Baseline Antimüllerian Hormone Level Does Not Serve as a Predictor of Uterine Fibroid Treatment Outcomes

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Objective: *To evaluate whether baseline serum antimüllerian hormone (AMH) concentration predicts symptom severity (SS) and quality of life (QOL) 1 year following uterine fibroid treatment with hysterectomy or non-hysteroscopic myomectomy.*

Methods: *A large multi-institutional observational cohort study enrolled individuals undergoing uterine fibroid therapies from 11/11/2015-9/29/2019. We measured serum AMH concentrations before treatment (baseline) for a subset of participants younger than 45 years at enrollment. QOL was assessed at baseline and 1 year after treatment. Propensity score methods adjusted for selection bias and confounding variables and estimated differences in 1-year scores between treatment groups (hysterectomy vs myomectomy) with a weighted general linear model.*

Results: *Baseline median AMH concentration was higher for the myomectomy group (n=143) than for the hysterectomy group (n=129) (1.4 vs 0.7 ng/mL, P=.002) and mean (SD) SS scores were higher for the hysterectomy group than for the myomectomy group (61.3 [22.7] vs 50.6 [25.9], P<.001). After 1 year, all scores had improved for both groups. After adjustment for other baseline characteristics, 1-year posttreatment SS and QOL scores did not differ according to baseline AMH level (≤1.0 vs >1.0 ng/mL) for either group.*

Conclusions: *Baseline serum AMH level did not modify health-related QOL outcomes at 1 year following uterine fibroid treatment.*

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BACKGROUND

Uterine leiomyomas—also termed myomas or uterine fibroids (UFs)—are a leading cause of morbidity among individuals of reproductive age and a major cause of health disparities.[1,2] Symptomatic UFs are associated with considerably impaired health-related quality of life (HR-QOL)[3, 4] measured by both general and disease-specific validated scales.

High-quality evidence about the comparative effectiveness of UF treatment options is lacking, and no biomarkers of treatment response are known. Since 2015, the Comparing Options for Management: Patient-Centered Results for Uterine Fibroids (COMPARE-UF) observational cohort study (NCT02260752, clinicaltrials.gov), has been comparing the effectiveness of UF procedures among participants who underwent scheduled surgical or procedural UF treatment.[5-11] Findings of the COMPARE-UF trial indicate that myomectomy and hysterectomy improve both short-term and long-term QOL for patients, and the level of improvement varies by procedure type and route (i.e., abdominal vs minimally invasive). Antimüllerian hormone (AMH) is a glycoprotein hormone with homology to transforming growth factor β that is synthesized by granulosa cells in antral and preantral ovarian follicles and thus can serve as a biomarker of functional ovarian reserve.[12]

Clinically, AMH is a reliable predictor of ovarian response among patients undergoing fertility treatment[13] but not of spontaneous fertility in patients aged 30 to 44 years.[14] One prior cohort study reported that lower baseline serum AMH levels were associated with reduced rates of subsequent interventions for patients with UFs undergoing uterine artery embolization or magnetic resonance–guided focused ultrasound surgery (MRgFUS).[15] Because fibroid growth and symptomatology decrease as ovarian function wanes during the perimenopausal transition, we hypothesize that AMH levels may serve as a biomarker for response to UF treatment. Studies evaluating the extent to which AMH concentrations modify the association between UF treatment and QOL are even more scarce. Thus, the goal of our analyses was to examine the extent to which the association between UF treatment and QOL 1 year after UF surgical treatment (myomectomy and hysterectomy) varies according to AMH level at time of UF treatment.

MATERIALS AND METHODS

Details regarding the COMPARE-UF study design and methods have been reported previously.[5] Briefly, the Duke Clinical Research Institute in Durham, North Carolina, served as the research data and coordinating center for the trial, and the following 8 clinical centers enrolled participants: Mayo Clinic Collaborative Network, University of California Fibroid Network, Henry Ford Health System, University of Mississippi Medical Center, University of Michigan, University of North Carolina, Brigham and Women's Hospital/Harvard Medical School Collaboration, and Inova Health System.

COMPARE-UF was conducted at multiple clinical centers throughout the US to provide geographic and demographic diversity and to ensure appropriate representation of self-identified Black or African American participants because these patients are affected more frequently by this disease, have a greater extent of disease, and have an earlier age of onset.[2]

Study Population

Investigators enrolled consecutive eligible patients scheduled to undergo procedural interventions for UFs at a facility affiliated with a COMPARE-UF study clinical center under a common Institutional Review Board protocol. Participants were at least 18 years old, premenopausal, and had documented UFs. Participants were enrolled from November 11, 2015, through August 29, 2019. Studied interventions included hysterectomy (abdominal, laparoscopic/robotic, and vaginal), myomectomy (abdominal, hysteroscopic, and laparoscopic/robotic), endometrial ablation, laparoscopic radiofrequency UF ablation, uterine artery embolization, MRgFUS, and progestin-

releasing intrauterine devices. The current analyses focused on the 2 most common treatments: hysterectomy and myomectomy.

Serum Collection and AMH Analysis

Women under the age of 45 years were offered enrollment in the AMH substudy reported here. Those who consented to this substudy had a blood sample drawn before treatment (baseline) and a second sample drawn 1 year after undergoing UF treatment. Immediately after blood collection, serum was isolated and frozen at −80 at each participating clinical site. Samples were shipped on dry ice to Mayo Clinic for analysis. Duplicate serum samples were assayed for AMH concentrations in a single lot by using an ultrasensitive enzyme-linked immunoassay (Ansh Labs) at Mayo Clinic Laboratories in Rochester, MN. The limit of detection for the assay was 0.03 ng/mL, and the normal range for women aged 13 to 44 years was 0.9 to 9.5 ng/mL.

