Efficacy of predictive models for polycystic ovary syndrome using serum levels of two antimüllerian hormone isoforms (proAMH and AMH_{N,C})

Michael W. Pankhurst, Ph.D., a Soulmaz Shorakae, M.D., c,d Raymond J. Rodgers, Ph.D., b Helena J. Teede, Ph.D., c,d and Lisa J. Moran, Ph.D. b,c

a Department of Anatomy, School of Biomedical Sciences, University of Otago, Dunedin, New Zealand; b The Robinson Research Institute, School of Medicine, University of Adelaide, Adelaide, South Australia, Australia; c Monash Centre for Health Research Implementation, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia; and d Diabetes and Vascular Medicine Unit, Monash Health, Melbourne, Victoria, Australia

Objective: To compare total antimüllerian hormone (AMH), proAMH, AMH_{N,C}, and the ratio of the two forms in predictive models for polycystic ovary syndrome (PCOS) diagnosis. Total AMH consists of proAMH (inactive precursor) and AMH_{N,C} (receptor-competent), but neither isoform has been tested individually for their ability to predict PCOS diagnosis.

Design: Cross-sectional study using biobanked samples collected between July 2008 and January 2010.

Setting: Not applicable.

Patient(s): Overweight, premenopausal women aged 18–45 years with PCOS (n = 45, with 21 fulfilling National Institutes of Health diagnostic criteria and 24 fulfilling European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE) criteria, but not National Institutes of Health criteria) and without PCOS (n = 23 controls).

Intervention(s): None.

Main Outcome Measure(s): Serum concentrations of proAMH and total AMH (proAMH and AMH_{N,C} combined) were determined by immunoassay. The AMH_{N,C} concentrations were calculated by subtraction ([AMH_{N,C}] = [total AMH] – [proAMH]). Relative levels of proAMH were expressed as the AMH prohormone index (API = [ProAMH]/[Total AMH] × 100).

Result(s): In women with PCOS, total AMH, proAMH, and AMH_{N,C} levels were higher, and the API was lower (P = .010), than in controls indicating increased conversion of proAMH to AMH_{N,C}. Receiver-operating characteristic analysis for proAMH (area under the curve [AUC] = 0.82), AMH_{N,C} (AUC = 0.86), and API (AUC = 0.70) did not improve the prediction for PCOS when compared with total AMH (AUC = 0.86).

Conclusion(s): The proAMH and AMH_{N,C} do not appear to improve the ability to predict a diagnosis of PCOS beyond total AMH assays. However, the ratio of inactive proAMH precursor to receptor-competent AMH_{N,C} (API) differs in women with PCOS relative to unaffected controls indicating that AMH signaling mechanisms may be altered in women with PCOS. (Fertil Steril 2017;108:851–7. ©2017 by American Society for Reproductive Medicine.)

Key Words: Predictive models, receiver operator characteristic analysis, proprotein, prohormone, testosterone

Discuss: You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/19241-24488

Received June 8, 2017; revised July 24, 2017; accepted August 7, 2017.

M.W.P. reports grants from Health Research Council of New Zealand. S.S. has nothing to disclose. R.J.R. has nothing to disclose. H.J.T. reports fellowship for research activities from NHMRC Australia. L.J.M. has nothing to disclose.

Supported by funding from the Health Research Council of New Zealand (grant number 14-441), Monash University and the NHMRC Centre for Research Excellence in the Evaluation, Management and Care Needs of Polycystic Ovary Syndrome (PCOS) and Related Health Implications (grant number APP107844). Initial funding was received from the Diabetes Australia Research Trust. L.J.M. is supported by a SACVRDP Fellowship; a program collaboratively funded by the NHF, the South Australian Department of Health and the South Australian Health and Medical Research Institute (grant number AC115374) and a National Heart Foundation Future Leader Fellowship (grant number 101169). H.J.T. holds an NHMRC Practitioner Fellowship and 5.S. holds an NHMRC scholarship (grant number APP1074512).

