Associations of Breast Cancer Risk Factors with Breast Density in Hispanic Women[1]

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Abstract

Although there has been much research on the factors associated with breast density, most studies did not include Hispanic women or relied on semiquantitative methods of assessing density. Using data from the Chicago Breast Health Project, which targeted Hispanic women and assessed density quantitatively using full-field digital mammography, we assessed cross-sectional associations of breast cancer risk factors with percentage of breast density.

Between November 2000 and June 2002, 296 Hispanic women recruited from three community health centers in Chicago, Illinois completed a health and lifestyle questionnaire, had their height and weight measured, and underwent screening mammography. The average percentage of total breast area occupied by fibroglandular tissue was computed from each mammographic view. Associations of breast cancer risk factors with percentage of breast density were assessed using multivariate linear regression analyses.

Overall, the mean percentage of breast density was 17.6%. In multivariate analysis, older age was associated with lower density ($P = 0.03$), and density was lower among postmenopausal than premenopausal women ($\beta = 5.2\%$; $P = 0.002$). Body mass index was significantly inversely related to percentage of breast density ($P < 0.00001$). Women currently taking hormone replacement therapy had a higher percentage of breast density ($\beta = 3.3\%$; $P = 0.03$). In premenopausal women, cigarette smokers had a marginally higher percentage of density ($\beta = 6.23\%$; $P = 0.06$) compared with nonsmokers, but there was no relationship for postmenopausal women. Other breast cancer risk factors were not associated with density.

In summary, breast density was strongly and inversely associated with age, body mass index, and menopausal status, and positively associated with hormone replacement therapy use and cigarette smoking. Additional research focusing on relationships of other, potentially modifiable, factors with the extent of breast density is warranted to better understand the interindividual variability in density among Hispanic women.

Introduction

It has long been recognized that the radiographic appearance of the breast varies according to differences in the relative distributions of fat and FA[3] (1). The extent of mammographically detected fibroglandular breast tissue has been referred to as parenchymal patterns or as percentage of breast density, and is one of the strongest known risk factors for breast cancer (2, 3). Indeed, results of a meta-analysis of eight cohort studies showed a 5-fold greater risk of breast cancer for women in the highest compared with the lowest strata of density (4). Many breast cancer risk factors such as age, menopausal status, parity, obesity, and current use of HRT, particularly those that contain progestin, are also associated with mammographic breast density (3, 5–10). Furthermore, the utility of breast density as a surrogate marker in studies of breast cancer prevention has been suggested (2).

Hispanics are the fastest growing ethnic group in the United States (11). Thus, the health needs of this ethnic group are an important public health priority. Specifically, there is a paucity of data on breast cancer and breast cancer risk factors for Hispanic women, which is particularly concerning, because it is the most commonly occurring cancer, and the most common cause of cancer mortality in this ethnic group (12). Although three studies published previously of breast density included large numbers of Hispanic women (10, 13, 14), none of these studies described associations of breast cancer risk factors with percentage of breast density for Hispanic women separately. Because the distribution of breast cancer risk factors (*e.g.,* level of obesity and parity) could differ between Hispanics and non-Hispanic whites, we believe it is important to describe these associations for Hispanics to better understand the factors related to the interindividual variability in density in this large, ethnic group.

The CBHP was an integrated health care delivery/health education/research project targeting clients of three health centers that serve primarily Hispanic communities in Chicago. This project was designed to provide timely access to a state-of-the-art mammography screening center, and education regarding

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[3] The abbreviations used are: FA, fibroglandular tissue; HRT, hormone replacement therapy; CBHP, Chicago Breast Health Project; BMI, body mass index; BA, breast area; CEE, conjugated equine estrogen.