Data Collection and Follow-up

HR-QOL was assessed[16] via a self-administered questionnaire at baseline and 1 year after UF treatment with the Uterine Fibroid Symptom–HR-QOL (UFS-QOL), which is a validated disease-specific instrument, and the 5-Level EuroQol-5 Dimension (EQ-5D-5L), which is a validated instrument for general HR-QOL.[4,17,18] Both instruments use a 5-point Likert scale. The UFS-QOL consists of an 8-question symptom severity scale (SSS) and 29 questions related to HR-QOL; the total UFS-QOL measure also has 6 component subscales measuring activity, concern, control, energy, self-consciousness, and sexual function.[16] All scores are measured with a 100-point scale, and a higher SSS score indicates more symptoms, whereas a higher total UFS-QOL score indicates better QOL.[16] The EQ-5D-5L is measured with a visual analog scale (VAS), in which a score of 100 represents best imaginable health.[4, 17, 18] For the self-care, usual activities, and pain and discomfort questions on the EQ-5D-5L, we summarized the percentage of respondents reporting the top 3 Likert categories (moderate, severe, and extreme) [4,17,18].

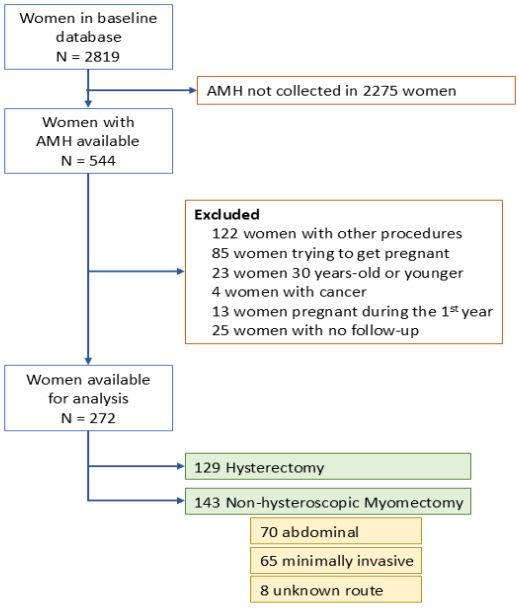
Statistical Analyses

We initially compared mean (SD) or median (IQR) values between groups for normally distributed and nonnormally distributed data, respectively. Propensity score methods were used to adjust for baseline characteristics of participants who for baseline characteristics of participants who underwent different UF treatments.16,19 The propensity score was estimated for each patient through a logistic regression model with hysterectomy procedure (yes or no) as the dependent variable and the following patient characteristics as the independent variables: age, race/ethnicity, insurance type, time since UF diagnosis, previous UF procedures, heavy menstrual bleeding, prior pregnancies, and components of the UFS-QOL and EQ-5D-5L VAS. Interactions between baseline serum AMH concentration and key variables were also included in the propensity score model. Continuous variables were assessed for nonlinearity by fitting restricted cubic splines. The estimated propensity scores were used to derive overlapping weights.[19] QOL outcomes at 1 year (UFS-QOL total score and components and EQ-5D-5L VAS) were compared between treatment groups by using a weighted general linear model with robust variance estimates.

Baseline variables with missing values were multiply imputed by using the full-conditional specification method in SAS PROC MI (SAS Institute Inc). To conduct imputations, we included all important confounders and additional variables available in the COMPARE-UF dataset. Because of the low percentage of missing data for any given covariate (<5%), we used a single imputation data set in this analysis, which is consistent with previous publications from this registry and prior sensitivity analyses that showed no difference from using multiple imputation.

Our initial analysis of serum AMH levels used a categorical variable (high vs low) with a cut point at the median concentration of all participants. We

Figure 1: Flow Diagram of Patients Included in Analysis. Patients were enrolled in a large prospective multi-institutional clinical trial of uterine fibroid management.



also analyzed a cut point of 0.3 ng/mL or less because this concentration was used in a prior study analyzing UF outcomes according to pretreatment serum AMH levels.[15]

RESULTS

Among 544 participants who provided a baseline serum sample before undergoing UF treatment (Figure 1), we restricted our analyses to those who underwent hysterectomy or myomectomy because too few underwent the following treatments for analysis: hysteroscopic myomectomy (n=54), uterine artery embolization (n=29), MRgFUS (n=7), laparoscopic radiofrequency ablation (n=5), or other treatments including medical management (n=27). We also excluded participants with baseline serum samples who reported the following events in the year after hysterectomy or myomectomy: pregnancy (n=13), active pursuit of pregnancy (n=85), diagnosis of cancer (n=4), or loss to follow-up (n=25). We also excluded 23 participants aged 30 years because no participants in this age group underwent hysterectomy.[6, 8, 10] The final analytic sample included 272 participants aged more than 30 years, of whom 143 underwent myomectomy and 129 underwent hysterectomy by any surgical approach.

