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Breastfeeding and Mammographic Breast Density: A Cross-sectional Study

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Abstract

Breastfeeding is inversely associated with breast cancer risk but the associations of breastfeeding with mammographic breast density (MBD) are not clear. We investigated the association between breastfeeding and volumetric measures of MBD (volumetric percent density (VPD), dense volume (DV) and non-dense volume (NDV)) and evaluated whether it differs by race, menopausal status, and body mass index (BMI).

The study population was comprised of 964 women (67% non-Hispanic white, 29% non-Hispanic black) who had screening mammography at Washington University School of Medicine, St. Louis, MO. VPD, DV and NDV were $\log_{10}$ transformed. We performed multivariable linear regression models adjusted for age, BMI, family history of breast cancer, race, and age at menarche among all participants and exclusively in parous women.

Mean age was 50.7 years. VPD was 12% lower among women who breastfed 0–6 months, (10^β=0.88, 95%CI (0.79,0.98)) compared to nulliparous women. Breastfeeding was inversely associated with DV (parous never breastfed: 10^β=0.93, 95%CI (0.83,1.04), breastfed 0–6 months: 10^β=0.91, 95%CI (0.79,1.05), breastfed 7–12 months: 10^β=0.94, 95%CI (0.81,1.10), breastfed >12 months: 10^β=0.87, 95%CI (0.78,0.98), p-trend=0.03). BMI modified the association between breastfeeding and VPD. Women who breastfed for 0–6 months and had a BMI < 25kg/m^2 had lower VPD compared to nulliparous women, but among women with a BMI ≥ 25kg/m^2 there was no association (p-interaction=0.04).

In this diverse study population, the association of breastfeeding with VPD appears to be modified by BMI, but not by race or menopausal status. Future research exploring the associations of breastfeeding with other mammographic features are needed.

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Authors' contributions: ATT designed the study and acquired the data. KRG, and SX analysed the data. KRG, SX and BA, wrote the manuscript draft. ATT and KRG revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interest: Babatunde Adedokun is currently an employee at Amgen and he receives remuneration and has stock in Amgen. Work contributed by Dr. Adedokun was performed before his current employment and is not related to his work at Amgen. The other authors have no relevant financial or non-financial interests to disclose.

Introduction

Mammographic breast density (MBD) reflects the proportion of epithelial and stromal tissues relative to adipose tissue in the breast.(1) There is a positive association between breast density and risk of developing breast cancer. Women with ≥75 percent density experience an approximately 5-fold increased risk of developing breast cancer compared to women with <5 percent density.(2) Additionally, maintaining dense breasts or developing more dense breast tissue over time is positively associated with the risk of developing breast cancer.(3)

Breastfeeding is inversely associated with breast cancer risk. (4,5) Reproductive factors such as higher parity and older age at first birth are inversely and positively associated with MBD, respectively, but studies have reported conflicting associations between breastfeeding and MBD. (6–14) The inconsistent findings may arise from how breastfeeding and MBD were measured and differences in study populations.(6–8,10–14) To the best of our knowledge, there are no studies on the association between breastfeeding and volumetric measures of MBD, as previous studies used either categorical or area-based measures.

Existing studies also suggest differences in the association between breastfeeding and MBD by menopausal status. The Nurses' Health Study observed positive associations between breastfeeding duration with dense and non-dense area among premenopausal women but no associations among postmenopausal women.(6) There was a positive association between breastfeeding duration and percent density among premenopausal women in a study performed among women in the Mexican Teacher's Cohort, but no relationship was observed among postmenopausal women.(13) Various demographic factors are related to breastfeeding behaviors, including race.(15–17) Differences in breastfeeding initiation and duration exist between non-Hispanic white and non-Hispanic black women, with non-Hispanic white women more likely to breastfeed compared to non-Hispanic black women. (16,17) Not only are breastfeeding practices and duration different across race, but race is also associated with MBD. (18–20) Moore et al. recently reported that non-Hispanic black women were more likely to have extremely dense breasts but less likely to have heterogeneously dense breasts compared to non-Hispanic white women. However, they did not investigate breastfeeding in their study.(19) Although there has been an increase in breastfeeding initiation and duration among non-Hispanic black women over time, it is important to investigate the association between breastfeeding and MBD by race because the prevalence of breastfeeding remains lower in non-Hispanic black women across the United States compared to non-Hispanic white women.(17,21) Breastfeeding is inversely associated with risk of estrogen receptor negative (ER−) breast cancer and non-Hispanic black women have a higher risk of and ER− breast cancer.(22) If breastfeeding is associated with MBD in non-Hispanic black women, it could provide an insight into how breastfeeding duration influences breast parenchyma and may provide supporting evidence to conduct large cohort studies to assess the association between breastfeeding duration and breast cancer development in this population.