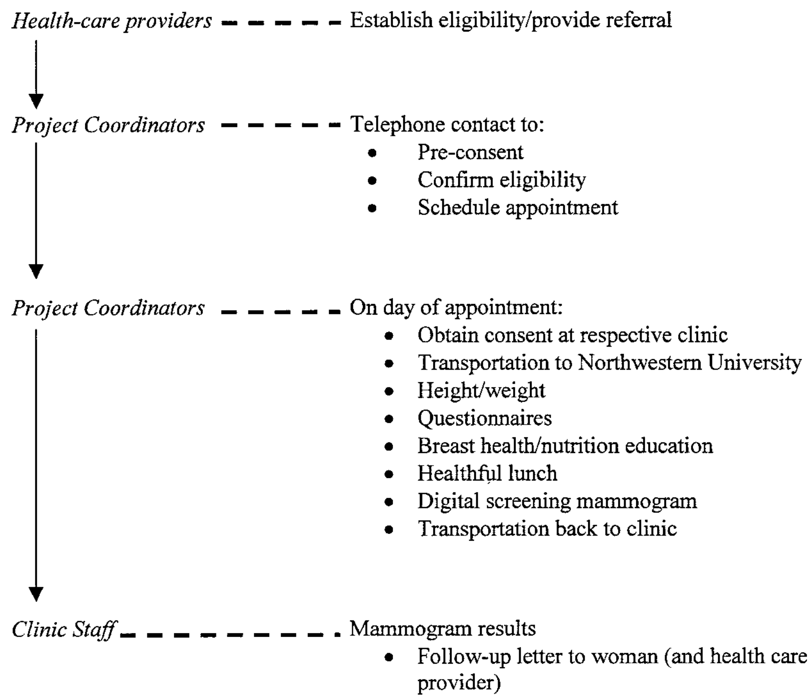

Fig. 1. CBHP study design.

the importance of breast cancer early detection and good nutrition. The primary research aims of this project were to examine cross-sectional associations of age, BMI, and sociodemographic and reproductive factors with breast density in Hispanic women. The CBHP is particularly well suited for a detailed analysis of these associations because of the availability of high-quality quantitative data on the extent of fibroglandular breast tissue determined from full-field digital mammography.

Materials and Methods

The CBHP Study Design and Sample. The design of CBHP is shown in Fig. 1. Briefly, healthcare providers from three clinics that serve large Hispanic communities referred eligible women for screening mammography to the project. Eligibility criteria included age 40 years and older, no personal history of breast cancer, not pregnant at the time of the study, no suspicious breast lumps, and no screening mammography within the last 12 months. On the day of the appointment, women provided written informed consent. The research protocol was approved by the Institutional Review Board of Northwestern University.

Between November 2000 and June 2002, a total of 504 women were referred to the project, and 325 women were screened. Among the 179 nonparticipants, 64% did not return phone calls and/or letters, or had a disconnected or a wrong telephone number, 32% did not want to participate, and 4% were ineligible for screening mammography. On the basis of information available on the referral form, there was no difference in the mean age of participants and nonparticipants (53 and 52 years, respectively; $P = 0.25$), and a there was a slightly higher proportion of women whose primary language is Spanish among participants than nonparticipants (90% and 85%, respectively; $P = 0.08$).

Among the 325 participants, we excluded 7 women who had screen-film mammography and 22 women who did not self-identify as Hispanic, resulting in a final sample size of 296 women who self-identified as Hispanic for this analysis. According to the self-reported information, ~63% of Hispanic women were born in Mexico, 15% were born in Puerto Rico, 7% were born in Guatemala, 13% were born in other Central or South American countries, and 2% were born in the United States.

Data Collection. Both of the data collection research interviewers were bilingual (Spanish/English) and bicultural (Hispanic), and were trained in interviewing and anthropometry measurements. All of the questionnaires were translated using a back translation approach (forward/backward/forward), which used two independent translations in sequence, from English to Spanish and then Spanish to English. Comparisons were made of the two versions in the original (English) language to identify inconsistencies and loss or change of meaning.

The health and lifestyle questionnaire was administered in-person by the interviewer, and included information on birth date, race/ethnicity, highest grade of education completed, reproductive and menstrual history, medical history, personal and family history of breast cancer in a first degree relative (*i.e.*, mother, daughter, or sister), current or past use of exogenous hormones, and alcohol and tobacco use. Weight and height were measured to the nearest 0.25 pounds and 0.25 inches with participants wearing no shoes. BMI was calculated as weight (kg) divided by height squared (m^2).