Reprint requests: Michael W. Pankhurst, Ph.D., Department of Anatomy, University of Otago, PO Box 913, Dunedin, 9054, New Zealand (E-mail: michael.pankhurst@otago.ac.nz).
Oligospermia. The AMH is a transforming growth factor β (TGF-β) superfamily member produced by granulosa cells (GCs) in developing ovarian follicles (7). The functions of AMH include inhibition of primordial follicle activation and regulation of GC sensitivity to FSH (8–10). The increased levels of circulating AMH in women with PCOS are thought to come from the greater number of follicles in polycystic ovaries (PCOs) and increases in AMH production per follicle (11, 12). It is still unclear whether alterations in AMH regulation exacerbate the reproductive features of PCOS, but there are positive associations between serum AMH levels and the degree of abnormal ovarian function in PCOS (13). The possibility that serum AMH levels could replace ultrasound in diagnosing polycystic ovary (PCO) morphology is currently being evaluated (14), but sensitivity and specificity can vary between study centers (15).

The AMH has two protein isoforms in circulation (16). It is synthesized as a cysteine-linked homodimer of the 560-amino acid preproprotein sequence that generates a 140-kDa proproprotein that is synthesized as a cysteine-linked homodimer of the 560-amino acid preproprotein sequence that generates a 140-kDa proproprotein that is converted to AMHN,C, when compared with FF from healthy women (16). Studies in mice indicate that proAMH and AMHN,C are cleared from blood at the same rate and proAMH is not converted to AMHN,C while in circulation (23). This strongly suggests proAMH to AMHN,C ratios in blood are indicative of extracellular proAMH cleavage rates within the ovary.

Circulating concentrations of proAMH and AMHN,C have not been quantified in women with PCOS, as clinical AMH assays measure total AMH, a combined measure of the two forms (24). However, analysis of follicular fluid (FF) from women with PCOS suggests that more proAMH produced is converted to AMHN,C when compared with FF from healthy women (22). The aim of the present study was to determine whether the ratios of proAMH or AMHN,C in serum are altered in women with PCOS relative to women without PCOS and to determine the ability of different AMH-related isoforms to predict a PCOS diagnosis.

**MATERIALS AND METHODS**

**Participants**

Study participants were women aged 18–45 years who were recruited between July 2008 and January 2010 as part of a previously published investigation (25). Participants were recruited through community advertisement. The PCOS was defined according to either National Institutes of Health criteria (two features of clinical or biochemical hyperandrogenism and chronic anovulation, and exclusion of other etiologies) (26) or the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) criteria (two of the three features of clinical or biochemical hyperandrogenism, PCO morphology, and oligoovulation or anovulation, and exclusion of other etiologies) (27). Control group participants were eligible if they had no history of diagnosed PCOS, no oligomenorrhea, or clinical or biochemical hyperandrogenism. Ultrasound was only requested for diagnostic purposes in women with only one other PCOS diagnostic feature. Ultrasound data were not collected as an experimental variable for analysis. Prospective participants were excluded if they were pregnant, smoking, had diabetes mellitus type 2, uncontrolled hypertension, had nonstable use of antihypertensives, were taking lipid-lowering or fish oil medications, or using hormonal (e.g., oral contraceptive [OC] pill), or insulin-sensitizing medication unless willing to cease medications for 3 months before study measurements. One woman with PCOS was using stable antihypertensive medication during the study. The study population consisted of 23 controls and 45 women with PCOS (21 qualifying for National Institutes of Health criteria and 24 diagnosed by Rotterdam criteria only). A priori power calculations indicated that this sample size was large enough to detect differences in the mean of one SD or more with β set to 0.95.

Institutional review board ethical approval was obtained from the Standing Committee on Ethics in Research Involving Humans for Monash University, the Human Research Ethics Committee of Monash Health, and the University of Otago Human Ethics Committee (Health). The study was conducted in accordance with the principles set out in the Declaration of Helsinki and all participants provided written, informed consent.

**Sampling**

Blood samples were taken in the morning between 8:00 and 10:00 AM. Blood samples were taken on days 0–14 of the ovarian cycle if the participant was regularly cycling, with the first day of menstrual bleeding recorded as day 0. Whole blood was stored on ice until centrifugation. Serum was collected and was stored at −80°C. Height, weight, and waist circumference data were also collected from each participant. Body mass index (BMI) was calculated by weight divided by height squared.