Our study population reflected the US population with symptomatic UFs (Table I). Most participants (54.1%) were aged 31 to 40 years, and 45.0% self-reported a race other than White (31.7% Black and13.3% other). Mean (SD) body mass index was 29.8 (8.4). UF symptoms persisted for a mean (SD) of 5.4 (6.2) years. Few patients (18.1%) had undergone prior interventional UF therapy, and 47.4% of participants had a history of anemia, with 7.5% of these participants requiring transfusion before study participation. Many baseline characteristics differed between the myomectomy and hysterectomy treatment groups (Table I). On average, participants who underwent myomectomy were younger, had a lower body mass index, and had an earlier age at UF diagnosis and onset of first symptoms than did those who underwent hysterectomy. More participants who underwent myomectomy had regular menses than did those who underwent hysterectomy. Fewer participants who underwent myomectomy had ever been pregnant, attempted conception for more than 1 year, or had other chronic medical

Table1 : Baseline Characteristics of COMPARE-UF Participants According to UF Treatment Type[a]

Characteristic	Total (N=272)	Myomectomy (n=143)	Hysterectomy (n=129)
Age group, y			
31-35	66 (24.3)	55 (38.5)	11 (8.5)
36-40	81 (29.8)	47 (32.9)	34 (26.4)
41-45	107 (39.3)	39 (27.3)	68 (52.7)
>45	18 (6.6)	2 (1.4)	16 (12.4)
Race	(n=271)	(n=142)	(n=129)
Black	86 (31.7)	49 (34.5)	37 (28.7)
White	149 (55.0)	70 (49.3)	79 (61.2)
Other	36 (13.3)	23 (16.2)	13 (10.1)
Hispanic ethnicity	18 (6.7)(n=269)	7 (5.0)(n=140)	11 (8.5)(n=129)
Private insurance	236 (87.4)(n=270)	120 (85.1)(n=141)	116 (89.9)(n=129)
BMI	29.8 (8.4)	28.2 (7.5)	31.6 (8.9)
Age at UF diagnosis, y	34.5 (6.4)	33.5 (5.3)	35.6 (7.3)
Any UF symptoms	258 (94.9)	136 (95.1)	122 (94.6)
Age at first UF symptoms, y	34.1 (6.9)	32.9 (6.0)	35.5 (7.6)
Duration of UF symptoms, y	5.4 (6.2)	4.8 (5.1)	6.0 (7.2)
Family history of UFs	134 (49.8)(n=269)	70 (49.3)(n=142)	64 (50.4)(n=127)
Any previous UF treatment	49 (18.1)(n=271)	19 (13.3)(n=143)	30 (23.4)(n=128)
Current contraception use	234 (86.0)	125 (87.4)	109 (84.5)
Regular, predictable menses	178 (65.9)(n=270)	108 (76.1)(n=142)	70 (54.7)(n=128)
History of anemia	128 (47.4)(n=270)	67 (47.2)(n=142)	61 (47.7)(n=128)
Requiring transfusion	20 (7.5)(n=268)	10 (7.0)(n=143)	10 (8.0)(n=125)
Ever pregnant	154 (57.0)(n=270)	64 (45.1)(n=142)	90 (70.3)(n=128)
≥2 pregnancies	108 (40.3)(n=268)	37 (26.2)(n=141)	71 (55.9)(n=127)
Ever tried for >1 year to get pregnant	47 (17.3)(n=271)	17 (12.0)(n=271)	30 (23.3)(n=129)
Previous medical condition[b]	106 (39.4)(n=269)	39 (27.5)(n=142)	67 (52.8)(n=127)
History of gynecologic symptoms[c]	43 (16.0)(n=269)	16 (11.3)(n=142)	27 (21.3)(n=127)
Tobacco use	19 (7.1)(n=269)	9 (6.3)(n=143)	10 (7.9)(n=126)
Alcohol use	208 (87.8)(n=237)	117 (93.6)(n=125)	91 (81.3)(n=112)
Marijuana use	25 (9.3)(n=269)	17 (12.0)(n=142)	8 (6.3)(n=127)
Surgical approach	(n=264)	(n=135)	(n=129)
Laparoscopic/robotic	169 (64.0)	65 (48.1)	104 (80.6)
Abdominal	95 (36.0)	70 (51.9)	25 (19.4)
Serum AMH concentration, ng/mL	1.8 (1.9)	2.0 (1.9)	1.5 (1.9)
Serum AMH concentration group			
≤1 ng/mL	139 (51.1)	59 (41.3)	80 (62.0)
>1 ng/mL	133 (48.9)	84 (58.7)	49 (38.0)

Abbreviations:
AMH, antimüllerian hormone; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); UF, uterine fibroid.

[a] Categorical data summarized as No. (%) of participants. Continuous data summarized as mean (SD).

[b] Previous medical conditions included high blood pressure, diabetes, asthma, thyroid problems, and blood clots in the legs or lungs.

[c] Gynecologic symptoms included polycystic ovary syndrome, endometriosis, and adenomyosis.

conditions than did those who had hysterectomy. Because of the differences between treatment groups for these baseline characteristics, we controlled for these variables in further analyses.

Mean (SD) serum AMH levels at baseline were lower in women who underwent hysterectomy (1.5 [1.9] ng/mL) than in those who underwent myomectomy (2.0 [1.9] ng/mL, P=.02).