The objective of this study is to investigate the association between breastfeeding and volumetric measures of MBD in a racially diverse study population and to determine whether menopausal status, race or (body mass index) BMI modify this association.

Materials and Methods

Study Population and Design

This study population consists of women who received their annual screening mammogram at the Joanne Knight Breast Health Center (BHC), at Siteman Cancer Center at Washington University School of Medicine, St. Louis, MO. Women who had their annual screening mammogram at the BHC were approached and screened for participation in the study. Eligibility criteria included: (i) age 35 to 64 years, (ii) ability to comply with all required study procedures and schedule; (iii) not having serious medical condition that would prevent the participant from returning for annual mammogram in 12 months, and (iv) not being pregnant. Exclusion criteria included: (i) history of any cancer, including breast cancer; (ii) history of breast augmentation, reduction, or implants; and (iii) history of selective estrogen receptor modulators (SERM) during the previous 6 months.

Participants completed a detailed questionnaire on demographic characteristics, reproductive factors, medication use, family history of breast cancer, alcohol use, tobacco use and adiposity at various ages. Further, participants' height and weight were measured using a stadiometer OMRON Full Body Sensor Body Composition Monitor and Scale Model HBF-514FC, respectively. Approval for the study was granted by the Institutional Review Board at Washington University School of Medicine, St. Louis, MO. All study participants provided written informed consent and the study was conducted in accordance with the Declaration of Helsinki.

Breastfeeding

Breastfeeding duration was derived by combining the number of months the women reported breastfeeding for their first, second and last child. The original breastfeeding duration variable was categorized into four groups ("0–3 months", "3–6 months", "7–12 months" and ">12 months"). To calculate cumulative duration of breastfeeding for all children, this variable combined breastfeeding duration across children and assumed the mother breastfed for the maximum number of months within each category for recoding purposes. Women who were nulliparous and those who had children but never breastfed were assigned to separate categories. The categories of breastfeeding duration analyzed were: "nulliparous", "parous never breastfed", "breastfed for 0–6 months", "breastfed for 7–12 months" and "breastfed for >12 months". Of the 906 parous women in the study, data on breastfeeding duration was available for 779 women, while 127 parous women were missing breastfeeding duration.

Mammographic Breast Density Assessment

Volpara version 1.5 (Matakina Technology Ltd) was used to evaluate volumetric measures of MBD - volumetric percent density (VPD), dense volume (DV), and non-dense volume (NDV) of the breast. (23,24) Volpara assesses measures of DV by averaging the mediolateral

oblique and cranial-caudal views of the left and right breasts. DV is the volume of fibroglandular tissue in the breast (cm^3). NDV is calculated as the difference between total breast volume (cm^3) and DV. VPD is the ratio of the volume of fibroglandular tissue (i.e., DV) to the total breast volume, expressed as a percentage.

Statistical Analysis

We calculated the participants' characteristics using percentages for categorical variables as well as means and standard deviations for continuous variables. We evaluated these characteristics across the different breastfeeding duration categories and performed chi-square and ANOVA tests to assess univariate associations. We performed complete case analyses of the associations between breastfeeding duration and MBD on 964 participants (excluding 127 parous women who were missing breastfeeding duration, 32 women who were missing MBD and additional 18 women who were missing values for confounding variables; flowchart of analytic sample presented in Supplemental Figure 1) and performed $\log_{10}$ transformations on VPD, DV, and NDV due to the skewed distribution.

We built multivariable-adjusted linear regression models to assess the associations between breastfeeding duration and MBD adjusting for age (continuous), BMI (continuous), family history of breast cancer in a first-degree relative (no, yes), race (non-Hispanic white, non-Hispanic black, other), and age at menarche (continuous). Models were also adjusted for alcohol use as well as use of oral contraceptives and hormone replacement therapy among premenopausal and postmenopausal women respectively. We additionally adjusted for body shape at age 10 which is based on the Stunkard scale/the figure rating scale. We recoded the original scale from 9 categories to 4 (1= body shapes 1 & 2, 2= body shapes 3 & 4, 3= body shape 5, and 4= body shapes 6–9).(25) Use of alcohol, oral contraceptives, hormone replacement therapy and body shape at age 10 were not included in the final models because they did not change the point estimates by >10%. Coefficients and 95% confidence intervals were back-transformed for easier interpretation. Tests for trend were performed by treating breastfeeding duration as an ordinal variable. To determine if menopausal status, race and BMI were effect modifiers on the association between breastfeeding duration and MBD, we added interaction terms to the multivariable linear regression models and conducted stratified analyses.

