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Evaluating Risk Factors for Differences in Fibroid Size and Number Using a Large Electronic Health Record Population

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Abstract

Objective: To evaluate individual characteristics of women with fibroids in relation to fibroid size and number.

Methods: This cross-sectional study involved 2,302 women (black and white, age range 18–87) with image- or surgery-confirmed fibroids from the Synthetic Derivative, a database of de-identified demographic and clinical information from patient electronic health records (EHRs) from the Vanderbilt University Medical Center. We performed multivariate regression analyses on the following outcomes: volume of largest fibroid, largest dimension of all fibroids, and number of fibroids (single vs multiple). Candidate risk factors included age at diagnosis, body mass index

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Contributors

Michael J. Bray, Todd L. Edwards, and Digna R. Velez Edwards designed the study.
Michael J. Bray and Sarah H. Jones contributed to data collection.
Michael J. Bray, Eric S. Torstenson, and Digna R. Velez Edwards analyzed the data.
All authors helped with manuscript drafting and critically reviewed the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This study was evaluated and approved by the Vanderbilt University Medical Center Institutional Review Board (IRB).

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Data will be made available on request.

(BMI), race, type 2 diabetes status, and number of living children (a proxy for parity). We assessed potential effect measure modification by race and both age and BMI using a likelihood ratio test.

Results: Black race was strongly associated with having multiple fibroids (adjusted odds ratio [aOR]: 1.83, 95% confidence interval [CI]: 1.49, 2.24) and larger fibroid volume (adjusted beta: 1.77, 95% CI: 1.38, 2.27) and greater largest dimension (adjusted beta: 1.28, 95% CI: 1.18, 1.38). Having multiple fibroids was most strongly associated with ages 43 to 47 (aOR = 3.37, 95% CI: 2.55, 4.46) compared with the youngest age group (ages 18 to 36). Having a larger number of living children was associated with having single a fibroid (aOR: 0.88, 95% CI: 0.78, 0.99).

Conclusions: Our findings suggest that different underlying etiologies are involved for women developing single versus multiple fibroids and small versus large fibroids.. Studies are needed of the mechanisms by which these characteristics influence fibroid formation and growth.

Keywords

uterine fibroids; leiomyomata; epidemiology; electronic health records

1. Introduction

The majority of women in the United States have at least one uterine fibroid by the age of menopause [1]. Fibroids are a major cause of hysterectomies [2], which are primarily done to manage symptoms [3] and cost the U.S. up to $34.4 billion annually in healthcare, treatment, and time lost from work [4]. Fibroids vary in size and number between women, leading to a range of symptoms including: pressure of the abdomen, chronic pelvic pain, and heavy or painful periods [5]. In addition, presence of multiple fibroids has associated with preterm birth and cesarean delivery, while large fibroids have associated with preterm premature rupture of membranes [6]. Increasing body mass index (BMI; kg/m^2) [7], nulliparity [8, 9], and being African American (compared to being white) [10–13] have previously been associated with fibroid risk. In contrast, women with type 2 diabetes are less likely to develop fibroids [14, 15].

Although fibroid risk factors have been well-documented [7, 8, 10–13], limited studies that examine factors of fibroid size and number exist. One potential reason for the lack of studies on fibroid characteristics is that fibroid size and number can only be assessed by imaging or surgical procedures (such as ultrasounds or hysterectomies). As a result, few studies have examined risk factors for fibroid characteristics. In a study by our group, we found an inverse relationship between age at menarche and fibroid number and size using the *Right From the Start* (2001–2010) cohort, in confirming reproductive hormonal exposure is a significant factor influencing fibroids [16]. A cross-sectional study of 988 women (630 cases) who had ultrasound results from the National Institute of Environmental Health Sciences Uterine Fibroid Study reported that decreased levels of insulin-like growth factor-I were associated with having small- (<2 cm) and medium- (≥2 to <4 cm) sized fibroid in white women, and decreased insulin levels were associated with having a large fibroid (≥4 cm), especially in black women [17]. In another cross-sectional study from the *Prospective Research on Ovarian Function Study*, fibroid characteristics, abstracted from pathology and operative notes, and key risk factors were compared between black and white women

(N=360) undergoing hysterectomies [18]. The authors found that black women, on average, had larger and more numerous fibroids than white women [18]. The authors also found that nulligravid black and white women were more likely to have larger fibroids, and nulligravid white women were more likely to have multiple fibroids than white women with one or more pregnancies [18].

