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Association Between Uterine Fibroids and Anti-Müllerian Hormone Concentrations Among African American Women

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Abstract

Objective: To evaluate the extent to which uterine fibroids are associated with Anti-Müllerian hormone (AMH) concentrations.

Design: Cross-sectional study.

Setting: Baseline data from Study of the Environment, Lifestyle and Fibroids Study which is a five-year longitudinal study of African American women.

Patients: 1,643 women aged 23–35 years without a known history of fibroids.

Exposure: Fibroid presence

Main outcome measure: The primary outcome was percent difference in mean AMH concentration in participants with fibroids compared to those without fibroids. The secondary outcomes were percent differences in mean AMH concentrations in participants with different numbers, sizes, types, and positions of fibroids, and percent difference in mean AMH concentration in participants with different uterine volumes.

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Results: At least one fibroid was identified on ultrasound in 362 participants (22.0%). There was a small difference in mean AMH concentrations in participants with fibroids (age-adjusted model: −4.6%, 95% CI: [−14.5%, 6.5%]; multivariable model: −4.6%, 95% CI: [−14.4%, 6.3%]). Mean AMH concentrations tended to decrease with increasing fibroid number. Although differences in AMH concentrations were not statistically significant, compared with no fibroids, mean percent differences in AMH concentrations for 1, 2–3, and ≥4 fibroids were −1.2% (95% CI: [−13.2%, 12.5%]), −7.1% (95% CI: [−23.3%, 12.5%]) and −17.5% (95% CI: [−38.2%, 10.0%]), respectively. There were no consistent associations between AMH concentrations and fibroid location or size, or uterine volume.

Conclusion: The presence of fibroids was not materially associated with AMH concentrations. Other than a monotonic inverse relationship between fibroid number and AMH concentrations, no other fibroid characteristics were consistently or appreciably associated, although associations were imprecise.

Keywords

Anti-Müllerian hormone; ovarian reserve; uterine fibroids; uterine leiomyomas

INTRODUCTION

Uterine fibroids, also called leiomyomas, are benign neoplasms of the uterus (1). Over 80% of black women and almost 70% of white women will develop at least one fibroid by the age of 50 (2), making these the most common tumors among females (3). Although fibroids can be asymptomatic, many women experience symptoms that disrupt their quality of life and cause other medical issues (1). Certain fibroids may impact reproductive outcomes (3) and negatively affect fertility (4). Given that fibroids are detected in up to 10% of women with infertility (4), a proportion of individuals with a history of fibroids may ultimately need to pursue fertility treatments, such as in vitro fertilization (IVF), to achieve a pregnancy.

One factor that influences IVF success is ovarian reserve as this predicts an individual's response to ovarian stimulation (5). A commonly utilized marker of ovarian reserve is anti-Müllerian hormone (AMH). AMH is a member of the transforming growth factor β (TGF-β) family that is released by the granulosa cells within the ovaries (6). As serum AMH concentrations are directly proportional to the number of ovarian follicles (6), AMH concentration can aid in assessing functional ovarian reserve (7) and has been demonstrated to predict oocyte yield after gonadotropin stimulation for IVF (5). In addition, some studies have demonstrated that AMH concentrations can assist in predicting time to menopause (8).

Despite the inverse association between ovarian reserve and age, AMH concentrations can vary widely among similarly-aged women (5). Although factors other than age have been investigated to determine their relationship with AMH concentrations (7), further insight into novel factors that may influence AMH concentrations is needed. One factor that has received little attention is the presence of fibroids. Although it has been suggested that certain treatments for fibroids may decrease AMH concentrations (9), it is unknown whether the presence of fibroids is associated with AMH concentrations. The ovaries are partially perfused by a branch of the uterine artery which also provides a blood supply to fibroids (10,

11) making it possible for fibroids to compromise blood flow to the ovaries, impact ovarian reserve as a consequence, and thus reduce AMH concentrations.

Given the high prevalence of fibroids among reproductive-aged women and the fact that some treatments for fibroids—or the fibroids themselves—may decrease AMH concentrations, we evaluated the extent to which fibroids and their characteristics are associated with AMH concentrations in a cohort of women aged 23–35 years.