Additionally we investigated the association between breastfeeding and MBD among parous women only. Excluding nulliparous women from the analyses may help to isolate the impact of breastfeeding, which may be influenced by parity. Time since last birth was considered as a confounding variable in these analyses but was not included in the final models because it did not influence the point estimates by >10%. We also performed additional sensitivity analyses to address women who had missing values for breastfeeding duration. Inverse probability weights were calculated to mimic the population where no participants had breastfeeding duration missing. Weights were added to the models and participants with breastfeeding duration missing were excluded.

All statistical tests were two-sided, and p values < 0.05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, Statistical Analysis System, RRID:SCR_008567).

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Results

Descriptive Statistics

The complete case analysis included 964 women with a mean age of 50.7 years (Table 1). Approximately 67% of the women were non-Hispanic white, and 29% were non-Hispanic black. The average BMI was 30.6 kg/m^2. Approximately 30% of the women in the study were parous but never breastfed, followed by women who breastfed for >12 months (25.0%), nulliparous women (23.7%), women who breastfed for 0–6 months (11.9%), and women who breastfed for 7–12 months (9.4%). Nulliparous women were younger and had a younger age at menarche than women who reported breastfeeding. Parous women who never breastfed had the youngest age at first birth (23.3 years) and the highest BMI ($32.4 kg/m^2$) compared to the other women. Women who breastfed for >12 months were likely to have the most children and also had the highest VPD (9.9%) but lowest DV ($80.5 cm^3$) and NDV ($1131.5 cm^3$).

Multivariable Analysis

All study participants—VPD was 12% lower among women who were parous but never breastfed, (10^β=0.88, 95% CI (0.81, 0.96)) and women who breastfed 0–6 months, (10^β=0.88, 95% CI (0.79, 0.98)) compared to nulliparous women (Table 2). Breastfeeding was not associated with VPD among women who breastfed 7–12 months or >12 months (p-trend=0.92). There was an inverse association between breastfeeding and DV (parous never breastfed: 10^β=0.93, 95% CI (0.83, 1.04), breastfed 0–6 months: 10^β=0.91, 95% CI (0.79, 1.05), breastfed 7–12 months: 10^β=0.94, 95% CI (0.81, 1.10), and breastfed >12 months: 10^β=0.87, 95% CI (0.78, 0.98) p-trend=0.03) (Table 2). There were no associations between breastfeeding and NDV.

Parous women only—In the analyses limited to parous women, there was a positive association between breastfeeding for 7–12 months and VPD (10^ β=1.12, 95%CI (1.00, 1.25)). There was no association between breastfeeding and DV, but an inverse trend was observed between breastfeeding duration and NDV (breastfed 0–6 months: 10^β=1.01, 95% CI (0.89, 1.16), breastfed 7–12 months: 10^β=0.91, 95% CI (0.78, 1.06), and breastfed >12 months: 10^β=0.90, 95% CI (0.80, 1.01) p-trend=0.04) (Table 2).

Interaction Analyses

All study participants—BMI modified the association between breastfeeding duration and VPD. Among women with BMI<$25 kg/m^2$, women who breastfed for 0–6 months had lower VPD compared to nulliparous women, but among women with a BMI ≥ $25 kg/m^2$ there was no association (p-interaction=0.04), (Table 3). Menopausal status and race did not modify the associations of breastfeeding with VPD, DV, or NDV (Table 3).

Parous women only—Similar findings were observed in the analyses limited to parous women; BMI, menopausal status and race did not modify the association between breastfeeding and any measure of MBD (Table 4).

Missing Data

The results from the analysis that utilized inverse probability weights to deal with missing data were consistent with the findings from the complete case analysis (Supplemental Table 1) hence; the results from the complete case analysis are not likely to be biased due to missing data.

Discussion

In the analyses across all study participants, we observed that women who breastfed for 0–6 months had lower VPD compared to nulliparous women, which appears to be driven by women with BMI < 25 kg/m^2. Breastfeeding was also inversely associated with DV in the analyses involving all study participants and with NDV in analyses limited to parous women.

Our findings with VPD are consistent with the current literature.(6,10–12) Tehranifar et al. observed similar associations between breastfeeding duration and percent density when assessing digitized films utilizing Cumulus software to calculate area measures of MBD.(10) They investigated this association in a comparable study population including non-Hispanic black and white women in their analyses.(10) Although their results are similar to ours, our sample size was larger, N=964 compared to N=191 in their study, which allowed us to stratify by race. Similar to the mostly null results between breastfeeding and VPD in our analyses limited to parous women, Yaghjyan et al. also found no association between breastfeeding duration and percent density among parous pre and postmenopausal women in the Nurses' Health Study, which also used digitized mammograms and Cumulus software to measure percent density based on breast area.(6) Another study in Korea observed no significant associations between breastfeeding and percent density within twins.(12) All of the aforementioned studies measured percent density using digitized mammograms and calculated area-based measures of MBD while we, to the best of our knowledge, are the first study to use volumetric measures of MBD calculated using Volpara.