Individual characteristics of a woman may put her at risk of developing single versus multiple fibroids or a small versus large fibroid. Knowing which of these characteristics is strongly associated with fibroid size and number might allow for better understanding of the mechanisms underlying individual variation in fibroid size and number. Our objective was to identify individual characteristics of a woman associated with fibroid size or number. We examined the association of fibroid volume, largest fibroid dimension, and fibroid number with candidate risk factors using a clinical population of 2,302 women identified from electronic health records (EHRs).

2. Materials and Methods

2.1. Study Population - The Synthetic Derivative

We conducted our analyses using subjects from the Synthetic Derivative, a clinical population at Vanderbilt University Medical Center [19] consisting of de-identified demographic and clinical information from patient EHRs. We used a previously validated phenotyping algorithm with a positive predictive value of 96% to identify fibroid cases [20]. The algorithm included black and white women who were 18 years or older, had at least one International Classification of Diseases, 9^{th} Revision (ICD-9) or current procedure terminology (CPT) code for pelvic imaging, and had at least one ICD-9 or CPT code indicating a fibroid diagnosis. Fibroid status for 2,302 cases was manually validated by examining image or surgical reports from patient EHRs. We manually extracted dimensions for each reported fibroid, number of fibroids, and relevant demographic information from pelvic imaging reports, including ultrasound, magnetic resonance imaging, and computed tomography scans or surgical reports from myomectomies and hysterectomies. Precedence for recording patient information was given to the first image report mentioning fibroids. If a patient's EHR lacked an image report citing fibroids, we entered patient data from the first surgical report describing their fibroids.

We abstracted fibroid number (single vs. multiple), volume of largest fibroid (cm^3), and largest dimension (cm) of all reported fibroids. The following formula for volume of an ellipsoid was used to calculate fibroid volume: length × width × height × 0.523. The largest fibroid dimension and volume measurements were log10-transformed to accommodate the assumption of normally distributed residuals for linear regression. For individuals with two recorded dimensions of their largest fibroid (35.6% of cases), we assigned the last measurement by averaging the initial two to calculate fibroid volume. For individuals with data for number of fibroids, some EHRs (18.6%) noted the presence of many fibroids but gave no specific number. Because of this limitation, we coded fibroid number as one versus multiple fibroids.

Abstracted clinical characteristics included age at diagnosis, BMI (continuous), selfreported or clinically identified race, type 2 diabetes status, and number of living children. We used previously published programming algorithms to abstract type 2 diabetes from EHRs [21]. Number of living children was chosen as a proxy for parity. In addition, we abstracted indication for imaging and fibroid location. This study was evaluated and approved by the Vanderbilt University Medical Center Institutional Review Board (IRB).

2.2. Statistical Analyses

We performed univariate and multivariate regression analyses for the following outcomes: volume of largest fibroid, largest dimension of all fibroids, and number of fibroids (single vs. multiple). Exposures included age at diagnosis, BMI, race, type 2 diabetes status, and number of living children (numbered 0 through 5 and 6 or more grouped together) as covariates. All multivariate regression analyses included age, BMI, and race as covariates. Age and BMI were not normally distributed and had nonlinear effect sizes; therefore, analyses were performed by grouping age into quintiles and BMI into World Health Organization (WHO) categories [22]. Too few underweight individuals were in our dataset (underweight N=27), so we combined individuals from the underweight and normal weight categories. We assessed potential effect measure modification by race across age quintiles and BMI categories using a likelihood ratio test. A likelihood ratio test p-value of 0.10 or less was considered an interaction.

In secondary analyses, multiple imputation was performed for missing data (number of living children) for each outcome to determine if missingness in this exposure affected our analyses. All exposures in the multivariate regression model and outcome were included in each multiple imputation data model. Each dataset was imputed ten times. To ensure consistency in multiple imputation analyses, the random number generation functions were seeded with the number 12,345. Multiple imputation analyses were largely consistent with effect sizes estimated from non-imputed data; therefore, we present and discuss results herein using non-imputed missing data. Lastly, Stata/SE 13 (College Station, Texas) was used for all statistical analyses.