MATERIALS AND METHODS

Study participants

The Study of Environment, Lifestyle, and Fibroids (SELF) is an ongoing prospective cohort study. 1,693 African American women aged 23–34 were recruited to participate from November 2010 through December 2012. To be included in the study participants must have affirmed being “African American or Black” (additional ancestries could also have been affirmed) and must have been residents of the Detroit, MI metropolitan area. Participants were excluded if they had been diagnosed with uterine fibroids prior to enrollment. They were also excluded if they had a history of a hysterectomy, were taking medication to treat an autoimmune disorder (including: multiple sclerosis, Grave’s disease, scleroderma, lupus, or Sjogren’s), or had received radiation or chemotherapy. A previously published study has described the study design, methods, and recruitment (12). Prior to enrollment, women were seen for a clinic visit where height, weight, and blood pressure were measured and a blood draw was completed. Women also completed comprehensive self-administered questionnaires. For those who were pregnant at recruitment, the enrollment visit was delayed until after pregnancy (3–4 months). The institutional review boards of the participating institutions approved the study and participants provided written informed consent.

Assessment of AMH

Recruitment occurred during 2010–2012. At enrollment, up to 55 mL of blood was drawn from each participant. Blood collection was not timed with participants’ menstrual cycles given that most studies have demonstrated that AMH concentrations are generally stable throughout the menstrual cycle (6). Serum was stored at −80°C until analysis was performed. ln 2018, frozen samples were shipped to Ansh labs (Webster, Texas, USA) where AMH assays were performed using the picoAMH assay which is an ultrasensitive enzyme linked immunosorbent assay (ELISA). The same reagent lot was used for all samples. AMH values are presented in concentration of ng/mL with the lower limit of detection of the test being 1.3 pg/mL. The limit of blank, defined as the concentration below which analyte-free samples are found with a probability of 95 %, was 0.5 pg/mL. The limit of blank was calculated as the 95th percentile value from a minimum of n = 324 measurements of 4–6 analyte-free samples in each of 4 reagent lots. The measuring range was 6.0 to 1,150 pg/mL (0.043 pmol/L to 8.21 pmol/L). If necessary, specimens were diluted up to 20-fold prior to assay, thus extending the measuring range up to 23,000 pg/mL (23 ng/mL, 164 pmol/L). Intra-assay and inter-assay coefficients of variation were <5%. Serum AMH concentrations were available for 1,643 individuals.

Assessment of Uterine Fibroids and Fibroid Characteristics

Participants underwent screening for fibroids at their baseline visit. Fibroid presence was the exposure for this study. Details of ultrasound assessment of fibroids are included in a previously published study examining fibroid incidence and growth in this study population (13). Those performing the ultrasounds had at least three years of experience performing gynecologic ultrasounds and were registered diagnostic medical sonographers. The sonographers underwent additional training specific to the study to ensure that fibroid detection was standard amongst them. Ultrasounds were performed transvaginally with 2D equipment. Images were archived for quality control purposes. The lead sonographer reviewed 8% of each sonographer's ultrasounds monthly or at minimum one per sonographer.

Several details about fibroids were ascertained and recorded. These included fibroid presence, quantity, size, type, and position. Uterine length, anterior-posterior and transverse diameters were each measured twice and averaged to compute uterine volume for all women. Any fibroids or questionable fibroids greater than or equal to 0.5 cm in any of the three planes were counted; any number of fibroids larger than 10 was recorded as "10". Each of the six largest fibroids was measured three times in each plane and the diameters were averaged to compute fibroid volume. Fibroid size was then categorized into a five-level variable defined by the diameter equivalent of the volume. The six largest fibroids were also described by type and longitudinal, anterior-posterior, and transverse positions.

Assessment of Covariates

Body mass index (BMI) was calculated from height and weight data measured at the clinic by trained study staff. Other variables were collected from participants using computer assisted telephone interviews, computer assisted web-based interviews, self-administered hard-copy questionnaires, or through responses to questions administered by the study staff during the clinic visit. Participants were asked to report current use of hormonal contraceptives which included combined oral contraceptives, the etonogestrel/ethinyl estradiol vaginal ring, depot medroxyprogesterone acetate, etonogestrel implant, the ethinyl estradiol/norelgestromin transdermal patch, and the levonorgestrel intrauterine device. A current or prior diagnosis of any thyroid condition, polycystic ovarian syndrome (PCOS) or a history of "seeking care for difficulty conceiving" was obtained by participant self-report.