Screening mammography was obtained using an Food and Drug Administration-approved clinical full-field digital mammography system (GE Senographe 2000D; GE Medical Systems, Milwaukee, WI). Full-field digital mammography images are acquired on this system with $1,920 \times 2,304$ pixels, each pixel being 100 μm (10^{-4} m) in size, with 14-bit signal depth (16,384 signals levels) per pixel. A reviewer blinded to the radiologist report and patient history analyzed the digital image to determine the percentage of breast fibroglandular density measured from the craniocaudal and medio-lateral oblique images by: (*a*) determining the area of the entire breast, excluding nipple markers and pectoralis major muscle along the chest wall, by summing the number of pixels containing BA; (*b*) determining a threshold signal value that best separated fibroglandular regions from the fatty background; and (*c*) determining the area of FA within the breast by summing the number of pixels within the fibroglandular region. For each woman, percentage of breast density was calculated as the number of pixels filled with FA divided by the number of pixels for the entire BA, excluding markers and pectoralis major muscle (FA/BA). This calculation was done separately for the medio-lateral oblique and craniocaudal views of both right and left breasts, and percentage of breast density was determined by taking the mean of the percentage of density from both views of both breasts.

Statistical Methods. Women who reported that their menstrual periods had stopped completely were classified as postmenopausal, and all of the other women were classified as premenopausal. Age was stratified into ~5-year age groups, and the oldest age group included women aged 61–76 years. Highest level of education was classified as less than high school, high school graduate, or more than high school. Cutpoints for quintiles of BMI were computed for all of the women. The use of HRT and cigarettes were classified as never, past, or current. Age at first birth, numbers of live births, age at menarche, and age at menopause were categorized into four approximately equal groups, and alcohol intake was categorized as nondrinker, <1 drink/week, and ≥1 drinks per week. Women were also classified according to family history of breast cancer in a first-degree relative (*i.e.*, no, yes, and do not know). Percentage of breast density was treated as a continuous variable for all of the analyses. Univariate associations were examined by comparing the mean percentage of density across levels of each variable using ANOVA for premenopausal and postmenopausal women separately, and for all of the women combined.

Associations of each variable with percentage of breast density also were determined using multiple linear regression analysis. The variables included in the final model were age, BMI, and number of births as continuous variables. HRT use and cigarette smoking were each dichotomized (*i.e.*, current *versus* past/never), because there was no meaningful difference in percentage of density for past and never-users for each variable. For the combined analysis, a dichotomous variable for menopausal status was included. The variables in the final model were those that appeared to be associated ($P \leq 0.25$) with percentage of density in univariate analyses. Other variables (*i.e.*, education, age at first live birth, age at menarche, age at menopause for postmenopausal women, alcohol intake, and family history of breast cancer) were not associated with breast density in the multivariable models, nor did they change the β-coefficients for the variables included in the model by >10%.

Table 1 Distributions of sociodemographic, reproductive, health, and lifestyle characteristics with mean (SD) percentage of breast density among Hispanic women

Characteristic	Premenopausal (n = 105)		Postmenopausal (n = 191)	
	n	(%[a])	n	(%[a])
Age group (yrs.)				
40–45	68	(65)	7	(4)
46–50	29	(28)	28	(15)
51–55	8	(8)	49	(26)
56–60	0	(0)	49	(26)
≥61	0	(0)	58	(30)
Education				
<High school	62	(59)	130	(68)
High school	36	(34)	49	(26)
>High school	7	(7)	12	(6)
Body mass index (kg/m^2)				
18.6–27.2	16	(15)	42	(22)
27.3–29.8	29	(28)	31	(16)
29.9–32.1	21	(20)	39	(20)
32.2–35.4	18	(17)	41	(21)
35.5–51.2	21	(20)	38	(20)
Number of births				
0	4	(4)	6	(3)
1–2	33	(31)	33	(17)
3–4	43	(41)	69	(36)
≥5	25	(24)	83	(43)
Age at first birth for parous women (yrs.)				
≤18	36	(36)	62	(34)
19–21	23	(23)	61	(33)
22–24	16	(16)	25	(14)
≥25	25	(25)	37	(20)
Age at menarche (yrs)[b]				
≤11	18	(17)	31	(16)
12	18	(17)	30	(16)
13	29	(28)	46	(24)
14	20	(19)	42	(22)
≥15	19	(18)	42	(22)
Age at menopause (yrs)[c]				
22–42			41	(22)
43–46			38	(20)
47–50			55	(29)
51–59			53	(28)
Use of hormone replacement therapy				
Never	95	(90)	114	(60)
Past	5	(5)	27	(14)
Current	5	(5)	50	(26)
Cigarette smoking				
Never	81	(77)	148	(77)
Past	13	(12)	33	(17)
Current	11	(10)	10	(5)
Alcohol intake				
Non-drinker	81	(77)	165	(86)
<1 drink/week	18	(17)	19	(10)
≥1 drink/week	6	(6)	7	(4)
First degree family history of breast cancer				
No	96	(91)	170	(89)
Yes	2	(2)	13	(7)
Don't know	7	(7)	8	(4)