Table 2 : Baseline Serum AMH Concentration According to Participant Characteristics and UF Treatment

Characteristic	Median (IQR) serum AMH concentration, ng/mL		
	Total	Myomectomy	Hysterectomy
All women	1.0 (0.4-2.5)	1.4 (0.7-2.8)	0.7 (0.2-2.3)
Age group			
≤40 y	1.8 (0.9-3.3)	1.9 (0.9-3.1)	1.2 (0.6-3.3)
>40 y	0.5 (0.2-1.5)	0.6 (0.3-1.5)	0.5 (0.2-1.5)
Race			
Black	1.3 (0.5-3.1)	1.5 (0.9-3.1)	1.0 (0.3-3.0)
White	0.9 (0.3-2.5)	1.5 (0.7-2.8)	0.6 (0.2-1.8)
Other	1.0 (0.3-2.2)	1.0 (0.5-2.6)	0.7 (0.3-2.0)
Race and age group			
Black and ≤40 y	1.7 (1.0-3.8)	2.0 (1.2-4.4)	1.3 (0.6-3.6)
Black and >40 y	0.5 (0.3-1.5)	0.4 (0.4-0.9)	0.7 (0.1-3.0)
White and ≤40 y	1.9 (0.8-3.2)	1.9 (0.8-2.8)	1.9 (0.8-3.3)
White and >40 y	0.5 (0.2-0.9)	0.6 (0.3-1.5)	0.4 (0.1-0.9)
Other and ≤40 y	1.0 (0.8-2.1)	1.2 (0.8-2.4)	–[a]
Other and >40 y	0.7 (0.3-2.3)	0.7 (0.1-3.1)	1.3 (0.3-2.2)

Abbreviations:
AMH, antimüllerian hormone; UF, uterine fibroid.
[a] Only 1 participant in the other race and ≤ 40 y age group underwent hysterectomy during the study period; therefore, median (IQR) values were not calculated.

Among all study participants, the mean (SD) baseline AMH concentration was 1.8 (1.9) ng/mL (Table I), and the median (IQR) AMH concentration was 1.0 (0.4-2.5) ng/mL (Table II). For participants 40 years or younger, two-thirds had a serum AMH concentration greater than 1.0 ng/mL. The distribution of AMH concentrations did not markedly differ among self-reported race groups or groups defined by both age and race. Although both treatment groups had high UF symptom severity at baseline, as measured by the SSS of the UFS-QOL, participants who underwent hysterectomy had a higher mean (SD) SSS score (61.3 [22.7]) at baseline than did those who underwent myomectomy (50.6 [25.9], P<.001) (Table III). However, HR-QOL scores from both the UFS-QOL and EQ-5D-5L were similar for both treatment groups except for the UFS-QOL sub score for concern, which was appreciably higher among participants who underwent myomectomy (47.4 [34.8]) than for those who underwent hysterectomy (44.2 [28.3], P=.02). At 1 year after UF treatment, both adjusted and unadjusted HR-QOL scores had improved for all validated QOL measures in both treatment groups. However, participants undergoing had better (higher) HR-QOL scores and lower SSS scores than participants undergoing myomectomy, and these scores did not differ from baseline AMH levels (Table IV). We also performed 2 additional sensitivity analyses to validate these results. First, we analyzed all participants enrolled in COMPARE-UF who were not enrolled in this sub study but were older than 40 years, which approximated women with low

Table 3 : Baseline HR-QOL Scores According to UF Treatment[a]

HR-QOL measure	Total (N=272)	Myomectomy (n=143)	Hysterectomy (n=129)	P
		UFS-QOL		
Symptom severity	55.6 (25.0)	50.6 (25.9)	61.3 (22.7)	<.001
Total HR-QOL	46.2 (26.8)	48.5 (28.0)	43.1 (24.7)	.14
Activity	47.2 (29.8)	49.3 (30.9)	38.2 (27.5)	.20
Concern	43.0 (31.9)	47.4 (34.8)	44.2 (28.3)	.02
Control	47.7 (27.5)	46.3 (29.7)	49.2 (25.0)	.38
Energy	47.2 (27.9)	49.6 (30.9)	44.5 (23.8)	.12
Self-consciousness	42.4 (31.5)	44.5 (32.4)	39.4 (29.9)	.23
Sexual function	48.4 (33.9)	51.7 (35.3)	44.8 (32.0)	.10
EQ-5D-5L				
VAS score	70.6 (19.9)	72.6 (19.7)	68.4 (19.8)	.09
Moderate or higher self-care	6 (2.2)	5 (3.5)	1 (0.8)	.22
Moderate or higher usual activities	44 (16.2) (n=271)	22 (15.4) (n=143)	22 (17.2) (n=128)	.69
Moderate or higher pain and discomfort	127 (46.7)	63 (44.1)	64 (49.6)	.36

Abbreviations:
EQ-5D-5L, 5-Level EuroQol-5 Dimension; HR-QOL, health-related quality of life; UF, uterine fibroid; UFS-QOL, Uterine Fibroid Symptom–health-related quality of life; VAS, visual analog scale.
[a] Continuous HR-QOL score data summarized as mean (SD), and EQ-5D-5L dimensions summarized as No. (%) of participants.

ovarian reserve, and observed similar results (data not shown). Second, we repeated this analysis with a baseline serum AMH concentration of 0.3 ng/mL as a more stringent cut point to represent markedly decreased ovarian reserve and again observed no meaningful differences in unadjusted or adjusted HR-QOL scores between treatment groups (P≥08) (Table V).

Surgical approach is an important factor for HR-QOL at 1 year after myomectomy. 8 Therefore, we performed sub analyses of baseline participant characteristics, baseline HR-QOL scores, and HR-QOL scores at 1 year after treatment stratified by dichotomized baseline serum AMH concentration (≥1.0 vs >1.0 ng/mL) for participants who underwent laparoscopic/robotic myomectomy (n=65) or abdominal myomectomy (n=70) (Tables VI-VIII). Women who underwent laparoscopic/robotic myomectomy had a lower baseline mean (SD) body mass index (26.4 [6.7]) than did those who underwent abdominal myomectomy (30.0 [7.9], P=.006), but these cohorts were otherwise similar with respect to other baseline characteristics (P≥07) (Table VI). Baseline HR-QOL scores did not differ between the surgical approaches (P≥.07) (Table VII).