Statistical Analysis

For this study, we analyzed only baseline data from SELF. The primary outcome was percent difference in mean AMH concentration in participants with fibroids compared to those without fibroids. The secondary outcomes were percent differences in mean AMH concentrations in participants with different numbers, sizes, types, and positions of fibroids, as well as percent difference in mean AMH concentration in participants with different uterine volumes.

We assessed the distribution of AMH concentrations and that of the explanatory variables of interest (presence of fibroids, number of fibroids, uterine volume, and fibroid size, type, and position in each of the three planes). For analyses using the explanatory variables of

fibroid size, type, and position, characteristics of the largest fibroid were used. Separate analyses were also performed where only participants with a single fibroid were included (N=228). Means or medians (with standard deviations [SD] or interquartile ranges [IQR]) were calculated for continuous variables, while proportions were calculated for categorical variables. As AMH concentrations were not normally distributed, we compared median AMH concentrations of women with fibroids compared to those of women without fibroids using two-sample Wilcoxon rank-sum tests.

We used a multivariable linear regression model to estimate the percent difference in mean AMH concentration (β) and the corresponding 95% confidence intervals (CI) associated with each of the explanatory variables of interest. The covariates included in the multivariable models are: age, age^2, BMI, current use of any hormonal contraceptive, self-reported history of any thyroid condition, "seeking care for difficulty conceiving" and PCOS. We controlled for age using both linear and quadratic terms because of the non-linear association between age and AMH concentrations. We controlled for BMI, current use of hormonal contraceptives, any thyroid condition, and "seeking care for difficulty conceiving" as all these factors were found to be associated with AMH concentrations in previous analyses of this cohort (14). We also controlled for a self-reported diagnosis of polycystic ovarian syndrome (PCOS) given that AMH concentrations are associated with a history of PCOS in the literature (15). Although menstrual cycle length was also found to be associated with AMH concentrations in previous analyses of this cohort, cycle length can only be assessed accurately when a woman is off hormonal contraceptives. Therefore, given that we controlled for hormonal contraceptive use, menstrual cycle length was not included in the models.

We used multivariable models to assess trend of fibroid number and fibroid size. We treated fibroid number as categorical and adjusted for the same covariates discussed above. For the analysis of fibroid number, all participants were included. We also assessed trend for fibroid size, adjusting for all covariates discussed above. This analysis included participants with a single fibroid and those without fibroids (n= 1509).

For all analyses, we log-transformed AMH concentrations to account for non-normality and right-skewness in the distribution. All analyses were carried out using Statistical Analysis Software version 9.4 (SAS Institute, Cary, NC).

RESULTS

Baseline Characteristics

Of the 1,693 African American women enrolled in SELF, serum AMH concentrations were available for 1,643 individuals. There were no appreciable differences in baseline characteristics between those who did and did not have serum available for analysis (Supplemental Table 1). The mean age of participants (±SD) considered in this analysis was 29.2 ± 3.4 years (Table 1). The median AMH concentration was 4.07 ng/mL (IQR: 2.29–6.70). 362 participants (22.0%) were documented to have at least one fibroid on ultrasound. The majority of participants with fibroids had only one (63%), while 26.0% had

two or three fibroids and 11.0% had four or more fibroids. Additional fibroid characteristics of participants are presented in Table 2.

AMH and Fibroids

Unadjusted median AMH concentrations were lower among participants with ultrasound-detected fibroids at baseline (3.65 ng/mL, IQR: 2.09–5.79) than among participants without fibroids (4.25 ng/mL, IQR: 2.34–7.00), p<.001. In multivariable-adjusted analyses, the mean percent difference in AMH concentrations was attenuated (−4.6%, 95% CI: [−14.4%, 6.3%]) (Table 3).