3. Results

Our study population included 2,302 individuals with fibroids (Table 1). Their mean age (± SD) was 45.5 years ± 12, and the majority were overweight (29%) or obese (44%). The average BMI (± SD) was 30.4 kg/m^2. The mean volume (± SD) of largest fibroid and mean largest fibroid dimension (± SD) were 71.4 cm^3 ± 202 cm^3 and 3.7 cm ± 3 cm, respectively. Fibroid number was dichotomized (single vs. multiple), and more women (52%) had multiple fibroids.

Fibroid number

Increasing age had a nonlinear association with having multiple fibroids (Table 2). The strongest association was observed when comparing ages 43 to 47 to the referent group (ages 18 to 36) (adjusted odds ratio [aOR]: 3.37, 95% confidence interval [CI]: 2.55, 4.46). Black race associated with having multiple fibroids (aOR: 1.83, 95% CI: 1.49, 2.24), while

having a higher number of living children was associated with having fewer fibroids (aOR: 0.88, 95% CI: 0.78, 0.99). BMI and type 2 diabetes were not associate with fibroid number. We did not observe evidence of effect measure modification by race on age or BMI for analyses of fibroid number (age - p = 0.739, BMI - p = 0.632).

Fibroid size (volume and largest dimension)

Increasing age had a nonlinear association with both fibroid volume and largest fibroid dimension (Table 3 and Table 4).The strongest effect of age on fibroid volume (adjusted beta: 1.57, 95% 1.12, 2.22) (Table 3) and dimension (adjusted beta: 1.19, 95% CI: 1.07, 1.32) (Table 4) was for women between 48 and 54 years of age. Black race also associated with increasing fibroid volume (adjusted beta: 1.77, 95% CI: 1.38, 2.27) and larger dimensions (adjusted beta: 1.28, 95% CI: 1.18, 1.38). BMI, type 2 diabetes, and number of living children were not associated with fibroid volume or largest dimension. There was no effect modification by race on age or BMI for our analyses of fibroid volume (age - p = 0.281, BMI - p = 0.172) or largest dimension (age - p = 0.414; BMI - p = 0.144).

4. Discussion

In this analysis of individual characteristics as they relate to fibroid size and number, we observed no synergistic interaction of race with age or race with BMI. This suggests effects of age and BMI do not fundamentally vary by race so that they can be considered primary rather than joint influences on fibroid size and number. Increasing age was nonlinearly associated with fibroid number and size, with risk peaking at premenopause/early menopause and then declining for subsequent age groups. This is consistent with overall fibroid risk which also increases until menopause [1]. Our findings are also consistent with a study of women undergoing hysterectomies that observed postmenopausal women had smaller and fewer fibroids compared to premenopausal women [23]. However, the authors found little difference in fibroid risk with regards to menopausal status [23]. Our findings combined with prior studies support a hormonal influence on size and number of fibroids, which become relatively dormant after menopause. Fibroids have not been documented in prepubescent girls [24], confirming fibroids have a hormonal component. A plausible model is that fibroids form and progress as a result of cumulative exposure to hormones, including estrogen and progesterone. In effect with increasing age women have greater exposure time as well as more cumulative calendar time in which to develop one or more fibroids. After menopause, estrogen and progesterone fall and fibroid progression/development is stunted.

BMI was not associated with fibroid number or size in our study. However, in a previous study of women who had a hysterectomy, increasing BMI was associated with fibroid risk but not with largest fibroid dimension [7]. This lack of an association between BMI and fibroid size or number could mean that BMI influences fibroid risk and not progression. This may suggest that the increased exposure to estrogen resulting from increasing obesity [13] is not a driver for larger or multiple fibroids.

