SUPPLEMENTAL RESULTS

Relationship of AMH to Body Mass Index

We found that AMH levels are inversely correlated with body mass index (BMI) in PCOS (Supplemental Fig. 1), in confirmation of an earlier report (1). We tested the possibility that the lower AMH of PCOS-A than of PCOS-T is a function of their differing degrees of obesity (Table 1). We compared the morbidly obese (BMI ≥ 40 kg/m^2) subsets of PCOS-A with positive SDAST (n = 10) and of PCOS-T (n = 10). In the absence of a significant difference in BMI ($P=.12$), AMH levels remained significantly lower in this PCOS-A subset than in this PCOS-T subset (5.3 $\pm$ 0.8 vs. 11.0 $\pm$ 1.0 ng/mL; $P<.01$) and were not significantly different from the others in their respective groups. Our data suggest that the low AMH of PCOS-A is independent from obesity and is instead related to milder ovarian dysfunction.

Within-Group Relationships of AMH to Age, Ovarian Volume, and Ovarian Function

Age (Supplemental Fig. 2A). A significant inverse relationship of AMH to age was found only in the V-NO group. Insignificant positive correlations were found in the other groups.

Ovarian volume (Supplemental Fig. 2B). In addition to being significant across groups, the AMH correlation with ovarian volume was significant across both volunteer groups ($r = 0.317$; $P=.022$) and tended toward significance across both PCOS groups ($r = 0.244$; $P=.07$). The correlation of AMH with ovarian volume tended toward significance within the V-NO ($P=.09$) and PCOS-A ($P=.052$) groups.

SDAST (Supplemental Fig. 2C). AMH correlated with the testosterone response to SDAST across volunteer groups ($r = 0.351$; $P<.02$) and tended to do so across PCOS groups ($r = 0.225$; $P=.098$). It tended to correlate with SDAST outcome in the V-NO group ($P=.08$), but was not related to SDAST results in any other individual group.

GnRHag test (Supplemental Fig. 2D). AMH correlated with the 17-OHP response to GnRHag testing across volunteer groups ($r = 0.465$; $P=.001$) and across PCOS groups ($r = 0.306$; $P<.025$). It correlated significantly with GnRHag test outcome in the V-NO ($P<.005$) and PCOS-A ($P<.05$) groups. We conclude that significant cross-group relationships are not necessarily sustained in individual study groups.

Relation of AMH to Ovarian Function Parameters

SDAST and GnRHag test results correlated significantly across groups ($r = 0.67$), as previously reported (2). The correlation between these tests of ovarian androgenic function was significant within the PCOS-T group ($r = 0.524$; $P<.001$) and across PCOS groups ($r = 0.46$; $P<.0001$), but not within the PCOS-A group ($r = 0.23$) or within ($r \leq 0.32$) or across ($r = 0.12$) volunteer groups.

AMH levels correlated significantly with both SDAST and GnRHag test results across groups ($r = 0.489$–0.513), as discussed in the main text and shown in Figure 2E and F.

We further analyzed the data to determine whether AMH differed among subgroups that had diverse relationships among polycystic ovary and ovarian androgenic function test status. Supplement Figure 3 shows the data in relationship to the degree of elevation of the AMH level.

Ninety-five percent of V-NO had AMH levels <6.2 ng/mL (Supplemental Fig. 3A). Interestingly, the one V-NO outlier with asymptomatic baseline hyperandrogenemia also had abnormal SDAST and AMH (Supplemental Fig. 3B). Ninety-six percent of V-PCO had an AMH level <10.7 ng/mL (68% were <6.2 ng/mL; Supplemental Fig. 3A and B). AMH levels did not differ significantly among volunteer subgroups (Table 2). AMH was elevated (>6.2 ng/mL) in 21% of those with normal androgenic ovarian function (subgroup 2a, lavender circles in lower-left quadrants of Supplemental Fig. 3A and B) and 62.5% of those who were normoandrogenemic with high post-GnRHag 17-OHP peaks (subgroup 2b, lavender circles in lower-right quadrants of Supplemental Fig. 3). Notably, each member of the V-PCO subgroup with baseline hyperandrogenemia (subgroup 2c), which has PCOS according to Rotterdam criteria, had an abnormal response to SDAST, GnRHag test, or both, but only one-half (Supplemental Fig. 3B) had AMH elevation.