AMH concentrations tended to decrease with increasing fibroid number. Compared with no fibroids, mean percent differences in AMH concentrations for 1, 2–3, and ≥4 fibroids were −1.2% (95% CI: [−13.2%, 12.5%]), −7.1% (95% CI: [−23.3%, 12.5%]) and −17.5% (95% CI: [−38.2%, 10.0%]), respectively (Table 3). When only participants with fibroids were analyzed, compared to those with one fibroid, mean percent differences in AMH concentrations for 2–3 and ≥4 fibroids were −7.6% (95% CI: [−23.6%, 11.8%]) and −20.5% (95% CI: [−39.2%, 3.9%]) (Supplemental Table 2). When a trend test was performed for categorical fibroid number, there was no significant association with AMH concentration (p=0.189)

There was no clear association between type of fibroid and AMH concentration. Relative to participants without fibroids, in women with fibroids, participants whose largest fibroid was submucosal had 16.7% higher AMH concentrations (95% CI: [−20.5, 71.2%]), while those whose largest fibroid was intramural had 4.8% lower AMH concentrations (95% CI: [−16.0%, 7.9%]) and those whose largest fibroid was subserosal or pedunculated had 8.8% lower AMH concentrations (95% CI: [−25.0%, 11.0%]) (Table 3). As demonstrated in Table 4, in participants with a single fibroid there was also no clear association between fibroid type and AMH concentration. Relative to participants without fibroids, those with submucosal fibroids had 20.1% higher AMH concentrations (95% CI: [−28.6, 102.0%]), while those with intramural fibroids had 0.5% higher AMH concentrations (95% CI: [−13.2%, 16.4%]) and those with subserosal or pedunculated fibroids had 11.2% lower AMH concentrations (95% CI: [−33.0%, 17.7%]). When only participants with fibroids were compared, there was also no significant association between fibroid type and AMH concentration (Supplemental Table 2)

Total uterine volume showed little association with AMH concentration. There was also no significant association between size of the largest fibroid and AMH concentration in participants with fibroids, when compared to those without fibroids (Table 3). When participants with a single fibroid were examined, fibroid size also showed no material association with AMH concentration (Table 4). When a trend test was performed for fibroid size, there was no significant association with AMH concentration either (p=0.642).

When all participants with fibroids were compared to those without fibroids, anterior-posterior, transverse or longitudinal position of the largest fibroid was not associated with AMH concentration (Table 3). There were also no appreciable associations between fibroid position and AMH concentration when participants with a single fibroid were examined

(Table 4). In addition, when only participants with fibroids were compared, there was no significant association with size or position of the largest fibroid and AMH concentration (Supplemental Table 2).

Results were not significantly different when analyses that only adjusted for age were performed (Supplemental Table 3). There were also no differences in results when analyses did not adjust for current use of hormonal contraceptives (Supplemental Table 3).

DISCUSSION

In this cross-sectional study of over 1,600 reproductive-aged African American women without a history of diagnosed fibroids, median AMH concentrations were not appreciably different among women with and without ultrasound-detected fibroids at enrollment. There was some evidence suggestive of an inverse monotonic relationship between fibroid number and AMH concentrations, but no consistent evidence of an association with fibroid size, type or position, albeit results were imprecise. These data suggest that fibroids and their characteristics are not likely to be strong predictors of AMH concentrations.

In this study individuals with more fibroids had lower AMH concentrations than those with fewer fibroids. AMH concentrations were 17% lower among women with four or more fibroids relative to women without fibroids, although the association between AMH and fibroid number was imprecise. When considering biological rationale for the potential relationship between fibroid number and AMH concentration, it is relevant to consider perfusion of the uterus and ovaries. Uterine fibroids mainly receive their peripheral blood supply from the uterine arteries (16). The ovaries are also perfused by a branch of the uterine artery, in addition to the ovarian artery (10, 11). It seems possible that fibroids could impact blood supply to the ovaries. In the presence of fibroids, the uterine artery and its branches can be distorted (10). Increased blood velocity and decreased resistance index in the uterine arteries have also been reported in women with uterine fibroids (17, 18). In women who have undergone ligation of the internal iliac artery, which supplies the uterine artery, AMH levels have been found to be lower (11). Further, when the impact of uterine artery embolization (UAE), which involves occlusion of the arteries perfusing the uterus, on ovarian reserve has been examined some studies have shown decreased AMH levels after UAE, though results have been mixed (9, 19–21). Although the ovary has a collateral blood supply and thus does not rely on perfusion from the uterine artery alone, it still seems plausible that an increased number of fibroids could lead to altered blood flow to the ovaries. It is logical to suspect that this may in turn reduce AMH concentrations.

