

GENERAL GYNECOLOGY

Relationship between hysterectomy and admixture in African American women

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OBJECTIVE: Most studies suggest that hysterectomies are more common in African American women than in other ethnic groups. To assess this ethnic surgical disparity in a novel way, our main goal was to determine whether admixture (the proportion of sub-Saharan African or European origin in individuals) is associated with hysterectomy frequency in African American women in the Women's Health Initiative.

STUDY DESIGN: In this retrospective study, we used ancestry informative single nucleotide polymorphisms to estimate admixture proportions in >10,000 African American women from the Women's Health Initiative. Logistic regression models were used to assess the association between admixture and self-reported history of hysterectomy with and without controls for relevant covariates. Multinomial logistic regression models were used to assess the association between admixture and self-reported age of hysterectomy. We also considered other potential risk factors (adiposity, hypertension, and education) for hysterectomy accounting for admixture.

RESULTS: African admixture was a strong risk factor after the adjustment for multiple covariates (odds ratio, 1.85; $P < .0001$). The admixture risk for hysterectomy was highest for those procedures that were performed in the 35–39 age range (odds ratio, 3.08; $P < .0001$) and least evident in oldest ages (≥ 45 years old). Our analyses also suggest that adiposity, hypertension, and education were associated independently with hysterectomy in this population group.

CONCLUSION: These results suggest that higher African admixture is associated with higher frequencies of hysterectomy and that genetic studies that specifically target African American women and diseases that are associated with hysterectomy may be especially useful in understanding the pathogenesis and underlying cause of this disparity in health outcome.

Key words: ancestry, ancestry informative markers, fibroid tumors, Women's Health Initiative

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Hysterectomy is the most common gynecologic surgery in the United States.¹ African American women have a higher risk of hysterectomy compared with other ethnic groups.^{2,3} Explanations for this higher risk include less access to more conservative treatments because of lower socioeconomic status (SES), higher population density in the southern United States where hysterectomy

is more common, and psychosocial factors that affect patient and/or physician preferences towards hysterectomy over other treatments.³⁻⁶ However, the higher hysterectomy rates in African American women may also reflect differences in the prevalence of diseases for which hysterectomy is performed. African American women have a higher prevalence of uterine leiomyomas (fi-

broid tumors),³ although the cause is not well understood.

In African American women, 60-70% of hysterectomies are performed for fibroid tumors compared with 29-33% for non-Hispanic white women.^{1,7,8} The odds of African American women having fibroid tumors as an indication for hysterectomy ranges from 2.7–9.4 compared with women without African ancestry.^{3,9-11} African American women experience fibroid tumors at younger ages and have more rapid fibroid growth and larger tumor volumes than women of European descent.² Although the effect of psychosocial or environmental factors should not be discounted, differences in fibroid behavior could also suggest an underlying biologic cause that includes genetic polymorphisms and/or expression.^{12,13} Some estimates place genetics as a primary factor for fibroid tumors, with heritability estimates that range from 26–80%, with most estimates at >50%¹⁴⁻¹⁶; the diagnosis of fi-

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broid tumors is associated with several genetic loci in Japanese women.¹⁷

To explore the possible influence of genetics on the higher rate of hysterectomy in African American women, we investigated whether the relative proportion of sub-Saharan African (referred to here as African) is associated with hysterectomy. We used a set of ancestry informative single nucleotide polymorphisms (SNPs)^{18,19} to estimate admixture accurately in >10,000 self-identified African American participants of the Women's Health Initiative (WHI). In addition, we examined whether education, body mass index (BMI), and hypertension are associated with a history of hysterectomy (after adjustment for admixture) and whether these factors influence the admixture-associated risks for hysterectomy.

MATERIALS AND METHODS

This study was a cross-sectional analysis of self-identified African American participants in the WHI. WHI is the largest US health study of postmenopausal women aged 50-79 years and includes >160,000 women who were recruited between 1993 and 1998.^{20,21} Our study included 10,439 African American women for whom DNA samples were genotyped and baseline hysterectomy information and other study covariates were available. The WHI provided access to clinical data and DNA samples under appropriate Human Institutional Review Board approval, and the study design was approved by the National Institutes of Health Heart, Lung and Blood Institute as part of a BAA for the WHI. The study was otherwise exempt from institutional review board approval.