We observed an inverse association between breastfeeding duration and DV such that women who breastfed for >12 months had lower DV than nulliparous women who had never breastfed. Similar to our study, a study, by Li et al., found an inverse association between breastfeeding and dense area among Chinese women, but a positive association among Australian women.(14) Other studies that investigated the association between breastfeeding duration and dense area observed positive associations.(6,12,14) Yaghjyan et al. found a positive association between breastfeeding duration and dense area particularly among premenopausal women.(6) Since this study was conducted among women in the Nurses' Health Study, it is possible that study subjects are demographically and socioeconomically different from our study population.

Breastfeeding duration may be influenced by various factors including educational background and socioeconomic status.(15,26) The relationship between breastfeeding duration and dense area/volume may not be transportable across the study populations due to these potential demographic and socioeconomic differences. Other studies that observed a positive association between breastfeeding duration and dense area were conducted among women who lived in countries other than the United States.(12,14) Breastfeeding behaviors differ by not only race but also country.(27) Non-Hispanic black women breastfeed for shorter durations of time compared to women of other race/ethnicities in the United States.(17,21) Our study also showed that approximately half of parous women who never breastfed were non-Hispanic black, but there was no difference in the association between breastfeeding duration and DV by race in this study. Also MBD may be different by ethnicity. Since the association between breastfeeding duration and MBD is not consistent across race and geographical location, it is possible breastfeeding may be influencing dense area/volume differently across races other than non-Hispanic black vs non-Hispanic white.

We did not observe any associations between breastfeeding duration and NDV in analyses involving all study participants, but we observed an inverse trend between breastfeeding duration and NDV in the analyses limited to parous women. After stratifying by menopausal status there is no association between breastfeeding duration and NDV among postmenopausal parous women, which is similar to findings in the Mexican Teacher's Cohort and Nurses' Health Study.(6,13) Our study found an inverse association between breastfeeding and NDV in premenopausal parous women, which differs from the non-significant findings in the Mexican teacher's cohort and positive association observed in the Nurses' Health Study.(6,13) Observations of an inverse association between breastfeeding duration and NDV could potentially be explained by changes in adiposity from breastfeeding, but this relationship is not clearly established.(28) Future research is necessary to understand why these differences across the studies are present.

Women who are parous and breastfeed experience structural, cellular and DNA changes in the breast that may prevent the development of certain subtypes of breast cancer.(4,29–31) Breastfeeding is protective against breast cancer beyond the impact of parity and mechanisms such as reduction in lifetime ovulatory cycles, which reduces exposure to estrogen may explain this effect.(5,32) A meta-analysis investigating the association between breastfeeding and breast cancer by subtype found the strongest inverse association between breastfeeding and ER− breast cancer.(31,33) Breastfeeding duration is often higher in low and middle-income countries compared to high-income countries but the inverse relationship with ER− cancer remains consistent.(34–36) Certain changes in the breast tissue appear to benefit women who breastfed for long durations (>12 months), hence breastfeeding has only been consistently associated with a reduction in breast cancer risk among women who breastfeed for long durations.(4) Given that MBD is a strong risk factor for breast cancer and the inconsistences on the associations of breastfeeding with MBD, especially percent density, it is possible that other features of breast parenchyma may mediate the association between breastfeeding and breast cancer development.

Strengths/Limitations

There are several strengths to this study including a relatively large sample size with information on reproductive and demographic variables that were assessed as confounders and effect modifiers. An additional strength is that this study has a modest sample size of non-Hispanic black women, which provided the opportunity to investigate the association between breastfeeding and MBD measures among non-Hispanic black women and non-Hispanic white women separately. Also, to our knowledge, this study is the first to explore the association between breastfeeding duration and volumetric measures of MBD. Previous studies have mainly utilized area-based and qualitative measures of MBD. Volumetric and area measures of percent density have been found to be highly correlated (r =0.93), but the correlation between dense volume and dense area is not as strong (r=0.55). (37) Area based measures may be impacted by compression and density may appear different visually.(38)