**Hormone Assays**

Total AMH was measured with the AMH Gen II ELISA (Beckman Coulter, Cat# A79765, following field safety notice
FSN–20434–3, June 2013) according to the manufacturer’s instructions. The proAMH was measured according to a modified protocol of the Gen II assay, as previously described (28). The AMH Gen II calibrators (Beckman Coulter, Cat# A79766) were used for quantification in total AMH immunoasays and a recombinant human proAMH standard was used for quantification in proAMH immunoasays (28). All samples were measured in a single batch and a human AMHN,C preparation was included to serve as a negative control for the proAMH assay. Cross-detection of AMHN,C in the proAMH assay was <4%. The intra-assay coefficients of variations (CVs) were 3.8% and 7.5% for the total AMH and proAMH assays, respectively. Sample concentrations were calculated from standard curves fitted to quadratic equations (Prism 6, Graphpad Software). Total AMH and proAMH concentrations for each sample were calculated from the mean of duplicate assays. The AMHN,C concentrations were calculated as [total AMH] - [proAMH]. The AMH prohormone index (API) was calculated to determine the relative ratio of proAMH-to-AMHN,C: API = [proAMH]/[total AMH] × 100. Testosterone was assayed with a liquid chromatography-mass spectrometry according to previously published procedures (29). Sex hormone-binding globulin (SHBG), fasting insulin, lipids, and blood glucose were measured as previously reported (25). The free androgen index (FAI) was calculated as (T × SHBG)/100 and homeostasis assessment of insulin resistance was calculated as (Fasting glucose × Insulin)/22.5.

**Statistical Analysis**

All analyses were conducted with SPSS statistics v22.0 (IBM). In all analyses involving API, three individuals from the control group were excluded as their assay values for total AMH and proAMH were at or below the detection limit, which precludes generation of accurate API values. In analyses involving other AMH-related variables (total AMH, proAMH, and AMHN,C), these individuals were given values equivalent to the limit of detection of the assays (0.6 pmol/L). Comparisons between means were conducted with general linear models with Tukey’s B post-hoc test when more than two groups were analyzed. The Box–Cox test was used to determine the appropriate log-transformations when non-normality of data and heterogeneity of variances was present (total AMH, proAMH, and AMHN,C data sets). Pearson correlation was used to determine the relationship between total AMH and API.

Univariate and multivariate prediction models for PCOS were conducted using receiver operating characteristic (ROC) curves for total AMH, proAMH, AMHN,C, and the API. Variables for inclusion in multivariate prediction models for PCOS were determined by univariate logistic regression analysis based on hypothesis testing. Variables tested for association with PCOS included age, BMI, weight, waist circumference, T, SHBG, FAI, fasting insulin, fasting glucose, and homeostasis assessment of insulin resistance. The final multivariate regression models included age, waist circumference, and FAI as the variables with the strongest relationship on significance or hypothesis testing. The optimal balance between false-positive and false-negative discovery rates was determined by calculating the maximal Youden index across the ROC space (30).

**RESULTS**

The anthropomorphic and biochemical characteristics of the study population are listed in Table 1, as previously reported in Moran et al. (25). Mean total AMH, proAMH, and AMHN,C levels were higher in women with PCOS when compared with controls, with the differences being statistically significant (Fig. 1A–1C; P < .001). The API values were lower on average in women with PCOS compared with controls (P = .010) (Fig. 1D). The API values for 48.9% of the women with PCOS (22/45) were below the interquartile range of the control women, indicating that proAMH cleavage tends to occur at a faster rate in women with PCOS. In contrast, the proportion of women in the PCOS group with values above the interquartile range of control women was 75.6%, 71.1%, and 77.8% for total AMH, proAMH, and AMHN,C, respectively.

