TITLE: AN AMH-BASED SCREENING TOOL IS BOTH SENSITIVE AND SPECIFIC FOR PREDICTING A DIAGNOSIS OF PCOS BY ROTTERDAM CRITERIA.

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BACKGROUND: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-aged females and can present with insulin resistance, metabolic syndrome, and infertility. In the U.S., the Rotterdam criteria are commonly used for diagnosis, requiring 2 out of 3 criteria, one being polycystic ovarian morphology (PCOM) on ultrasound. AMH levels are strongly correlated with follicle number per ovary (FNPO) and have been proposed as a surrogate marker for PCOM in the 2023 International Evidence-based Guideline for PCOS assessment and management.

OBJECTIVE: To evaluate whether a PCOS screening tool using anti-Müllerian hormone (AMH) levels in lieu of polycystic ovarian morphology (PCOM) can reliably identify patients who meet the Rotterdam criteria for PCOS.

MATERIALS AND METHODS: Patients with PCOS were diagnosed by ultrasound-based Rotterdam criteria and included 516 subjects from the multi-site PPCOS II trial and patients from a tertiary academic center's multidisciplinary PCOS clinic. The control cohort included 617 participants from the Ovarian Aging Study (OVA), a community-based cohort of ovulatory women not seeking treatment for fertility. Receiver operating curves were used to calculate age-stratified AMH thresholds to predict PCOM, defined as FNPO >20 with groups aged 25-29, 30-34, and 34-39. These age-stratified AMH thresholds were used as one of the three criteria for the diagnosis of PCOS, in addition to oligomenorrhea (<8 menstrual cycles per year) and biochemical hyperandrogenism (free androgen index >6 ng/dL).

The AMH thresholds were initially calculated from a randomly selected age-matched training group which comprised roughly one-quarter of the total cohort (n=388). The thresholds were then validated against the remainder of the cohort (n=745), termed the experimental group, to create a modified Rotterdam criteria using the original Rotterdam criteria as the gold standard. Two AMH assay sources were utilized: one from the University of Virginia (UVA), which used ELISA (Ansh Labs), and a second from the multidisciplinary PCOS clinic, which used multiple labs and assays available in the community (e.g., Quest, Labcorp).

RESULTS: The subjects in the validation group exhibited significant demographic differences, with non-PCOS patients being older and having lower BMI, waist/hip ratios, and AMH levels compared to those with PCOS (Table 1). The age-stratified AMH threshold to predict PCOM was 6.75 ng/dL for patients aged 25-29 and 6.25 ng/dL for patients aged 30-39. Using these thresholds, the modified Rotterdam criteria accurately identified PCOS (per original Rotterdam criteria) in 219 out of 298 patients and correctly predicted the absence of PCOS in 409 out of

447 patients in the validation group, yielding an overall sensitivity of 73.5% and specificity of 91.5%.

CONCLUSIONS: The modified Rotterdam criteria incorporating age-stratified AMH thresholds demonstrate high sensitivity and specificity for predicting a diagnosis of PCOS as defined by the traditional Rotterdam criteria. The use of AMH offers a non-invasive and objective alternative to transvaginal ultrasound for screening patients for PCOS. Further research is warranted to evaluate the performance of this screening tool prospectively in more heterogeneous populations, with varied AMH assays, and among patients with differing ovulatory statuses.

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REFERENCES:

1. Teede H, Chau Thien Tay, Laven J, et al. Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *Fertility and Sterility*. 2023;120(4):767-793. doi:https://doi.org/10.1016/j.fertnstert.2023.07.025

TABLES/FIGURES:

Table 1: Validation Group Subject Characteristics

	OVA (n=447)	PCOS (n=298)	P value
Age (years)	33.1 (4.2)	30.6 (3.6)	<0.001
BMI	27.1 (7.3)	30.5 (9.1)	<0.001
Waist/hip ratio	0.79 (0.08)	0.83 (0.10)	<0.001
AMH	5.4 (4.0)	10.2 (7.7)	<0.001

KEYWORDS: polycystic ovary syndrome, anti-mullerian hormone, polycystic ovarian

morphology, Rotterdam criteria