When all participants with fibroids were examined, no single type of fibroid was strongly associated with AMH concentrations, although only the largest type of fibroid was included in the analysis. When participants with only one fibroid were examined, subserosal or pedunculated fibroids were associated with 11% lower AMH concentrations, possibly supporting a hypothesis that fibroids in those locations may alter blood flow accordingly. However, the lack of a clear association with uterine volume and the inconsistent results for fibroid size (i.e., the smallest fibroids were associated with the lowest AMH concentrations)

make the mechanism for an effect unclear. Thus, the results seen for fibroid number and AMH concentrations could also be due to chance.

The association between presence of fibroids and AMH concentrations is an important relationship to examine given the prevalence in reproductive-aged women and the clinical consequences if an association does exist. While work is still being done to better understand how AMH concentrations provide insight into female reproduction and to determine how and whether clinical care should be altered as a result, studies have shown that AMH concentration may be beneficial in not only in predicting time to menopause (8) but also in determining how individuals will respond to infertility treatment, particularly IVF. AMH concentrations are correlated with the number of oocytes retrieved with IVF (22) and higher oocyte yield is associated with higher live birth rates (23). Together these data suggest that individuals with lower AMH concentrations may have reduced pregnancy rates with IVF. If AMH concentrations were to be lower in the presence of fibroids, menopause timing may be influenced and IVF success rates may be compromised in individuals with fibroids.

This study has several strengths. It examines a large number of reproductive-aged African American women. If a relationship between fibroids and AMH concentrations does exist, the association is particularly relevant to African American women, who are disproportionately affected by fibroids (24). In addition, African American women with fibroids develop them at a younger age and have an increased severity of disease (24). More than 20% of participants had fibroids, thereby ensuring high statistical power to evaluate our hypotheses. Another strength was the systematic collection of numerous fibroid characteristics through ultrasound, which has high sensitivity and specificity relative to histologic evidence. Given that participants with known fibroids were excluded, ultrasound was used to diagnose fibroids and the study did not rely on participants' self-report. Importantly, ultrasounds were performed by experienced sonographers who underwent specialized training. Finally, to ensure consistency in the data, a single lab assay was used to obtain all AMH concentrations.

Study limitations include the cross-sectional design, which makes the temporality of associations unclear, and the fact that SELF was designed to enroll women without a previous diagnosis of fibroids. Assuming that all women with fibroids at enrollment had asymptomatic fibroids, their fibroids were likely to be newer, smaller, and less representative of the full spectrum of disease in the general population. Moreover, the fibroids may not have been present long enough to have an influence on AMH concentrations. Thus, we cannot rule out the possibility that symptomatic fibroids are associated with AMH levels. It is also possible that this study investigated women too early in their reproductive years for fibroids to have an influence on AMH concentrations. The incidence of ultrasound-detected fibroids in African American women has been shown to be 26% by age 30 (25), 60% by age 35 and over 80% by age 50 with a mean age at diagnoses of 33 years (2). Thus, our findings may not generalize to older women. Finally, results were imprecise for the analyses of fibroid characteristics, due to the limited variation in fibroid size and number among cases and the large sample size needed to comprehensively evaluate fibroid type and location.

CONCLUSIONS

These data suggest that uterine fibroids are not likely to be strong determinants of AMH concentrations in young reproductive-aged African American women. The presence of fibroids was not materially associated with AMH concentrations. Other than a monotonic inverse relationship between fibroid number and AMH concentrations, no other fibroid characteristics were consistently or appreciably associated, although associations were imprecise. Further investigation into the relationship between fibroids and AMH levels among older women and women with symptomatic disease may be warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Capsule:

Fibroid presence was not materially associated with Anti-Müllerian hormone (AMH) concentrations. Besides a monotonic inverse relationship between fibroid number and AMH, no other fibroid characteristics were consistently or appreciably associated.