[a] For some characteristics, the percentage of women may not add to 100% because of rounding.
[b] Excludes 1 premenopausal woman missing data on age at menarche.
[c] Excludes 4 postmenopausal women missing data on age at menarche.

Results

Among the 296 Hispanic participants, the mean (SD) percentage of breast density was low (17.6%; 10.5%), with a range of 1.9–54.6%. The distributions of premenopausal women and postmenopausal women across strata of selected sociodemographic, reproductive, health, and lifestyle characteristics are shown in Table 1. As expected, a much higher proportion of postmenopausal women (>80%) were >50 years of age compared with premenopausal women (8%). Most women had less than a high school education, and were overweight or obese, although there was a slightly higher proportion of postmenopausal women than premenopausal women in the lowest quintile of BMI. The distributions of premenopausal and postmenopausal women were similar across strata of age at first birth and age at menarche. Although the proportion of women who were nulliparous was similar for pre- and postmenopausal women, postmenopausal women were more likely to have had $\geq$5 live births. Less than 25% of postmenopausal women reported their age at menopause as $\leq$42 years of age. A higher proportion of postmenopausal women reported ever using HRT than premenopausal women (40% *versus* 10%). In this group of women, the overall prevalence of cigarette smoking and alcohol use was low; however, premenopausal women were more likely to be current smokers (10% *versus* 5%), and to drink alcohol (23% *versus* 14%) than postmenopausal women. Most women ($\geq$80%) reported no family history of breast cancer in a first-degree relative.

For postmenopausal women, the mean (SD) percentage of breast density was lower than for premenopausal women [15.1% (9.2%) and 22.2% (11.0%), respectively; $P < 0.0001$]. This difference was apparent for each age group (see Table 2). As expected, age was statistically significantly inversely associated with percentage of breast density. This association appeared to be stronger for postmenopausal women, although there was a trend of lower density with older age among premenopausal women. In simple linear regression analysis modeling age as a continuous independent variable, the mean decline in breast density was -0.06%/year ($P = 0.86$) in premenopausal women and -0.21%/year ($P = 0.02$) in postmenopausal women. There was a statistically significant inverse association between BMI and percentage of breast density, and this association was stronger for premenopausal women than postmenopausal women. Current cigarette smokers had a higher density than never or past smokers; this difference was only significant in the combined analysis of premenopausal and postmenopausal women. Similarly, in the combined analysis, there was a trend of lower density with higher number of births, although these results should be interpreted with caution because of the small number of women who were nulliparous in this sample. In addition, percentage of breast density was higher among current HRT users compared with never or past users, but this difference achieved statistical significance only for postmenopausal women. Education, age at first live birth, age at menarche, age at menopause, alcohol intake, and family history of breast cancer in a first degree relative were not associated with percentage of breast density for premenopausal, postmenopausal, or all women combined.