There are limitations of this study including potential misclassification of the exposure. Breastfeeding duration was categorized into approximately 3 to 6 month time periods for the first, second and last children. Categories were combined across children to achieve the final breastfeeding duration for each woman. This may lead to a loss of information and potential misclassification of the exposure if women breastfed the minimum duration of each breastfeeding category per child. It may also mitigate the presence of a linear relationship. Since breastfeeding appears to have a threshold effect with breast cancer, benefitting women who breastfeed for very long durations (>12 months) the most, categorizing breastfeeding duration should not impact the findings in this study.(4) Additionally, breastfeeding duration data was available only for the first, second and last children. Participants who had more than three children may be misclassified into lower breastfeeding duration categories if they breastfed the children born between the second and last for a longer duration. However, the majority of study participants had three children or less and the unavailability of data for other children is unlikely to have any impact on the results given the consistently null findings. Also, we are unable to differentiate between women who breastfed exclusively compared to those who did not. Future studies with information on exclusive breastfeeding practices can evaluate this. It is possible the full extent of the association between breastfeeding and MBD was not apparent in our study due to unmeasured confounding or inability to adjust for certain variables because of potential collinearity, especially between parity and breastfeeding duration even after performing analyses on parous women separately. Since we investigated the association between breastfeeding duration and several measures of MBD and assessed this association across potential effect modifiers it is possible, due to the multiple comparisons, significant associations observed were due to chance. Lastly, although this study had a relatively large sample of non-Hispanic black and non-Hispanic white women, there was a limited number of women from other races/ethnic groups, hence, study results may not be generalizable to them.

In conclusion, we observed an inverse association between breastfeeding and VPD for women who breastfeed for 0–6 months, but not women who breastfeed for longer periods. Breastfeeding may protect against breast cancer development by acting through other features and patterns within the breast parenchyma that are not captured in volumetric

measures of MBD. Future studies looking at the associations of breastfeeding with breast radiomics and microscopic features are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Prevention Relevance Statement:

Breastfeeding for up to 6 months may be associated with lower VPD among women with a BMI<25kg/m^2. The potential role of MBD in mediating the associations of breastfeeding with breast cancer risk in a select group of women deserves further evaluation.

Table 1.

Characteristics of 964 women recruited during annual screening mammography at the Joanne Knight Breast Health Center, Washington University School of Medicine, St. Louis, MO.*

	Total (N=964)	Nulliparous (N=228)	Parous never breastfed (N=289)	0–6 months (N=115)	7–12 months (N=91)	>12 months (N=241)	p
	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	
Age, year	50.7 (7.1)	48.8 (7.1)	52.2 (6.7)	52.1 (7.0)	53.3 (6.9)	49.2 (6.8)	<0.0001
Age at menarche, year	12.7 (1.6)	12.6 (1.5)	12.7 (1.7)	12.8 (1.6)	12.6 (1.6)	12.9 (1.6)	0.31
Age at first birth, year [a]	25.6 (6.2)	-	23.3 (6.1)	27.3 (6.4)	26.0 (5.8)	27.3 (5.4)	<0.0001
Body Mass Index, kg/m^2	30.6 (7.8)	31.2 (8.8)	32.4 (7.9)	30.0 (6.1)	29.6 (7.1)	28.5 (7.2)	<0.0001
Race							
Non-Hispanic white	645 (66.9)	176 (77.2)	140 (48.4)	73 (63.5)	66 (72.5)	190 (78.8)	
Non-Hispanic black	279 (28.9)	43 (18.9)	144 (49.8)	38 (33.0)	20 (22.0)	34 (14.1)	<0.0001
Other Race	40 (4.2)	9 (4.0)	5 (1.7)	4 (3.5)	5 (5.5)	17 (7.1)	
Menopause status							
Premenopausal	613 (63.6)	167 (73.3)	157 (54.3)	63 (54.8)	46 (50.6)	180 (74.7)	<0.0001
Postmenopausal	351 (36.4)	61 (26.8)	132 (45.7)	52 (45.2)	45 (49.5)	61 (25.3)	
Family history of breast cancer							
Yes	228 (23.7)	65 (28.5)	52 (18.0)	27 (23.5)	30 (33.0)	54 (22.4)	0.01
No	736 (76.4)	163 (71.5)	237 (82.0)	88 (76.5)	61 (67.0)	187 (77.6)	
Parity number							
Nulliparous	228 (23.7)	228 (100)	-	-	-	-	
1–2 children	480 (49.8)	-	210 (72.7)	90 (78.3)	63 (69.2)	117 (48.6)	<0.0001[b]
≥3 children	256 (26.6)	-	79 (27.3)	25 (21.7)	28 (30.8)	124 (51.5)	
Current alcohol use[c]							
Yes	627 (65.2)	152 (66.7)	155 (53.8)	79 (69.3)	64 (70.3)	177 (73.4)	<0.0001
No	335 (34.8)	76 (33.3)	133 (46.2)	35 (30.7)	27 (29.7)	64 (26.6)	
Mammographic density[d]							
Volumetric Percent density, %	8.5 (6.4)	9.4 (7.3)	6.8 (4.9)	7.6 (4.9)	9.0 (6.5)	9.9 (7.3)	<0.0001
Dense volume, cm^3	96.1 (83.9)	104.2 (92.3)	103.6 (95.0)	87.4 (56.0)	104.1 (111.0)	80.5 (53.2)	0.02