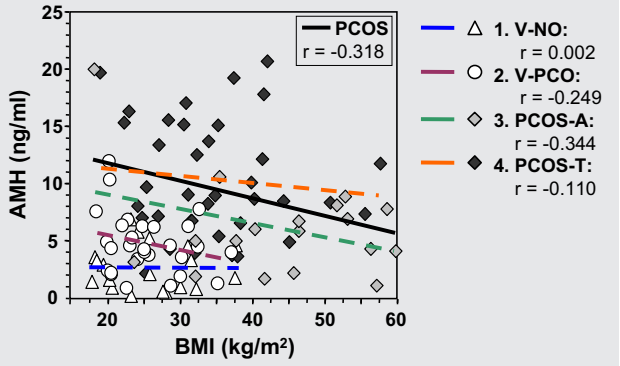
AMH levels did not differ significantly different between the PCOS-A subgroups with and without evidence of ovarian hyperandrogenism (Table 2). Among PCOS-A subgroup 3a, those with normal ovarian androgenic function tests (green symbols in the lower-left quadrants of Supplemental Fig. 3), AMH was appropriate for polycystic ovary status in 6 of 7 patients (Supplemental Fig. 3A and B); the other had obesity as the only apparent source of androgen, a classic polycystic ovary, and a very high AMH level (20 ng/mL; Supplemental Fig. 3C). Among PCOS-A subgroup 3b, those with atypical functional ovarian hyperandrogenism (i.e., elevated post-SDAST testosterone level, but normal GnRHag test, green diamond-shaped symbols in the upper-left quadrants of Supplemental Fig. 3A and B), AMH levels were elevated (>6.2 ng/mL) in 45%, but appropriate for polycystic ovary status (<10.7 ng/mL) in all. AMH >10.7 ng/mL distinguished PCOS-T from V-PCO with 96% specificity and from PCOS-A with 94% specificity (Supplemental Fig. 3C vs. Supplemental Fig. 3A and B).

These subgroup analyses indicate that, although AMH levels correlate significantly with the outcomes of specific tests for ovarian androgenic function, AMH elevation is associated with the presence of a polycystic ovary independently from ovarian hyperandrogenism.

SUPPLEMENTAL REFERENCES

1. Piouka A, Farmakiotis D, Katsikis I, Macut D, Gerou S, Panidis D. Anti-mullerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels. Am J Physiol Endocrinol Metab 2009;296:E238–43.
2. Rosenfield RL, Mortensen M, Wroblewski K, Littlejohn E, Ehrmann DA. Determination of the source of androgen excess in functionally atypical polycystic ovary syndrome by a short dexamethasone androgen-suppression test and a low-dose ACTH test. Hum Reprod 2011;26:3138–46.