Type 2 diabetes was also not associated with fibroid number or size in our study. Diabetes has inversely associated with fibroid risk in prior studies, including a study by our group that observed an OR of 0.61 (95% CI: 0.47, 0.80) for the association [15]. However, studies

evaluating the association between diabetes and fibroid size or number are limited. One study evaluated the association between diabetes metabolites and fibroid size in white and black women and observed an inverse association between insulin-like growth factor-I and fibroid size in both white and black women [17]. The authors had approximately 92 individuals with diabetes (including gestational diabetes) and could not perform association analyses between diabetes and fibroid size [17]. The lack of an association between type 2 diabetes and fibroid number and size could mean that our sample size was too small with 317 diabetic women. Further larger powered studies are necessary to better understand the association between type 2 diabetes and fibroids size and number. Additionally, it is possible that the effect of diabetes on fibroids is due to exposure to specific diabetes medications, which we did not evaluate in our analyses.

Parity was not consistently documented in the EHRs, and we used number of living children as a proxy. We observed that having more children was associated with single fibroids, suggesting that the hormonal effects of pregnancy may reduce the number of fibroids present. This is consistent with prior studies that showed uterine involutions during childbirth are associated with loss of fibroids [25]. This is also consistent with literature showing that women with higher parity are at reduced risk for fibroids (relative risk: 0.5, 95% CI: 0.4, 0.6) [9]. The protective effects of carrying a child to term could not only decrease the risk of having fibroids but also the number of fibroids. We also observed trends showing an increased number of living children associated with smaller fibroid sizes. In addition, we cannot rule out the possibility that women with multiple fibroid may be less able to become pregnant and have children. Future studies need to examine if a higher number of children (increased parity) is associated with decreased fibroid number or if having less children is a byproduct of having multiple fibroids.

Limitations in our study exist. Race was determined by a third-party source such as a physician or nurse to be either black or white. We note that there may be dissimilarities in the risks of different fibroid characteristics between African and African American women. However, were unable to distinguish country of origin from medical records and therefore summarized data only according to race (black and white). Our study population represents patients from within Vanderbilt University Medical Center. We cannot rule out that women had previous treatment (surgical or hormonal at other medical institutions). In addition, we did not assess fibroid treatments prior to imaging event and note that there may differences in fibroid size and number from women who previously sought treatment.

Using a dataset of EHRs consisting of women with image- or surgery-confirmed fibroids, we found that black race was associated with multiple and larger fibroids. We also observed that increasing age was nonlinearly associated with multiple and larger fibroids, with the trends for these fibroid characteristics varying across age groups. Lastly, we observed that multiple fibroids (but not size) were associated with an increasing number of living children. A strength of our study is focusing on women with fibroids rather than directly comparing to controls. Prior studies examining the relationship between fibroid characteristics and risk factors compared each characteristic to controls. With that approach, it is difficult to determine if the observed effect is due to a woman having a fibroid or differences in fibroid

size or number. Our findings suggest that different underlying etiologies are involved for women developing single versus multiple fibroids and small versus large fibroids.

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References

[1]. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. American journal of obstetrics and gynecology. 2003; 188(1):100–7. [PubMed: 12548202]

[2]. Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990–1997. Obstetrics and gynecology. 2002; 99(2):229–34. [PubMed: 11814502]

[3]. Parker WH. Uterine myomas: management. Fertility and sterility. 2007; 88(2):255–71. [PubMed: 17658523]

[4]. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. American journal of obstetrics and gynecology. 2012; 206(3):211 e1–9. [PubMed: 22244472]

[5]. Zimmermann A, Bernuit D, Gerlinger C, Schaefers M, Geppert K. Prevalence, symptoms and management of uterine fibroids: an international internet-based survey of 21,746 women. BMC women's health. 2012; 12:6. [PubMed: 22448610]

[6]. Ciavattini A, Clemente N, Delli Carpini G, Di Giuseppe J, Giannubilo SR, Tranquilli AL. Number and size of uterine fibroids and obstetric outcomes. The journal of maternal- fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2015; 28(4):484–8.