	Total (N=964)	Nulliparous (N=228)	Parous never breastfed (N=289)	0–6 months (N=115)	7–12 months (N=91)	>12 months (N=241)	p
	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	N (%) or mean (SD)	
Non-dense volume, cm^3	1450.4 (1423.7)	1442.5 (1502.8)	1777.6 (1666.7)	1416.5 (1319.7)	1318.7(1105.0)	1131.5 (1067.8)	<0.0001
Log_{10}-Mammographic density							
Volumetric Percent density, %	0.8 (0.3)	0.9 (0.3)	0.8 (0.2)	0.8 (0.2)	0.9 (0.3)	0.9 (0.3)	<0.0001
Dense volume, cm^3	1.9 (0.3)	1.9 (0.3)	1.9 (0.3)	1.9 (0.2)	1.9 (0.3)	1.8 (0.2)	0.02
Non-dense volume, cm^3	3.0 (0.4)	3.0 (0.4)	3.1 (0.4)	3.0 (0.3)	3.0 (0.3)	2.9 (0.4)	<0.0001

*Presented as N. (%) for categorical variables or mean (SD) for continuous variables. N = Number, % = column percentage, SD = standard deviation

*a.*4 parous women were missing age at first birth

*b.*Chi-square test across parous never breastfed, 0–6 months, 7–12 months, and >12 months groups.

*c.*2 participants are missing alcohol use information

*d.*Mammographic density indicators are not normally distributed. Kruskal-Wallis tests were conducted instead of ANOVA. These indicators were log_{10} transformed to follow approximately normal distributions.

Table 2.

Associations of breastfeeding duration with mammographic breast density measures [a]

Breastfeeding Duration	N	Volumetric Percent Density 10^β (95%CI)	Dense Volume (cm^3) 10^β (95%CI)	Non-dense Volume (cm^3) 10^β (95%CI)
All women	964			
Nulliparous	228	Reference	Reference	Reference
Parous never breastfed	289	**0.88 (0.81, 0.96)**	0.93 (0.83, 1.04)	1.07 (0.95, 1.20)
0–6 months	115	**0.88 (0.79, 0.98)**	0.91 (0.79, 1.05)	1.07 (0.93, 1.24)
7–12 months	91	1.00 (0.89, 1.13)	0.94 (0.81, 1.10)	0.96 (0.82, 1.11)
>12 months	241	0.95 (0.87, 1.04)	**0.87 (0.78, 0.98)**	0.94 (0.84, 1.05)
P trend		0.92	**0.03**	0.10
Parous women	736			
Parous never breastfed	289	Reference	Reference	Reference
0–6 months	115	0.99 (0.89, 1.09)	0.98 (0.86, 1.12)	1.01 (0.89, 1.16)
7–12 months	91	**1.12 (1.00, 1.25)**	1.02 (0.88, 1.18)	0.91 (0.78, 1.06)
>12 months	241	1.06 (0.98, 1.16)	0.94 (0.84, 1.06)	0.90 (0.80, 1.01)
P trend		0.07	0.38	**0.04**

[a.] Models were adjusted for age (continuous), age at menarche (continuous), BMI (continuous), race (non-Hispanic white, non-Hispanic black, other), and family history of breast cancer (yes, no). Mammographic breast density measures were $\log_{10}$ transformed due to the skewed distribution. Coefficients were back-transformed for easy interpretation. CI = confidence intervals, MBD= mammographic breast density. Bold indicates statistical significance ($p<0.05$).

Table 3.