Similarly, unadjusted and adjusted HR-QOL scores at 1 year after UF treatment stratified by serum AMH concentrations of 1.0 ng/mL or less vs more than 1.0 ng/mL did not differ between surgical approaches (P≥13) (Table VIII).

Table 4 : Mean HR-QOL Scores at 1 Year After UF Treatment According to Dichotomized Baseline AMH Concentration (≤1.0 vs >1.0 ng/mL)

HR-QOL measure/AMH level	Unadjusted				Adjusted[a]			
	Myomectomy	Hysterectomy	Difference in score (95% CI) [b]	P	Myomectomy	Hysterectomy	Difference in score (95% CI) [b]	P
UFS-QOL								
Symptom severity				.86				.26
≤1.0 ng/mL	17.1	7.6	−9.5 (−14.7 to 4.3)		20.2	6.3	−13.9 (−20.2 to 7.6)	
>1.0 ng/mL	16.8	7.9	−8.8 (−14.3 to 3.3)		15.9	7.2	−8.8 (−15.0 to2.5)	
Total HRQOL				.76				.42
≤1.0 ng/mL	87.4	95.2	7.8 (2.4 to 13.3)		86.0	97.0	11.1 (5.7 to 16.4)	
>1.0 ng/mL	87.6	94.2	6.6 (0.9 to 12.4)		86.8	94.2	7.4 (0.3 to 14.4)	
Activity				.75				.87
≤1.0 ng/mL	89.6	96.1	6.5 (0.9 to 12.0)		89.0	97.5	8.5 (2.5 to 14.5)	
>1.0 ng/mL	90.5	95.6	5.2 (−0.6 to 10.9)		87.5	95.2	7.7 (−0.2 to 15.6)	
Concern				.46				.22
≤1.0 ng/mL	83.7	97.9	14.1 (7.9 to 20.3)		79.7	98.8	19.1 (10.6 to 27.6)	
>1.0 ng/mL	86.8	97.6	10.8 (4.3 to 17.3)		85.5	97.7	12.2 (5.1 to 19.3)	
Control				.78				.34
≤1.0 ng/mL	89.9	96.0	6.1 (0.3 to 12.0)		88.8	97.5	8.7 (3.2 to 14.1)	
>1.0 ng/mL	86.8	94.1	7.3 (1.2 to 13.5)		89.2	93.5	4.1 (−3.5 to 11.6)	
Energy				.90				.54
≤1.0 ng/mL	88.7	94.1	5.4 (−0.6 to 11.4)		88.0	96.4	8.3 (3.4 to 13.3)	
>1.0 ng/mL	86.9	93	6.0 (−0.3 to 12.2)		87.3	92.6	5.4 (−2.6 to 13.3)	
Self-conscious				.55				.50
≤1.0 ng/mL	82.3	92.0	9.7 (2.1 to 17.3)		81.9	95.1	13.2 (6.0 to 20.4)	
>1.0 ng/mL	85.2	91.5	6.3 (−1.6 to 14.3)		82.6	91.3	8.7 (−2.2 to 19.6)	
Sexual function				.83				.68
≤1.0 ng/mL	85.4	92.2	6.8 (−1.0 to 14.6)		82.9	95.2	12.3 (2.8 to 21.8)	
>1.0 ng/mL	87.8	93.4	5.6 (−2.8 to 13.9)		86.3	95.8	9.5 (0.2 to 18.8)	
EQ-5D-5LVAS				.78				.73
≤1.0 ng/mL	83.4	80.3	−3.1 (−7.9 to 1.8)		81.9	82.7	0.9 (−5.0 to 6.7)	
>1.0 ng/mL	83.6	81.5	−2.0 (−7.1 to 3.0)		83.4	82.8	−0.5 (−5.8 to 4.8)	

Abbreviations:
AMH, antimüllerian hormone; EQ-5D-5L, 5-Level EuroQol-5 Dimension; HR-QOL, health-related quality of life; UF, uterine fibroid; UFS-QOL, Uterine Fibroid Symptom–health-related quality of life; VAS, visual analog scale.
[a] Values were adjusted for age, race/ethnicity, insurance type, time since UF diagnosis, prior UF treatment, heavy menstrual bleeding, previous pregnancies, and components of the UFS-QOL and EQ-5D-5L VAS.
[b] Difference in HR-QOL score was determined by subtracting the score for the myomectomy group from that of the hysterectomy group.

Table 5: Mean HR-QOL Scores at 1 Year After UF Treatment According to Dichotomized Baseline Serum AMH Concentration (≤0.3 vs >0.3. ng/mL)[a]