[7]. Dandolu V, Singh R, Lidicker J, Harmanli O. BMI and uterine size: is there any relationship? International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2010; 29(6):568–71. [PubMed: 20881854]

[8]. Parazzini F. Risk factors for clinically diagnosed uterine fibroids in women around menopause. Maturitas. 2006; 55(2):174–9. [PubMed: 16533580]

[9]. Parazzini F, Negri E, La Vecchia C, Chatenoud L, Ricci E, Guarnerio P. Reproductive factors and risk of uterine fibroids. Epidemiology. 1996; 7(4):440–2. [PubMed: 8793374]

[10]. Ligon AH, Morton CC. Genetics of uterine leiomyomata. Genes, chromosomes & cancer. 2000; 28(3):235–45. [PubMed: 10862029]

[11]. Ligon AH, Morton CC. Leiomyomata: heritability and cytogenetic studies. Human reproduction update. 2001; 7(1):8–14. [PubMed: 11212080]

[12]. Morton CC. Genetic approaches to the study of uterine leiomyomata. Environmental health perspectives. 2000; 108(Suppl 5):775–8. [PubMed: 11035981]

[13]. Walker CL, Stewart EA. Uterine fibroids: the elephant in the room. Science. 2005; 308(5728): 1589–92. [PubMed: 15947177]

[14]. Wise LA, Palmer JR, Stewart EA, Rosenberg L. Polycystic ovary syndrome and risk of uterine leiomyomata. Fertility and sterility. 2007; 87(5):1108–15. [PubMed: 17241625]

[15]. Velez Edwards DR, Hartmann KE, Wellons M, Shah A, Xu H, Edwards TL. Evaluating the role of race and medication in protection of uterine fibroids by type 2 diabetes exposure. BMC women's health. 2017; 17(1):28. [PubMed: 28399866]

[16]. Velez Edwards DR, Baird DD, Hartmann KE. Association of age at menarche with increasing number of fibroids in a cohort of women who underwent standardized ultrasound assessment. American journal of epidemiology. 2013; 178(3):426–33. [PubMed: 23817917]

[17]. Baird DD, Travlos G, Wilson R, Dunson DB, Hill MC, D'Aloisio AA, London SJ, Schectman JM. Uterine leiomyomata in relation to insulin-like growth factor-I, insulin, and diabetes. Epidemiology. 2009; 20(4):604–10. [PubMed: 19305350]

[18]. Moorman PG, Leppert P, Myers ER, Wang F. Comparison of characteristics of fibroids in African American and white women undergoing premenopausal hysterectomy. Fertility and sterility. 2013; 99(3):768–776 e1. [PubMed: 23199610]

[19]. Roden DM, Pulley JM, Basford MA, Bernard GR, Clayton EW, Balser JR, Masys DR. Development of a large-scale de-identified DNA biobank to enable personalized medicine. Clinical pharmacology and therapeutics. 2008; 84(3):362–9. [PubMed: 18500243]

[20]. Feingold-Link L, Edwards TL, Jones S, Hartmann KE, Velez Edwards DR. Enhancing uterine fibroid research through utilization of biorepositories linked to electronic medical record data. Journal of women's health. 2014; 23(12):1027–32.

[21]. Kho AN, Hayes MG, Rasmussen-Torvik L, Pacheco JA, Thompson WK, Armstrong LL, Denny JC, Peissig PL, Miller AW, Wei WQ, Bielinski SJ, Chute CG, Leibson CL, Jarvik GP, Crosslin DR, Carlson CS, Newton KM, Wolf WA, Chisholm RL, Lowe WL. Use of diverse electronic medical record systems to identify genetic risk for type 2 diabetes within a genome-wide association study. Journal of the American Medical Informatics Association : JAMIA. 2012; 19(2):212–8. [PubMed: 22101970]

[22]. Obesity: preventing and managing the global epidemic Report of a WHO consultation, World Health Organization technical report series. 2000; 894:i–xii. 1. [PubMed: 11234459]

[23]. Cramer SF, Patel A. The frequency of uterine leiomyomas. American journal of clinical pathology. 1990; 94(4):435–8. [PubMed: 2220671]

[24]. Stewart EA. Uterine fibroids. Lancet. 2001; 357(9252):293–8. [PubMed: 11214143]

[25]. Baird DD, Dunson DB. Why is parity protective for uterine fibroids? Epidemiology (Cambridge, Mass.). 2003; 14(2):247–50.