Associations of breastfeeding duration with mammographic breast density measures by menopause status, race and BMI[a]

		Volumetric Percent Density		Dense Volume (cm^3)		Non-dense Volume (cm^3)	
	N	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**
Menopausal status							
Premenopausal[b]			0.75		0.06		0.19
Nulliparous	167	Reference		Reference		Reference	
Parous never breastfed	157	**0.86 (0.77, 0.96)**		0.96 (0.86, 1.07)		1.11 (0.99, 1.24)	
0–6 months	63	0.90 (0.78, 1.04)		1.05 (0.92, 1.21)		**1.20 (1.04, 1.38)**	
7–12 months	46	1.00 (0.85, 1.18)		0.95 (0.81, 1.11)		0.95 (0.81, 1.12)	
>12 months	180	0.94 (0.85, 1.04)		**0.90 (0.82, 1.00)**		0.97 (0.87, 1.07)	
Postmenopausal[b]			0.68		0.30		0.28
Nulliparous	61	Reference		Reference		Reference	
Parous never breastfed	132	0.96 (0.84, 1.09)		0.86 (0.68, 1.10)		0.95 (0.75, 1.21)	
0–6 months	52	0.91 (0.78, 1.07)		**0.74 (0.55, 1.00)**		0.85 (0.64, 1.14)	
7–12 months	45	1.08 (0.91, 1.27)		0.90 (0.66, 1.22)		0.85 (0.63, 1.15)	
>12 months	61	0.98 (0.84, 1.14)		0.83 (0.62, 1.10)		0.89 (0.67, 1.17)	
P-interaction		0.68		0.11		0.21	
Race							
Non-Hispanic white[c]			0.59		**0.04**		0.25
Nulliparous	176	Reference		Reference		Reference	
Parous never breastfed	140	0.93 (0.84, 1.04)		0.93 (0.81, 1.07)		1.01 (0.87, 1.16)	
0–6 months	73	**0.87 (0.76, 1.00)**		0.90 (0.76, 1.07)		1.07 (0.90, 1.28)	
7–12 months	66	1.02 (0.88, 1.17)		0.93 (0.78, 1.12)		0.93 (0.77, 1.12)	
>12 months	190	0.95 (0.86, 1.05)		**0.87 (0.76, 0.99)**		0.94 (0.82, 1.07)	
Non-Hispanic black[c]			0.55		0.97		0.60
Nulliparous	43	Reference		Reference		Reference	
Parous never breastfed	144	0.87 (0.76, 1.01)		0.98 (0.79, 1.20)		1.14 (0.93, 1.40)	
0–6 months	38	0.97 (0.81, 1.16)		0.98 (0.75, 1.27)		1.02 (0.79, 1.32)	
7–12 months	20	0.96 (0.77, 1.20)		1.08 (0.79, 1.48)		1.13 (0.83, 1.55)	
>12 months	34	0.97 (0.80, 1.17)		0.95 (0.73, 1.25)		0.98 (0.75, 1.28)	
P-interaction		0.48		0.96		0.67	
BMI							
BMI<25[d]			0.81		0.33		0.52
Nulliparous	59	Reference		Reference		Reference	
Parous never breastfed	49	0.81 (0.65, 1.01)		**0.71 (0.56, 0.92)**		0.92 (0.69, 1.22)	

		Volumetric Percent Density		Dense Volume (cm^3)		Non-dense Volume (cm^3)	
	N	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**
0–6 months	28	**0.75 (0.58, 0.96)**		0.86 (0.65, 1.15)		1.22 (0.88, 1.68)	
7–12 months	30	1.00 (0.78, 1.27)		1.00 (0.76, 1.33)		1.02 (0.74, 1.40)	
>12 months	96	0.91 (0.77, 1.09)		0.82 (0.67, 1.00)		0.91 (0.73, 1.15)	
BMI ≥25[d]			0.64		0.05		0.07
Nulliparous	169	Reference		Reference		Reference	
Parous never breastfed	240	0.94 (0.85, 1.04)		0.98 (0.87, 1.11)		1.06 (0.93, 1.20)	
0–6 months	87	1.03 (0.91, 1.17)		0.92 (0.79, 1.08)		0.91 (0.77, 1.07)	
7–12 months	61	1.06 (0.92, 1.22)		0.93 (0.78, 1.11)		0.89 (0.74, 1.07)	
>12 months	145	0.98 (0.88, 1.09)		0.89 (0.78, 1.01)		0.93 (0.81, 1.07)	
P-interaction		**0.04**		0.13		0.20	

[a] Mammographic breast density measures were $\log_{10}$ transformed due to the skewed distribution. Coefficients was back-transformed. CI = confidence intervals, MBD= mammographic breast density, BMI=body mass index. Bold indicates statistical significance ($p<0.05$), some CI may not appear significant due to rounding.

[b] Models were adjusted for age (continuous), age at menarche (continuous), BMI (continuous), race (non-Hispanic white, non-Hispanic black, other), and family history of breast cancer (yes, no).

[c] Models were adjusted for age (continuous), age at menarche (continuous), BMI (continuous), and family history of breast cancer (yes, no). Other races were excluded from the interaction analysis because of the small sample size

[d] Models were adjusted for age (continuous), age at menarche (continuous), race (non-Hispanic white, non-Hispanic black, other), and family history of breast cancer (yes, no).