	Unadjusted				Adjusted			
HR-QOL measure/AMH level	**Myomectomy**	**Hysterectomy**	**Difference In score (95% CI) [c]**	**P**	**Myomectomy**	**Hysterectomy**	**Difference in score (95% CI) [c]**	**P**
USF-QOL								
Symptom severity				.11				.28
≤0.3 ng/mL	23.1	7.6	–15.5 (–23.6 to 7.4)		23.9	7.1	–16.8 (–27.9 to –5.7)	
>0.3 ng/mL	15.9	7.8	–8.1(–12.4 to-3.8)		17.0	7.0	–10.0 (–14.9 to –5.1)	
Total HR-QOL				.32				.50
≤0.3 ng/mL	85.7	96.6	11.0(2.5 to 19.4)		87.8	98.9	11.2(3.9 to 18.4)	
>0.3 ng/mL	87.8	93.9	6.1 (1.6 to 10.6)		86.6	94.6	8 (2.5 to 13.5)	
Concern				.36				.49
≤0.3 ng/mL	81.7	98.2	16.5 (6.8 to26.2)		80.6	99.4	18.8(5.7 to 32.0)	
>0.3 ng/mL	86.1	97.5	11.4 (6.2 to 16.5)		83.9	97.6	13.7 (7.7 to 19.7)	
Activity				.45				.96
≤0.3 ng/mL	88.6	97.2	8.6 (0.0 to 17.2)		91.8	98.7	6.9 (–0.1 to 13.9)	
>0.3 ng/mL	90.4	95.2	4.9 (0.3 to 9.4)		88.5	95.7	7.2(1.3 to 13.0)	
Energy				.28				.36
≤0.3 ng/mL	84.9	95.3	10.4 (1.1 to 19.8)		89.1	99.0	9.9(2.8 to 17.1)	
>0.3 ng/mL	88.1	92.7	4.6 (–0.3 to 9.5)		87.8	93.4	5.6(–0.2 to 11.4)	
Control				.90				.83
≤0.3 ng/mL	91.2	98.2	6.9 (–2.2 to 16.1)		92.4	99.6	7.2(0.7 to 13.6)	
>0.3 ng/mL	87.6	93.8	6.2 (1.4 to 11.0)		88.1	94.2	6.2(0.1 to 12.3)	
Self-conscious				.31				.66
≤0.3 ng/mL	80.9	94	13.1 (1.2 to 25.0)		84.5	97.3	12.8(2.5 to 23.1)	
>0.3 ng/mL	84.5	90.6	6.1 (–0.2 to 12.4)		82.1	92.0	9.9 (1.7 to 18.0)	
Sexual function				.12				.37
≤0.3 ng/mL	80.6	95	14.4 (2.2 to 26.6)		80.3	98.9	18.6(–2.4 to 39.6)	
>0.3 ng/mL	87.8	91.3	3.5 (–3.0 to 10.0)		86.1	94.6	8.4(1.0 to 15.8)	
EQ-5D-5L VAS				.08				.30
≤0.3 ng/mL	80.4	83.4	3.0 (–4.6 to 10.6)		79.3	84.6	5.3(–6.4 to 16.9)	
>0.3 ng/mL	84.0	79.4	–4.6 (–8.5 to –0.6)		83.0	81.7	–1.3(–5.8 to 3.1)	

Abbreviations:
AMH, antimüllerian hormone; EQ-5D-5L, 5-Level EuroQol-5 Dimension; HR-QOL, health-related quality of life; UF, uterine fibroid; UFS-QOL, Uterine Fibroid Symptom–health-related quality of life; VAS, visual analog scale.
a Women with AMH ≤0.3 ng/mL (n=65; myomectomy, n=20; hysterectomy, n=45); women with AMH >0.3 ng/mL (n=207; myomectomy, n=123; hysterectomy, n=84).
b Values were adjusted for age, race/ethnicity, insurance type, time since UF diagnosis, prior UF treatment, heavy menstrual bleeding, previous pregnancies, and components of the UFS-QOL and EQ-5D-5L VAS.
c Difference in HR-QOL score was determined by subtracting the score for the myomectomy group from that of the hysterectomy group.

Table 6: Baseline Characteristics of Included Participants According to Myomectomy Surgical Approach[a].

Characteristic	Total (n=135)	Abdominal (n=70)	Laparoscopic/ robotic(n=65)	P
Age group, y				.93
31-35	52 (38.5)	27 (39)	25 (38)	
36-40	44 (32.6)	24 (34)	20 (31)	
41-45	37 (27.4)	18 (26)	19 (29)	
>45	2 (1.5)	1 (1)	1 (2)	
Race	(n=134)	(n=70)	(n=64)	.07
Black	49 (36.6)	32 (46)	17 (27)	
White	62 (46.3)	28 (40)	34 (53)	
Other	23 (17.2)	10 (14)	13 (20)	
Hispanic ethnicity	7 (5.3)(n=132)	3 (4)(n=70)	4 (6)(n=63)	.71
Private insurance	112 (84.2)(n=133)	59 (84)(n=70)	53 (84)(n=63)	.98
BMI	28.3 (7.5)	30.0 (7.9)	26.4 (6.7)	.006
Age at UF diagnosis, y	33.5 (5.4)	32.8 (4.8)	34.3 (5.9)	.09
Any UF symptoms	128 (94.8)	67 (96)	61 (94)	.71
Age at first UF symptoms, y	32.8 (6.1)	32.8 (5.8)	32.9 (6.4)	.92
Duration of UF symptoms, y	4.9 (5.2)	4.9 (5.2)	4.9 (5.3)	.99
Family history of UFs	66 (49.3)(n=134)	37 (54)(n=69)	29 (45)(n=65)	.45
Any previous UF treatment	17 (12.6)	9 (13)	8 (12)	.92
Current contraception use	117 (86.7)	60 (86)	57 (88)	.74
Regular, predictable menses	102 (76.1)(n=134)	56 (80)(n=70)	46 (72)(n=64)	.27
History of anemia	65 (48.5)(n=134)	36 (51)(n=70)	29 (45)(n=64)	.48
Requiring transfusion	9 (6.7)	6 (9)	3 (5)	.50
Ever pregnant	61 (45.5)(n=134)	29 (41)(n=70)	32 (50)(n=64)	.32
≤2 pregnancies	34 (25.6)(n=133)	15 (21)(n=70)	19 (30)(n=63)	.25
Ever tried for >1 year to get pregnant	17 (12.7)(n=134)	9 (13)(n=70)	8 (13)(n=64)	.95