The ROC analysis was used to examine the ability of the various AMH parameters to predict a diagnosis of PCOS (Supplemental Fig. 1). The predictive models using total AMH, proAMH, and AMHN,C produced similar area under the curve and similar optimal compromises between sensitivity and specificity, as determined by the Youden index (Table 2). The ROC curves for API were overtly different with lower area under the curve and lower specificity when the optimal compromise was calculated (Table 2). Combining all four AMH parameters in a multivariable model did not improve the predictive ability of the model (Table 2). However, the inclusion of key demographic and pathophysiological features (age, waist circumference, and FAI) as additional variables in multivariate models was able to improve the area under the curve for total AMH, proAMH, AMHN,C, and API ROC analysis (Table 2, Supplemental Fig. 2).

Possible interactions between the API and pathophysiological features of PCOS were investigated by subanalysis. No significant correlation was observed between total AMH concentration and API in women with (r = −0.108, P = .650)

---

### TABLE 1

**Participant demographic characteristics.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PCOS (mean ± SD)</th>
<th>Control (mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>33.1 ± 5.8</td>
<td>37.6 ± 8.1</td>
<td>.02</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>92.4 ± 19.0</td>
<td>79.6 ± 12.3</td>
<td>.002</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>34.0 ± 6.0</td>
<td>29.4 ± 3.9</td>
<td>.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>102.5 ± 15.1</td>
<td>90.9 ± 10.0</td>
<td>.002</td>
</tr>
<tr>
<td>T (ng/mL)</td>
<td>0.3 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>.1</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>34.0 ± 15.1</td>
<td>52.0 ± 15.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Free androgen index</td>
<td>8.5 ± 5.3</td>
<td>2.9 ± 1.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fasting insulin (mU/L)</td>
<td>20.2 ± 12.5</td>
<td>13.4 ± 4.9</td>
<td>.002</td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>4.8 ± 0.4</td>
<td>4.8 ± 0.3</td>
<td>.7</td>
</tr>
<tr>
<td>HOMA</td>
<td>4.3 ± 2.6</td>
<td>2.8 ± 1.1</td>
<td>.002</td>
</tr>
</tbody>
</table>

*Note:* HOMA = homeostasis assessment of insulin resistance; PCOS = polycystic ovary syndrome; SHBG = sex hormone-binding globulin.

Pankhurst. AMHN,C and proAMH levels in women with PCOS. Fertil Steril 2017.
or without PCOS ($r = -0.259$, $P = .086$; Fig. 2A). However, there was an apparent L-shaped curve among the women with PCOS. Those with low total AMH levels exhibited API values that occupied a similar range to the control group. In contrast, women with PCOS and higher total AMH levels had API values that were almost exclusively below the median API level for control women. Hence, there were no women with PCOS who simultaneously had high total AMH levels and high API. A similar pattern was observed between T levels and API, where no women with PCOS and high T levels had API above the median level for controls (Fig. 2B). Cycle irregularity was also found to differentiate women with PCOS according to API, as those with regular cycles were not different from controls but significant differences were observed between controls and women with PCOS and irregular cycles (Fig. 2C).

**DISCUSSION**

The current study suggests that specific proAMH and AMH$_{NC}$ measurements do not offer improved prediction of PCOS when compared with total AMH. Our total AMH findings are consistent with prior studies that have investigated total AMH as a predictor of PCOS (15). The inclusion of all AMH parameters in multivariate models showed no appreciable improvement, but inclusion of demographic and pathophysiological features increased the predictive capacity of each AMH parameter. Although the API had comparatively poor efficacy for the prediction of PCOS, we demonstrated an increased conversion of proAMH to AMH$_{NC}$ in the women with PCOS that may be associated with certain features of PCOS such as cycle irregularity or hyperandrogenism.

The PCOS has multiple phenotypes based on the presence of diagnostic features and the severity of clinical reproductive symptoms are variable. Of the three diagnostic features, PCO morphology is the strongest determinant of increased AMH levels in PCOS, but the presence of either hyperandrogenism or oligo/amenorrhea has also been shown to be associated with further elevations in AMH levels (13). This is consistent with the observation that the women with PCOS with either high levels of AMH or T, or irregular cycles, consistently had more rates of AMH activation, as represented by low API. A larger sample size will be required to determine the approximate level of total AMH or T that distinguishes these two subpopulations. Although elevated AMH production may be a consequence of PCO morphology, it is also possible that it plays a role in the ovarian dysfunction in PCOS. If so, the higher rates of conversion of inactive proAMH to receptor-competent AMH$_{NC}$ in the women with PCOS could further exacerbate the ovarian pathology.