Table 1:

Baseline characteristics of 1643 SELF participants, 2010–2012

	Fibroid presence	
	Yes (n=362)	**No (n=1281)**
Age at enrollment, y (mean ± SD; range)[a]	30.5 ± 3.1; 23–35	28.8 ± 3.5; 23–35
Body mass index, kg/m^2 (mean ± SD; range)	33.8 ± 9.0; 18.1–65.0	33.7 ± 9.8; 15.9–79.4
AMH, ng/mL (median, IQR)	3.65 (3.2)	4.25 (4.7)
AMH, ng/mL (range)	<0.06–28.1	<0.002–55.7
Education (%)		
High school/GED or less	18.0	23.2
Some college, associate's, or technical degree	45.6	51.2
Bachelor's or graduate degree	36.5	25.5
Annual household income (%)		
Less than $20,000	41.7	46.9
$20,000–50,000	35.1	36.9
More than $50,000	22.9	15.3
Current smoker (%)	18.5	19.4
Current user of hormonal contraception (%)	26.0	28.6
Menstrual cycle length (%)		
25–35 days	66.9	60.4
<25 days	21.8	20.5
>35 days or irregular	5.8	10.2
One or less period in past 12 months	5.0	8.1
Unknown	0.6	0.8
History of polycystic ovarian syndrome (%)	2.5	3.4
History of abnormal menstrual bleeding (%)	10.8	11.6
History of thyroid condition (%)	3.6	2.7
History of seeking care for difficulty conceiving (%)	6.6	5.6
History of previous birth (%)	52.5	63.4
Number of pregnancies (mean ± SD; range)[b]	3.0 ± 1.9; 1–11	3.1 ± 2.0; 1–15
Uterine volume, cm^3 (mean ± SD; range)	126.5 ± 87.5; 29.9–890.1	95.9 ± 47.2; 8.4–395.6

SELF=Study of Environment, Lifestyle and Fibroids; SD=standard deviation; IQR=interquartile range; AMH= Anti-Müllerian Hormone; GED=general equivalency degree.

[a]Women ages 23–34 were recruited, but some women had turned 35 by the time that all baseline activities and enrollment were completed.

[b]Among gravid women.

Table 2:

Fibroid characteristics in participants with fibroids (n=362)

	Among all participants with fibroids[a] (n=362)	Among participants with only a single fibroid (n=228)
Number of fibroids (mean ± SD; range)	1.8 ± 1.4; 1–10	1.0
Fibroid size (cm)		
Mean (± SD; range) Categorical (%)	2.0 ± 1.5; 0.4–9.0	1.7 ± 1.4; 0.4–9.0
<1	25.1	35.1
1-<2	40.1	40.4
2-<3	14.4	10.1
3-<4	8.3	4.8
≥4	10.5	7.0
Type of Fibroid (%)		
Submucosal	6.1	5.3
Intramural	69.1	76.3
Subserosal	21.5	16.2
Pedunculated serosal	3.3	2.2
Anterior-posterior position (%)		
Anterior	45.0	45.2
Middle	14.1	14.0
Posterior	40.9	40.8
Transverse position (%)		
Right	41.7	42.1
Middle	22.7	21.1
Left	34.5	35.1
Unclear position	1.1	1.8
Longitudinal position (%)		
Fundus	37.6	31.6
Corpus	58.6	64.5
Lower uterine segment/cervix	3.9	3.9

[a]Only characteristics of the largest fibroid were included for participants with more than one fibroid

Table 3:

The association between fibroid characteristics and AMH concentrations in all participants with fibroids