Previous medical condition[b]	**39 (29.1)(n=134)**	**22 (31)(n=70)**	**17 (27)(n=64)**	**.54**
Serum AMH concentration, ng/mL	2.1 (2.0)	2.2 (2.0)	2.0 (2.0)	.57
Serum AMH concentration group				.38
≤1.0 ng/mL	55 (40.7)	26 (37)	29 (45)	
>1.0 ng/mL	80 (59.3)	44 (63)	36 (55)	

Abbreviations:

AMH, antimüllerian hormone; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); UF, uterine fibroid.
[a] Categorical data summarized as No. (%) of participants. Continuous data summarized as mean (SD).
[b] Previous medical conditions included high blood pressure, diabetes, asthma, thyroid problems, and blood clots in the legs or lungs.

Table 7 : Baseline HR-QOL Scores According to Myomectomy Surgical Approach[a].

HR-QOL measure	Total (n=135)	Abdominal (n=70)	Laparoscopic/robotic (n=65)	P
USF-QOL				
Symptom severity	50.0 (26.2)	51.3 (27.1)	48.7 (25.3)	.56
Total QOL	48.5 (28.3)	46.8 (29.3)	50.3 (27.2)	.48
Concern	47.7 (35.2)	44.2 (33.8)	51.4 (36.6)	.24
Activity	49.1 (31.1)	47.5 (32.2)	50.7 (30.0)	.56
Energy	50.2 (31.0)	48.9 (31.6)	51.6 (30.5)	.62
Control	46.4 (30.3)	46.4 (31.0)	46.5 (29.7)	.98
Self-conscious	44.1 (32.2)	39.0 (32.5)	49.4 (31.2)	.07
Sexual function	52.5 (35.4)	48.5 (36.4)	56.7 (34.0)	.18
EQ-5D-5L				
VAS score	73.0 (19.8)	72.2 (20.8)	74.0 (18.7)	.60
Moderate or higher self-care	5 (3.7)	4 (6)	1 (2)	.37
Moderate or higher usual activities	20 (14.8)	13 (19)	7 (11)	.20
Moderate or higher pain and discomfort	60 (44.4)	32 (46)	28 (43)	.76

Abbreviations:
EQ-5D-5L, 5-Level EuroQol-5 Dimension; HR-QOL, health-related quality of life; UFS-QOL, Uterine Fibroid Symptom–health-related quality of life; VAS, visual analog scale.
a Continuous HR-QOL score data summarized as mean (SD), and EQ-5D-5L dimensions summarized as No. (%) of participants.

Table 8 : Mean HR-QOL Scores at 1 Year After UF Treatment According to Myomectomy Surgical Approach and Dichotomized Baseline AMH Concentration (£1.0 vs >1.0 ng/mL)

HR-QOL measure/AMH level	Unadjusted				Adjusted[a]			
	Abdominal	Laparoscopic/ robotic	Difference in score (95% CI) [b]	P	Abdominal	Laparoscopic/ robotic	Difference in score (95% CI) [b]	P
USF-QOL								
Symptom severity				.54				.62
≤1.0 ng/mL	16.1	17.2	–1.1 (–10.2 to 8.0)		18.3	20.9	–2.6 (–19.6 to 14.5)	
>1.0 ng/mL	18.4	15.8	2.6 (–4.9 to 10.1)		18.3	15.9	2.4 (–6.8 to 11.6)	
Total QOL				.69				.31
≤1.0 ng/mL	87.8	86.6	1.3 (–8.2 to 10.7)		88.1	82	6.1 (–7.4 to 19.5)	
>1.0 ng/mL	86.7	87.9	–1.3 (–9.1 to 6.6)		89.5	89	0.5 (–6.7 to 7.7)	
Concern				.18				.31
≤1.0 ng/mL	86.3	81.6	4.8 (–7.1 to 16.7)		85.2	77.1	8.1 (–11.2 to 27.4)	
>1.0 ng/mL	83.7	89.4	–5.7 (–15.6 to 4.2)		86.9	89.8	–2.9 (–11.3 to 5.5)	
Activity				.59				.45
≤1.0 ng/mL	91.2	86.8	4.3 (–5.4 to 14.1)		89.9	81.7	8.2 (–6.8 to 23.1)	
>1.0 ng/mL	90.5	89.6	0.9 (–7.2 to 9.0)		93.7	91.8	1.9 (–4.7 to 8.6)	
Energy				.71				.94
≤1.0 ng/mL	88.4	89.3	–0.9 (–11.0 to 9.2)		86.8	86.7	0.1 (–14.4 to 14.5)	
>1.0 ng/mL	85.0	88.4	–3.4 (–11.8 to 5.0)		88.5	89.1	–0.6 (–9.2 to 7.9)	
Control				.55				.13
≤1.0 ng/mL	91.7	87.6	4.1 (–6.4 to 14.5)		94.2	82.7	11.5 (0.3 to 22.7)	
>1.0 ng/mL	86.4	86.4	–0.1 (–8.7 to 8.6)		87.8	87.7	0.1 (–9.2 to 9.5)	
Self-conscious				.37				.79
≤1.0 ng/mL	79.2	85.7	–6.5 (–19.9 to 7.0)		83.1	79.9	3.2 (–13.9 to 20.2)	
>1.0 ng/mL	85.4	83.8	1.6 (–9.6 to 12.8)		88.6	82.7	6.0 (–6.2 to 18.1)	
Sexual function				.32				.68
≤1.0 ng/mL	81.3	87.5	–6.2 (–19.5 to 7.0)		86.2	80.7	5.6 (–14.4 to 25.5)	
>1.0 ng/mL	88.9	86.5	2.5 (–8.5 to 13.5)		89.9	89	0.9 (–8.7 to 10.5)	
EQ-5D-5L VAS				.44				.97
≤1.0 ng/mL	85.0	83.0	2.0 (–4.3 to 8.3)		85.4	83.9	1.5 (–6.7 to 9.6)	
>1.0 ng/mL	83.4	84.7	–1.2 (–6.5 to 4.0)		85.1	83.4	1.7(–4.4 to 7.8)	

