrease in ovarian volume and follicle number with age in women with PCOS and in women with regular menstrual cycles and no hyperandrogenism (7–9). We previously demonstrated that ovarian volume decreases log linearly and follicle number decreases linearly with

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age in women with PCOS and controls, studied both cross-sectionally and longitudinally (9). We have also demonstrated that virtually all women (97.3%) with PCOS diagnosed using the National Institutes of Health criteria have PCOM on ultrasound and those that do not are older and have higher FSH levels (10). These findings support the need for age-based PCOM criteria. Therefore, the objective of the study was to determine the follicle number and ovarian volume with the best sensitivity and specificity to distinguish PCOM on ultrasound in reproductive-age women within 5-year age groups.

MATERIALS AND METHODS

Subjects

All subjects were recruited as part of a genetics study with extensive phenotyping (10). PCOS subjects recruited at Massachusetts General Hospital in Boston from 2003 to 2013 were between the ages of 18 and 56 years (n = 544). PCOS subjects recruited in Iceland from 2003 to 2006 were between the ages of 18 and 40 years (n = 105). All subjects had oligomenorrhea (nine or fewer menstrual periods/year) and clinical and/or biochemical evidence of hyperandrogenism, fulfilling the National Institutes of Health criteria (11). Clinical hyperandrogenism was defined by [1] an elevated Ferriman-Gallwey score > 9 (12) or [2] acne on the face or back. Biochemical hyperandrogenism was defined as T > 63 ng/dL (2.8 nmol/L), DHEAS > 430 μg/dL (1.16 μmoL/L), or androstenedione levels > 3.8 ng/mL (13.3 nmol/L) (11).

Control subjects, ages 18–51 years, were recruited coincident with the PCOS subjects. Control subjects had regular menstrual cycles, 21–35 days, and no physical exam or biochemical evidence of hyperandrogenism in Boston (n = 666) and Iceland (n = 32). In Boston, all women were diagnosed with PCOS or confirmed as controls before the age of 40 years, but some came back at a later age for a longitudinal study (9). They were only included in the data at their second visit, providing a broader age range for assessment.

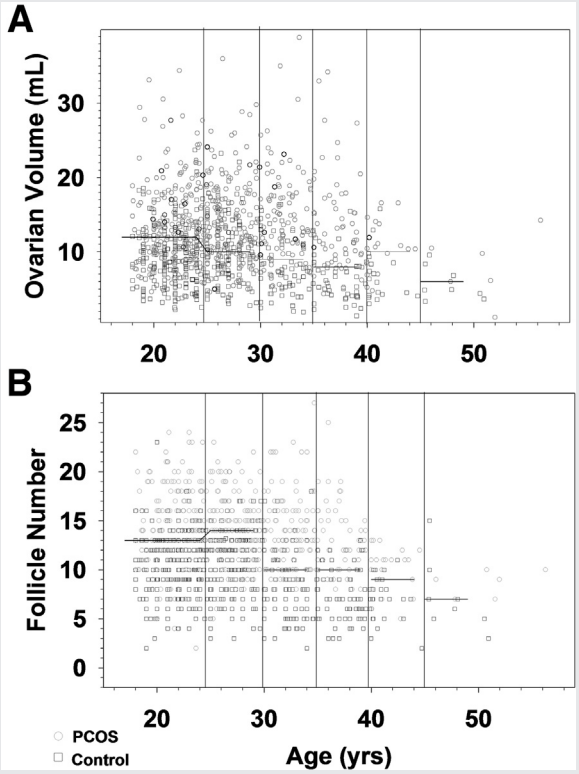
Subjects were excluded for a personal history or biochemical evidence of late-onset congenital adrenal hyperplasia (11). All subjects had normal thyroid function and PRL levels and a follicular-phase FSH level in the premenopausal range. Subjects were on no hormonal medication for at least 3 months, except for stable thyroid hormone replacement, and were not taking metformin.

The study was approved by the Partners Human Research Committee and the Data Protection Commission of Iceland and the National Bioethics Committee of Iceland. All subjects provided written informed consent.

Women with PCOS were studied ≥ 10 days after their last menstrual period to avoid the time period in which LH is suppressed after a P rise (13) and after a 12-hour fast (11). Control subjects were studied in the follicular phase. All subjects underwent a physical exam, blood draw for hormonal assessment, and oral glucose tolerance test at baseline. Ultrasounds were performed by one operator in Boston (J.M.A.), using the ATL HDI 1500 Ultrasound with a 4- to 8-mHZ convex array probe from 2003 to 2006. Ultrasounds were also performed by one operator in Iceland (trained by J.M.A.) using the ATL Envisor Ultrasound with a 4- to 8-mHZ convex array probe, which was well matched to the Boston device, from 2003 to 2006. In April 2006, the Boston group changed the ultrasound machine to a Phillips HD11 XE with a 4- to 8-mHZ endovaginal curved array transducer. In all cases, multiple images of the ovary were recorded. Ovarian volume was calculated using length × width × height in centimeters multiplied by 0.5233. All follicles were counted on a fixed image in a plane in which the maximum number of follicles was visualized. The maximum ovarian volume and maximum follicle number in the ovary with the maximum number of follicles was used for analysis, excluding the volume of an ovary with a dominant follicle (>10 mm) or a corpus luteum. Initial measurements were recorded in Boston and in Iceland and were over read by two observers (J.M.A, H.J.K, C.T.P., and/or C.K.W.). If readings were not in agreement, a consensus reading was agreed upon after review by all parties.

Using data from the Boston cohort, a receiver operating characteristic (ROC) curve was constructed for each (approximately) 5-year age group (18–24, >24–29, >29–34, >34–39, >39–44, and >44 years) for both ovarian volume and follicle number. Youden's index (sensitivity + specificity − 1) was used to choose the value that maximized the sensitivity and specificity across all possible results, rather than optimize one

FIGURE 1



(**A**) Ovarian volume and (**B**) follicle number in women with PCOS (*open gray circles*) and controls (*open black squares*) as a function of age. *Black horizontal lines* indicate the chosen cutoff to distinguish PCOM from normal morphology.

Kim. Age-based PCO morphology criteria. Fertil Steril 2017.