We estimated the proportion of African and European admixture using a validated set of ancestry informative markers (AIMs)^{18,19} that included 92 SNPs that enabled the accurate estimation of admixture proportions in African American women.^{18,19,22} Genotyping was performed by our group as previously described²² using the TaqMan OpenArrays system (ABI, Foster City, CA). The mean call rate was 97.1%. All AIM SNPs were in Hardy Weinberg equilibrium ($P > .005$) in parental populations, and the

mean width of the 90% Bayesian confidence intervals (CIs) was 0.2 for admixture estimates in our studies of groups of African and Hispanic American women.¹⁸ Although the mean width of CIs is larger for smaller AIM sets, the admixture proportions that were estimated in individuals who were assessed with these highly selected AIMs¹⁸ are correlated strongly with larger AIM sets. Correlations with larger sets of SNP AIMs (>500 SNPs) are >0.9 in the testing with Mexican American and African American admixed populations (unpublished data). For the current study, we did not include assessment of the Amerindian admixture because the African American participants showed a very low frequency of Amerindian admixture (mean, 0.019).

The African and European admixture contribution (a proportion that ranged from 0–100%) to each self-identified African American woman was assessed with the use of STRUCTURE (version 2.3.3; University of Chicago, Chicago, IL)²³ analyses of genotyping results with AIMs, as previously described.²² The analyses were performed under the assumption of 2 populations ($K = 2$) with 100,000 replicates and 100,000 burn-in cycles and representatives of parental population groups, as previously described.²² The results were consistent with <0.02 difference among each of 3 independent runs. We considered African admixture in data analyses because the results for European admixture mirror those for African admixture.

The primary outcome variable for all analyses was a self-reported history of hysterectomy at baseline. We also investigated the association between African admixture and self-reported age at hysterectomy and compared each age category with women who did not report hysterectomy. Age at hysterectomy was available in categories: < 30, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, and ≥ 60 years. We combined 50-54, 55-59, ≥ 60 years as ≥ 50 years to have a larger sample size for this category.

We considered the following baseline covariates: entry age, education, BMI, self-reported age at menarche, smoking history, alcohol intake, parity, and dia-

stolic blood pressure. These covariates have been reported in previous studies as factors that are associated or potentially associated with the frequency of hysterectomy and/or fibroid tumors.^{3-6,11,24,25} BMI was computed as measured weight (kilograms) divided by the square of measured height (square meters). Parity included the following categories: never pregnant, no full-term pregnancy; 1 child; 2, 3, or 4 children, and ≥ 5 children. We considered education with the following scale: high school or less; vocational education; some college, which included an associate degree, and college degree (BA/BS and above). Alcohol intake had the following scale: nondrinker, past drinker, <1 drink/month, <1 drink/week, 1 to <7 drinks/week, and ≥ 7 drinks/week. Smoking was categorized in the following manner: never smoker, <5 years, 5-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, and >50 years. Diastolic hypertension status (hypertensive or normotensive) was determined based on the participants' baseline diastolic blood pressure, as previously defined.²⁶

We conducted statistical analyses using SAS software (version 9.2; SAS Institute, Cary, NC). All statistical tests were 2-sided, and a probability value of < .05 was considered statistically significant. We used 10,439 participants for all analyses, except when diastolic blood pressure was used as a covariate ($n = 9792$) or for when we examined whether diastolic hypertension was associated with hysterectomy. This analysis included only individuals who were classified as hypertensive (blood pressure, >90 mm Hg) or normotensive (blood pressure, <80 mm Hg; $n = 7593$). Individuals with borderline blood pressures were not included in this analysis, which was consistent with our previous study.²⁶ Baseline characteristics of the women with and without hysterectomy were compared with the use of χ^2 tests for categorical variables and the Student t tests for continuous variables. To investigate the association between hysterectomy status and African admixture proportion, we obtained odds ratios (ORs) and 95% CIs using logistic regression models. The ORs described the effect of 100% African

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