Abbreviations:
AMH, antimüllerian hormone; EQ-5D-5L, 5-Level EuroQol-5 Dimension; HR-QOL, health-related quality of life; UF, uterine fibroid; UFS-QOL, Uterine Fibroid Symptom–health-related quality of life; VAS, visual analog scale.
[a] Values were adjusted for age, race/ethnicity, insurance type, time since UF diagnosis, prior UF treatment, heavy menstrual bleeding, previous pregnancies, and components of the UFS-QOL and EQ-5D-5L VAS.
[b] Difference in HR-QOL score was determined by subtracting the score for the laparoscopic/robotic group from that of the abdominal group.

DISCUSSION

UF growth and symptoms are dependent on the sex steroid hormones estrogen and progesterone. Although estrogens were classically considered an important contributor to UFs, progesterone is now known to be the more critical mediator of UF development, and estrogens permissively contribute to UFs through induction of the progesterone receptor.[20] Thus, the hypothesis that serum level of AMH a marker of ovarian function and thereby sex steroid production can modify the response to hysterectomy or myomectomy is reasonable. Moreover, UF symptoms generally wane for many people as they approach menopause, and decreased ovarian reserve (and AMH level) is a plausible contributor to this decrease in symptoms. However, this hypothesis was not supported by our findings.
At 1 year after surgical treatment, participants who underwent hysterectomy reported better QOL and less symptom severity than did those who underwent myomectomy. Participant AMH level before surgical treatment did not modify these associations. Therefore, baseline serum AMH level does not appear to be a useful biomarker for UF treatment outcomes at 1 year after hysterectomy or myomectomy. Additional studies are needed to investigate additional UF therapies, longer-term outcomes of UF treatment, and potential predictors of these outcomes.
This study was limited to a subset of participants, and our analyses excluded treatments other than myomectomy and hysterectomy. The follow-up period in this analysis was 1 year, and baseline serum AMH level could be an important determinant of HR QOL outcomes measured at longer follow-up times. Because the procedures that had the largest sample sizes (e.g., abdominal and laparoscopic/robotic myomectomy and hysterectomy) have the longest postoperative recovery times of UF treatments-, longer follow-up times may be necessary to observe clinically different outcomes according to baseline serum AMH level.
Although serum AMH level is a known predictor of pregnancy outcomes for women undergoing infertility treatment, only 1 prior study examined AMH level as a predictor of UF treatment outcomes, but that study was limited by small sample size.[15]
The range of serum AMH concentrations in study populations span 2 orders of magnitude, and this range is typically nonnormally distributed.[14, 21-23] The serum AMH levels linked to decreased reproductive function (i.e., reduced ovarian reserve) may differ from those associated with HR-QOL after UF treatment. Indeed, fertility begins to decrease for women in their mid-30s, but UF symptoms do not wane until women approach menopause, which typically occurs a decade or more later.
We first used the median serum AMH level of our study cohort (1.0 ng/mL), which is in the range of normal ovarian reserve. This median AMH level is similar to that reported in another cohort study, in which the median (1.27 ng/mL) AMH level in women aged 38 to 44 years was determined with the same assay used in our study.[14] A serum AMH level of 1.0 ng/mL is generally considered to be a normal level for a population seeking fertility care, such as in vitro fertilization, although our population was older than this core group.[14] Nevertheless, we did not observe any differences in HR-QOL outcomes by using an AMH concentration of 1.0 ng/mL as a cut point.
We next performed a sensitivity analysis with a cut point of 0.3 ng/mL, which generally represents markedly decreased ovarian reserve among those seeking fertility care. At this serum AMH level, the corresponding waning of sex steroid hormones would potentially augment positive outcomes of UF treatment, such as symptom improvement, because UFs are dependent on both estrogen and progesterone.

However, HR-QOL outcomes did not differ according to this AMH concentration cut point, and broadening our analysis according to age alone to represent decreased ovarian reserve resulted in similar findings.

The strengths of our study include its prospective design and racial and geographic heterogeneity of the study population. The broad baseline data collected (i.e., reduced potential for confounding variables), standardization of data for UF procedures facilitated adjustment for many potential confounders. This work was strengthened using validated methods for baseline serum AMH concentration measurement and validated measures for symptom severity and QOL (i.e., reduced potential for misclassification and dependent errors). However, long-term follow-up is critical to understanding the use of factors related to individual responses to various UF therapies. The likelihood of additional interventions for recurrent UFs or new formation of UFs increases with time after the primary intervention.[24] However, research on UF treatment recurrence has generally not been coupled with validated measures of symptom severity and QOL. Thus, additional follow-up of the COMPARE-UF cohort and analyses will provide a currently unreported longitudinal perspective that will be critical to the research question we addressed in this study.

CONCLUSION

Baseline serum AMH level did not modify standardized measures of health-related QOL outcomes at 1 year following surgical and interventional uterine fibroid treatment.

DECLARATIONS

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Conflicts of Interest

The other authors report no conflicts of interest.

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