Table 4.

Associations of breastfeeding duration with mammographic breast density measures by menopause status, race and BMI among parous women[a]

		Volumetric Percent Density		Dense Volume (cm^3)		Non-dense Volume (cm^3)	
	N	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**
Menopausal status							
Premenopausal[b]			0.16		0.23		**0.02**
Parous never breastfed	157	Reference		Reference		Reference	
0–6 months	63	1.04 (0.90, 1.19)		1.10 (0.96, 1.27)		1.09 (0.94, 1.25)	
7–12 months	46	1.15 (0.98, 1.35)		1.00 (0.85, 1.17)		0.88 (0.75, 1.03)	
>12 months	180	1.07 (0.96, 1.20)		0.95 (0.85, 1.06)		**0.89 (0.80, 1.00)**	
Postmenopausal[b]			0.49		0.98		0.68
Parous never breastfed	132	Reference		Reference		Reference	
0–6 months	52	0.94 (0.82, 1.08)		0.86 (0.67, 1.11)		0.92 (0.71, 1.18)	
7–12 months	45	1.10 (0.95, 1.28)		1.04 (0.80, 1.37)		0.92 (0.70, 1.21)	
>12 months	61	1.02 (0.89, 1.16)		0.97 (0.75, 1.24)		0.96 (0.74, 1.23)	
P-interaction		0.52		0.20		0.31	
Race							
Non-Hispanic white[c]			0.50		0.45		0.31
Parous never breastfed	140	Reference		Reference		Reference	
0–6 months	73	0.93 (0.81, 1.07)		0.97 (0.82, 1.16)		1.07 (0.90, 1.29)	
7–12 months	66	1.09 (0.94, 1.26)		1.02 (0.85, 1.23)		0.94 (0.78, 1.14)	
>12 months	190	1.01 (0.91, 1.13)		0.94 (0.82, 1.08)		0.95 (0.82, 1.10)	
Non-Hispanic black[c]			**0.04**		0.87		0.18
Parous never breastfed	144	Reference		Reference		Reference	
0–6 months	38	1.10 (0.96, 1.27)		1.00 (0.81, 1.23)		0.89 (0.72, 1.11)	
7–12 months	20	1.12 (0.93, 1.33)		1.11 (0.84, 1.46)		0.99 (0.75, 1.30)	
>12 months	34	1.14 (0.99, 1.33)		0.99 (0.79, 1.24)		0.85 (0.67, 1.06)	
P-interaction		0.42		0.91		0.70	
BMI							
BMI<25[d]			0.12		0.34		0.56
Parous never breastfed	49	Reference		Reference		Reference	
0–6 months	28	0.91 (0.70, 1.17)		1.23 (0.92, 1.65)		1.38 (0.99, 1.91)	
7–12 months	30	1.20 (0.92, 1.56)		**1.44 (1.07, 1.94)**		1.17 (0.84, 1.64)	
>12 months	96	1.12 (0.92, 1.38)		1.15 (0.91, 1.44)		1.00 (0.77, 1.29)	
BMI ≥25[d]			0.18		0.13		**0.04**

		Volumetric Percent Density		Dense Volume (cm^3)		Non-dense Volume (cm^3)	
	N	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**	**10^β (95%CI)**	**P trend**
Parous never breastfed	240	Reference		Reference		Reference	
0–6 months	87	1.10 (0.98, 1.23)		0.93 (0.81, 1.08)		0.86 (0.73, 1.01)	
7–12 months	61	1.13 (0.99, 1.29)		0.94 (0.80, 1.12)		0.84 (0.70, 1.01)	
>12 months	145	1.06 (0.96, 1.17)		0.90 (0.79, 1.03)		0.87 (0.76, 1.00)	
P-interaction		0.09		0.12		0.10	

a. Mammographic breast density measures were log10 transformed due to the skewed distribution. Coefficients was back-transformed. CI = confidence intervals, MBD= mammographic breast density, BMI=body mass index. Bold indicates statistical significance ($p<0.05$), some CI may not appear significant due to rounding.

b. Models were adjusted for age (continuous), age at menarche (continuous), BMI (continuous), race (non-Hispanic white, non-Hispanic black, other), and family history of breast cancer (yes, no).

c. Models were adjusted for age (continuous), age at menarche (continuous), BMI (continuous), and family history of breast cancer (yes, no). Other races were excluded from the interaction analysis because of the small sample size

d. Models were adjusted for age (continuous), age at menarche (continuous), race (non-Hispanic white, non-Hispanic black, other), and family history of breast cancer (yes, no).