Highlights

- The objective of this study was to identify the individual characteristics of a woman associated with fibroid size and number.
- Black race was associated with multiple and larger fibroids.
- Increasing age was nonlinearly associated with fibroid size and number, with risk peaking at premenopause/early menopause and then declining for subsequent age groups.
- The presence of multiple fibroids was associated with a larger number of living children (a proxy for parity) but the size of the fibroids was not.
- There are different underlying etiologies for single versus multiple fibroids and small versus large fibroids.

Table 1.

Demographic characteristics of Synthetic Derivative study population.

Characteristics	N	Study Population
Age (mean±SD)	2,302	45.5±12
18 to 36 (%)	510	22
37 to 42 (%)	438	19
43 to 47 (%)	442	19
48 to 54 (%)	493	21
55 to 87 (%)	419	18
BMI (kg/m^2) (mean±SD)	2,302	30.4±8
Underweight (<18.5) (%)	27	1
Normal Weight (18.5-24.9) (%)	606	26
Overweight (25-29.9) (%)	663	29
Obese (≥30) (%)	1,006	44
Race (%)	2,302	
White	1,616	70
Black	686	30
Indication for Imaging (%)[a]	1,375	
Pain	565	41
Pressure	39	2
Bleeding	848	62
Reproductive Ultrasounds[b]	120	9
Procedure Planning[c]	19	1
Fibroid Location (%)[a]	1,092	
Intramural	320	29
Submucosal	545	50
Subserosal	447	41
Pedunculated	77	7
Fibroid Volume (cm^3) (mean±SD)	1,307	71.4 (202)
Largest Fibroid Dimension (cm) (mean±SD)	1,777	3.7 (3)
Fibroid Number (%)	2,149	
1	1,042	48
>1	1,107	52
Type 2 Diabetes Status (%)	2,30f2	
No	1,985	86
Yes	317	14
Number of Children (%)	692	
0	160	23
1	107	15
2	242	35
3	113	16

Characteristics	N	Study Population
4	39	6
5	20	3
>6	11	2

BMI, body mass index; cm^3, cubic centimeters; SD, standard deviation.

[a] Some women had more than one indication of imaging or fibroid location.

[b] Fibroids were discovered during ultrasound procedures relating to pregnancy or fertility problems.

[c] Fibroids were discovered during ultrasound procedures unrelated to fibroids.

Table 2.

Association between fibroid number and exposure variables.

Exposure variables	N	Crude OR [95% CI]	Crude p-value	Adjusted[a] OR [95% CI]	Adjusted[a] p-value
Age	2,149				
18 to 36	474	1.00 (referent)	-	1.00 (referent)	-
37 to 42	405	1.79 [1.36, 2.34]	<0.001	1.85 [1.41, 2.44]	<0.001
43 to 47	417	3.07 [2.34, 4.04]	<0.001	3.37 [2.55, 4.46]	<0.001
48 to 54	465	2.09 [1.61, 2.72]	<0.001	2.48 [1.89, 3.25]	<0.001
55 to 87	388	1.84 [1.40, 2.41]	<0.001	2.17 [1.64, 2.89]	<0.001
BMI (kg/m^2)	2,149				
Normal Weight[b] (≤24.9)	595	1.00 (referent)	-	1.00 (referent)	-
Overweight (25-29.9)	623	1.21 [0.96, 1.51]	0.102	1.08 [0.85, 1.36]	0.527
Obese (≥30)	931	1.07 [0.87, 1.32]	0.513	0.93 [0.75, 1.16]	0.530
Race	2,149				
White	1,503	1.00 (referent)	-	1.00 (referent)	-
Black	646	1.52 [1.27, 1.84]	<0.001	1.83 [1.49, 2.24]	<0.001
Type 2 Diabetes Status	2,149				
No	1,858	1.00 (referent)	-	1.00 (referent)	-
Yes	291	0.94 [0.73, 1.20]	0.623	0.77 [0.59, 1.01]	0.055
Number of Living Children	631	0.93 [0.83, 1.04]	0.213	0.88 [0.78, 0.99]	0.036

CI = confidence interval; BMI = body mass index; kg/m^2 = kilograms per meter squared.

[a]Adjusted for age quintiles, WHO BMI categories, and race, respectively.