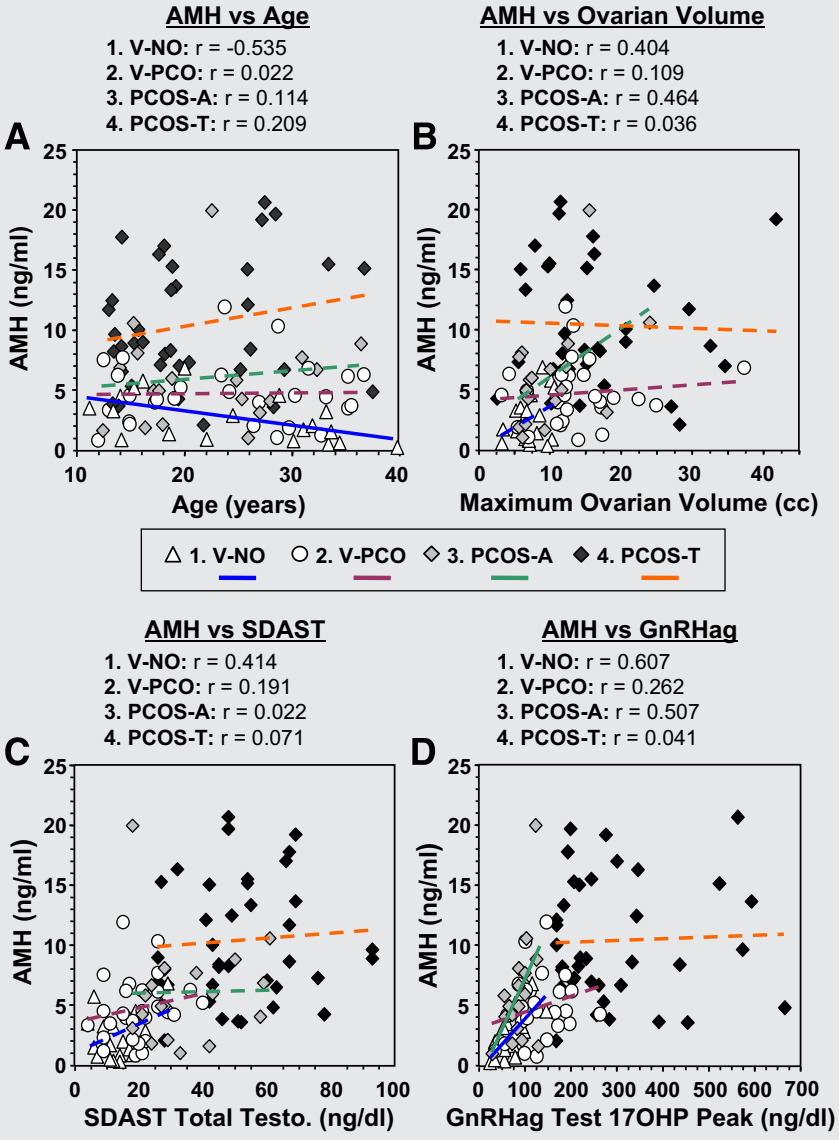
SUPPLEMENTAL FIGURE 1



Relationship of antimüllerian hormone (AMH) level to body mass index (BMI). A significant inverse correlation was seen across the polycystic ovary syndrome (PCOS) groups ($P<.02$, *solid trend line*), but there was not a significant correlation across all groups ($r = 0.09$) or within individual groups. *Dashed trend lines* indicate $P>.05$.

Rosenfield. AMH, PCO, and ovarian hyperandrogenism. Fertil Steril 2012.

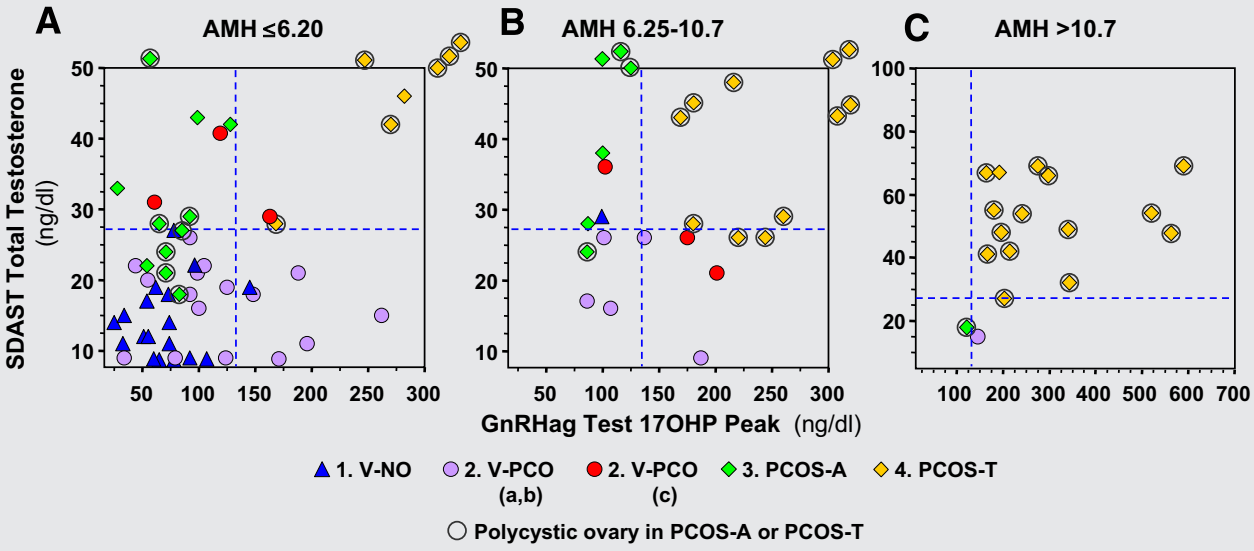
SUPPLEMENTAL FIGURE 2



Scatterplots illustrating the relationships of antimüllerian hormone (AMH) levels to age (A), maximum ovarian volume (B), post-SDAST testosterone (C), and post–GnRHag test 17-OHP peak (D). *Solid trend lines* indicate $P<.05$; *dashed trend lines* indicate $P>.05$. Relationships of AMH to these outcomes across all groups are discussed in the main text and shown in Figure 2C–2F.

Rosenfield. AMH, PCO, and ovarian hyperandrogenism. Fertil Steril 2012.

SUPPLEMENTAL FIGURE 3



Scatterplots of the relationships of antimüllerian hormone (AMH) levels to ovarian function parameters. The *axes* show the outcomes of tests for androgenic ovarian dysfunction (SDAST and GnRH agonist test); *dashed blue lines* show the cut-points that provide 95% specificity for distinguishing asymptomatic eumenorrheic volunteers with normal ovarian morphology from PCOS-T. Large circles indicate subjects with a polycystic ovary. (A, B) Outcomes of tests for PCOS types of ovarian dysfunction in the ranges observed in asymptomatic eumenorrheic volunteers without (V-NO) and with (V-PCO) a polycystic ovary; (C) (note expanded axis ranges) those with AMH levels that are inappropriately high for the presence of a polycystic ovary. The hyperandrogenemic V-PCO subgroup (2c) that meets Rotterdam criteria for PCOS is indicated in *red*.

Rosenfield. AMH, PCO, and ovarian hyperandrogenism. Fertil Steril 2012.