The proAMH cleavage is putatively orchestrated by proprotein convertase subtilisin/kexin-type-3 (PCSK3) and PCSK5 (20). Ovarian expression of these proteases is regulated by gonadotropins (31, 32) and LH in particular, exhibits increased secretion pulsatility, and reduced pulse-amplitude in women with PCOS (33). An LH-mediated change in ovarian PCSK3 and PCSK5 expression in PCOS is one possible explanation for the lowered API. The PCSKs activate a broad range of proteins including important ovarian TGF- β superfamily member proproteins including activins, inhibins, bone morphogenetic protein 15, and growth differentiation factor 9 (34–38). The proAMH cleavage site appears to be comparatively resistant to PCSK enzymes (20). If PCSK activity is increased in the PCOS ovary, then signaling pathways for multiple TGF- β ligands could be altered, potentially more than proAMH/AMH$_{NC}$.

The ability of total AMH, proAMH, and AMH$_{NC}$ to predict PCOS was relatively equivalent but API was overtly less effective. The AMH assays have been proposed as an alternative to ultrasound to detect PCO morphology (14), but studies tend to investigate AMH as a predictor of PCOS rather than PCO morphology (5, 6). Future research should determine whether AMH can be interchanged with ultrasound diagnosis because a single variable is unlikely to be able to diagnose a multisymptom condition such as PCOS. In keeping with this, we also report that a multivariate ROC analysis with all four AMH parameters was not improved relative to the univariate
analyses. However, AMH variables in combination with key demographic and pathophysiological variables improved the predictive model. It is likely that age improves the model by controlling for the large variation in AMH observed with age.

TABLE 2

Receiver operating characteristic analysis of the predictive ability of different antimüllerian hormone parameters.

<table>
<thead>
<tr>
<th>ROC analysis</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total AMH</td>
<td>proAMH</td>
</tr>
<tr>
<td>AUC (95% CI)</td>
<td>0.86 (0.73–0.94)</td>
<td>0.82 (0.69–0.91)</td>
</tr>
<tr>
<td>Optimal sensitivity (%)</td>
<td>75.6</td>
<td>71.1</td>
</tr>
<tr>
<td>Optimal specificity (%)</td>
<td>87.0</td>
<td>82.6</td>
</tr>
<tr>
<td>ROC P value</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Multivariate regression P value</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: AMH = antimüllerian hormone; AMHNC = cleaved AMH complex; API = AMH prohormone index; AUC = area under the curve; CI = confidence interval; proAMH = AMH proprotein; ROC = receiver operating characteristic.

a Analysis included one AMH-related variable as well as free androgen index, waist circumference, and age in the predictive model.
b Analysis included all four AMH variables (total AMH, proAMH, AMHNC, and proAMH).

Pankhurst. AMHNC and proAMH levels in women with PCOS. Fertil Steril 2017.

FIGURE 2

The relationships between AMH prohormone index (API) and total antimüllerian hormone (AMH) (A), T (testosterone) (B), and cycle regularity (C) in women with and without polycystic ovary syndrome (PCOS). Blue diamonds, control women; red circles, women with PCOS. The dashed line in (A) and (B) indicates the median of the control group. Data in (A) were analyzed by Pearson’s correlation and data in (C) by general linear models with Tukey’s B post-hoc test; groups that share the same letter annotation(s) did not exhibit statistically significant differences in the group means. Error bars, SEM; group sizes are indicated above the x-axis.

Pankhurst. AMHNC and proAMH levels in women with PCOS. Fertil Steril 2017.
agaging [39]. The FAI may increase the true positive detection rate by including some of women with PCOS who do not have AMH levels above the threshold in univariate analyses. The role of waist circumference is less clear, but AMH secreted from the ovary appears to diffuse into the extracellular fluid volume [23]. Waist circumference is correlated with extracellular fluid volume [40], which may act as another standardizing variable for AMH, but this hypothesis requires experimental confirmation. If predictive models based on clinical data are to be assessed for a PCOS diagnosis, there may be merit in using a multivariate approach. Further investigation is needed to determine whether age, FAI, and waist circumference findings can be replicated and whether additional variables can improve AMH-based prediction models.