	N	Estimate of % change in AMH (95% CI)	
Fibroids present		**Age-adjusted model[a]**	**Multivariable model[b]**
No	1281	Reference	
Yes	362	−4.6% (−14.5%, 6.5%)	−4.6% (−14.4%, 6.3%)
Number of fibroids [c]			
1	228	−1.3% (−13.4%, 12.5%)	−1.2% (−13.2%, 12.5%)
2–3	94	−5.6% (−22.3%, 14.7%)	−7.1% (−23.3%, 12.5%)
4 or more	40	−19.6% (−39.9%, 7.8%)	−17.5% (−38.2%, 10.0%)
Size of largest fibroid [c,d]			
<1cm	91	−11.0% (−27.0%, 8.4%)	−10.3% (−26.2%, 8.9%)
1 to <2cm	145	−1.9% (−16.4%, 15.1%)	−1.8% (−16.1%, 15.0%)
≥2cm	120	−4.0% (−19.4%, 14.4%)	−5.1% (−20.3%, 12.9%)
Type of largest fibroid [c,d]			
Submucosal	22	16.5% (−21.1%, 72.0%)	16.7% (−20.5%, 71.2%)
Intramural	250	−5.4% (−16.7%, 7.4%)	−4.8% (−16.0%, 7.9%)
Subserosal/Pendunculated	90	−6.7% (−23.5%, 13.8%)	−8.8% (−25.0%, 11.0%)
Anterior-posterior position of largest fibroid [c,d]			
Anterior	163	0.7% (−13.5%, 17.3%)	0.5% (−13.5%, 16.7%)
Middle	51	−11.9% (−32.1%, 14.2%)	−12.9% (−32.7%, 12.7%)
Posterior	148	−7.5% (−21.1%, 8.3%)	−7.2% (−20.6%, 8.5%)
Transverse position of largest fibroid [c,d]			
Right	151	−3.8% (−17.8%, 12.6%)	−3.2% (−17.1%, 13.0%)
Middle	82	−13.6% (−29.8%, 6.4%)	−12.0% (−28.4%, 8.1%)
Left	125	−0.5% (−16.1%, 18.0%)	−2.3% (−17.5%, 15.6%)
Longitudinal position of largest fibroid [c,d]			
Fundus	136	−6.9% (−21.0%, 9.8%)	−6.3% (−20.4%, 10.2%)
Corpus	212	−3.4% (−15.7%, 10.7%)	−3.5% (−15.6%, 10.4%)
Uterine volume (all women)			
<64.7cm^3 (1st quartile)	410	Reference	
64.7–89.3cm^3 (2nd quartile)	409	9.2% (−3.7%, 24.0%)	8.4% (−4.4%, 22.9%)
89.3–124.8cm^3 (3rd quartile)	413	−1.2% (−13.0%, 12.2%)	−1.7% (−13.4%, 11.5%)

	N	Estimate of % change in AMH (95% CI)	
Fibroids present		**Age-adjusted model[a]**	**Multivariable model[b]**
≥124.8cm^3 (4th quartile)	411	6.1% (−6.8%, 20.9%)	6.4% (−6.6%, 21.3%)

[a] The model adjusted for age and age^2

[b] The multivariable model adjusted for age, age^2, BMI, current use of any hormonal contraceptive, and self-reported history of any thyroid condition, “seeking care for difficulty conceiving”, or PCOS.

[c] Reference group is participants without fibroids

[d] All participants with fibroids included, but characteristics of largest fibroid used for analysis

Table 4:

The association between fibroid characteristics and AMH concentrations in participants with only a single fibroid[a]

	N	Estimate of % change AMH (95% CI)	
Fibroid size		**Age-adjusted model[b]**	**Multivariable model[c]**
<1cm	80	−12.8% (−29.4, 7.7%)	−11.0% (−27.7%, 9.6%)
1 to <2cm	92	−3.3% (−20.6%, 17.8%)	−3.6% (−20.7%, 17.2%)
≥2cm	50	22.0% (−6.3%, 58.8%)	20.0% (−7.7%, 56.0%)
Type of fibroid			
Submucosal	12	22.1% (−28.0%, 107.1%)	20.1% (−28.6%, 102.0%)
Intramural	174	−0.7% (−14.4%, 15.2%)	0.5% (−13.2%, 16.4%)
Subserosal/Pendunculated	42	−8.1% (−30.9%, 22.3%)	−11.2% (−33.0%, 17.7%)
Anterior-posterior position			
Anterior	103	4.3% (−13.5%, 25.8%)	4.1% (−13.4%, 25.1%)
Middle	32	6.8% (−23.0%, 48.1%)	6.1% (−23.4%, 47.1%)
Posterior	93	−9.1% (−25.3%, 10.6%)	−8.2% (−24.4%, 11.4%)
Transverse position			
Right	96	1.3% (−16.5%, 22.9%)	1.6% (−16.0%, 22.9%)
Middle	48	−14.1% (−34.3%, 12.4%)	−12.8% (−33.3%, 13.9%)
Left	80	2.5% (−16.9%, 26.6%)	2.2% (−17.1%, 25.9%)
Longitudinal position			
Fundus	72	−1.4% (−21.0%, 23.0%)	−0.7% (−20.2%, 23.5%)
Corpus	147	−1.2% (−15.8%, 16.0%)	−0.6% (−15.2%, 16.4%)

[a] Reference group is participants without fibroids

[b] The model adjusted for age and age^2

[c] The multivariable model adjusted for age, age^2, BMI, current use of any hormonal contraceptive, and self-reported history of any thyroid condition, “seeking care for difficulty conceiving”, or PCOS.