[b]Due to the limited number of underweight subjects (N=27), normal weight includes underweight individuals.

Table 3.

Association between fibroid volume and exposure variables.

Exposure variables	N	Crude Beta[c] [95% CI]	Crude p-value	Adjusted[a] Beta[c] [95% CI]	Adjusted[a] p-value
Age	1,307				
18 to 36	313	1.00 (referent)	-	1.00 (referent)	-
37 to 42	258	1.19 [0.85, 1.68]	0.311	1.22 [0.86, 1.71]	0.262
43 to 47	261	1.40 [0.99, 1.97]	0.054	1.47 [1.05, 2.07]	0.027
48 to 54	276	1.33 [0.95, 1.86]	0.102	1.57 [1.12, 2.22]	0.010
55 to 87	199	0.70 [0.48, 1.01]	0.055	0.81 [0.56, 1.18]	0.281
BMI (kg/m^2)	1,307				
Normal Weight[b] (≤24.9)	344	1.00 (referent)	-	1.00 (referent)	-
Overweight (25-29.9)	377	1.42 [1.05, 1.93]	0.025	1.31 [0.97, 1.78]	0.083
Obese (≥30)	586	1.32 [1.00, 1.75]	0.049	1.13 [0.85, 1.50]	0.408
Race	1,307				
White	844	1.00 (referent)	-	1.00 (referent)	-
Black	463	1.75 [1.38, 2.21]	<0.001	1.77 [1.38, 2.27]	<0.001
Type 2 Diabetes Status	1,307				
No	1,141	1.00 (referent)	-	1.00 (referent)	-
Yes	166	0.78 [0.55, 1.09]	0.149	0.72 [0.51, 1.02]	0.062
Number of Living Children	345	0.97 [0.82, 1.14]	0.696	0.93 [0.79, 1.11]	0.422

CI = confidence interval; BM = body mass index; kg/m^2 = kilograms per meter squared.

[a]Adjusted for age quintiles, WHO BMI categories, and race, respectively.

[b]Due to the limited number of underweight subjects (N=27), normal weight includes underweight individuals.

[c]Beta values are back-transformed to cm^3.

Table 4.

Association between largest fibroid dimension and exposure variables.

Exposure variables	N	Crude Beta[c] [95% CI]	Crude p-value	Adjusted[a] Beta[c] [95% CI]	Adjusted[a] p-value
Age	1,777				
18 to 36	408	1.00 (referent)	-	1.00 (referent)	-
37 to 42	345	1.05 [0.94, 1.18]	0.347	1.06 [0.95, 1.19]	0.264
43 to 47	345	1.13 [1.02, 1.27]	0.026	1.16 [1.04, 1.30]	0.007
48 to 54	381	1.11 [1.00, 1.24]	0.051	1.19 [1.07, 1.32]	0.002
55 to 87	298	0.88 [0.78, 0.98]	0.024	0.94 [0.84, 1.05]	0.284
BMI (kg/m^2)	1,777				
Normal Weight[b] (≤24.9)	491	1.00 (referent)	-	1.00 (referent)	-
Overweight (25-29.9)	510	1.10 [1.00, 1.21]	0.043	1.06 [0.97, 1.17]	0.200
Obese (≥30)	776	1.11 [1.02, 1.22]	0.015	1.05 [0.96, 1.14]	0.319
Race	1,777				
White	1,209	1.00 (referent)	-	1.00 (referent)	-
Black	568	1.28 [1.18, 1.38]	<0.001	1.28 [1.18, 1.38]	<0.001
Type 2 Diabetes Status	1,777				
No	1,545	1.00 (referent)	-	1.00 (referent)	-
Yes	232	0.98 [0.88, 1.08]	0.644	0.94 [0.84, 1.05]	0.278
Number of Living Children	491	0.98 [0.94, 1.03]	0.517	0.96 [0.92, 1.01]	0.155

CI = confidence interval; BMI = body mass index; kg/m^2 = kilograms per meter squared.

[a]Adjusted for age quintiles, WHO BMI categories, and race, respectively.

[b]Due to the limited number of underweight subjects (N=27), normal weight includes underweight individuals.

[c]Betas are back-transformed to cm.