Our observation of lower API in women with PCOS is consistent with immunoprecipitation experiments observing more conversion of proAMH to AMH\(_\text{N,C}\) in the FF of women with PCOS relative to controls [22]. Our results are not consistent with prior attempts to measure AMH\(_\text{N,C}\) in the serum of women with PCOS, which generated substantially lower API values, likely due to the severe assay interference [22]. This would normally invalidate an assay and preclude it from being used quantitatively.

In the present study, AMH\(_\text{N,C}\) concentrations were calculated by the subtraction of proAMH from total AMH concentrations. The validity of this has been verified by parallel and linear dilution characteristics between proAMH and total AMH assays [28].

Limitations of this study include the use of biobanked samples that were collected for a previous study [25] and the lack of ultrasound data in all women. Ultrasound was used to confirm the presence or absence of PCO in a subset of women, but data on ovarian morphology and antral follicle counts were not collected as experimental variables. Increases in per-follicle output have been observed in women with PCOS [11, 41] and this, in combination with increased numbers of antral follicles, is the likely explanation for the increased total AMH levels in serum. Incorporating antral follicle counts into future multivariate predictive models may enable AMH output per follicle to be estimated (Serum [Total AMH]/Antral follicle count) and assessed as a predictive variable.

The clearly defined case and control populations used in this study are ideal for investigating new parameters in predictive models. However, predictive tests for PCOS would ultimately aim to differentiate women presenting at clinics with PCOS from women with other conditions that display PCOS-like symptoms and women with one feature of PCOS who do not meet the criteria for diagnosis. Predictive models for PCOS involving AMH measurements have not been rigorously tested in different groups of patients with overlapping characteristics. Such populations are ideal for further testing of multivariate predictive models. Larger studies will be needed, as we were only able to assess four variables in the multivariate models given our sample size. Furthermore, our approach of multivariate logistic regression followed by ROC analysis is suitable for hypotheses testing but future research needs to investigate generation of nomograms or reference intervals.

In conclusion, the present study indicates that the rate of proAMH conversion to AMH\(_\text{N,C}\) is increased in women with PCOS in a manner dependent on severity of symptoms. However, API is not superior or equivalent to total AMH in predicting PCOS. The proAMH and AMH\(_\text{N,C}\) provide equivalent predictive ability to PCOS, but neither are superior to total AMH. Proprotein convertase activity in women with PCOS deserves further investigation as these enzymes have broad actions across multiple hormonal and growth factor signaling systems.

Acknowledgments: The authors thank Prof. L.S. McLennan for providing advice and his contribution to the conception of the study. Prof. David Handelsman is thanked for conducting the T assays and Mrs. N.J. Batchelor and Dr. Eveline Jona are thanked for providing technical assistance.

REFERENCES

15. Ilidromiti S, Kelsey TW, Anderson RA, Nelson SM. Can anti-Mullerian hormone predict the diagnosis of polycystic ovary syndrome? A systematic
SUPPLEMENTAL FIGURE 1

Receiver operating characteristic curves for the ability of total antimüllerian hormone (AMH) (A), AMH proprotein (proAMH) (B), cleaved AMH complex (AMH_{N,C}) (C), and AMH prohormone index (API) (D) to predict a diagnosis of polycystic ovary syndrome (PCOS).

Pankhurst. AMH_{N,C} and proAMH levels in women with PCOS. Fertil Steril 2017.
Multivariate receiver operating characteristic curves for the ability of total antimüllerian hormone (AMH) (A), AMH proprotein (proAMH) (B), cleaved AMH complex (AMH\textsubscript{N,C}) (C), and AMH prohormone index (API) (D) to predict a diagnosis of polycystic ovary syndrome (PCOS). Multivariate models were generated with PCOS status as the dependent and the AMH parameter, age, free androgen index (FAI), and waist circumference (WC) as the independent variables.

Pankhurst. AMH\textsubscript{N,C} and proAMH levels in women with PCOS. Fertil Steril 2017.