In multivariate linear regression analyses (Table 3), there were no differences in the direction of the relationships between each risk factor and percentage of breast density for premenopausal and postmenopausal women, although there appeared to be some differences in the strength and level of significance of these relationships for some variables. In particular, there was no meaningful relationship between age and percentage of breast density for premenopausal women, whereas older age was significantly associated with lower density for postmenopausal women. However, the test for interaction between age and menopausal status was not statistically significant ($P = 0.51$). Density was significantly lower (*i.e.*, 5.2%) among postmenopausal than premenopausal women. Higher BMI was significantly associated with a lower percentage of breast density for both groups of women. For women who reported currently taking HRT, percentage of breast density was higher compared with those who were not currently taking HRT; this difference was ~3.3% ($P = 0.03$) in the combined analysis. Among premenopausal women, current cigarette smokers had a marginally higher ($P = 0.06$) percentage of density compared with nonsmokers, but there was no meaningful relationship between cigarette smoking and breast density among postmenopausal women. The test for interaction between menopausal status and cigarette smoking was only marginally significant ($P = 0.11$). There was no evidence of an association between number of births and percentage of breast density in any analyses.

Discussion

As mentioned previously, three other studies of breast density included Hispanic women (10, 13, 14). However, none of these studies reported associations of breast cancer risk factors with breast density for Hispanics specifically. The CBHP project is the first study that we are aware of to examine these associations in this large ethnic group. Similar to studies of other racial/ethnic groups, we found significant inverse associations of age, BMI, and menopausal status with percentage of breast density, whereas current use of HRT and perhaps cigarette smoking were positively associated with density. However, we observed no meaningful relationships between percentage of breast density and number of births, age at first birth, age at menarche, age at menopause, family history of breast cancer in a first-degree relative, or alcohol intake.

It is well recognized that percentage of breast density is lower among postmenopausal women than among premenopausal women (3). This difference in density according to menopausal status is consistent with the hypothesis that cessation of ovarian steroid hormone production leads to changes in the distributions, and amounts of fibroglandular and fat tissue in the breast. Results of our study showed a weak inverse relationship of age with density for premenopausal women, and a stronger inverse relationship for postmenopausal women. It is plausible that a weak association of age with density among premenopausal women could be because of the strong influence of ovarian steroid hormone levels on the extent of dense tissue, which could mask subtle age-associated differences in percentage of density over a small age range; in our study, 92% of premenopausal women were 40–50 years of age. Indeed, our findings for premenopausal women are consistent with those of Boyd *et al.* (15), in which there was little reduction in percentage of breast density (2%) over a 5-year period. Alternatively, there are data, albeit controversial, indicating variability in mammographically detected breast density (13) and breast structure according to time in the menstrual cycle (16). Not accounting for this variability could attenuate modest associations of age with breast density in premenopausal women. In postmenopausal women, a significant inverse relationship of age with percentage of breast density could result from both an increase in the fat area and a decrease in the dense area of the breast because of reduced hormone exposure.

Greater BMI has been consistently associated with a higher risk of postmenopausal breast cancer but with a lower risk of premenopausal breast cancer (17–19). This difference in risk has been attributed to differences in sex hormone synthesis and metabolism for overweight/obese premenopausal women compared with overweight/obese postmenopausal women. Among premenopausal women, higher levels of BMI are associated with lower serum estrogen concentration, whereas among postmenopausal women there is a positive association between BMI and estrogen concentration (20). Nonetheless, most observational studies show inverse relationships between BMI (or weight) and percentage of breast density regardless of menopausal status (3). It has been proposed that increasing levels of BMI increase the fat area of the breast to a greater extent than the dense area, and therefore, the percentage of breast density would decrease with higher levels of obesity in

Table 2 Univariate associations of sociodemographic, reproductive, health, and lifestyle characteristics with mean (SD) percentage of breast density among Hispanic women

Characteristic	Premenopausal (n = 105)			Postmenopausal (n = 191)			All (n = 296)		
	Mean percentage of density	(SD)	P	Mean percentage of density	(SD)	P	Mean percentage of density	(SD)	P
Age group (yrs.)									
40–45	22.7	(10.9)		14.3	(8.4)		21.9	(10.9)	
46–50	21.6	(12.1)		18.1	(10.7)		19.9	(11.5)	
51–55	20.8	(9.7)	0.85	17.2	(10.1)		17.7	(10.0)	
56–60	–	–		13.5	(8.1)		13.5	(8.1)	
≥61	–	–		13.3	(8.1)	0.05	13.3	(8.1)	<0.0001
Education									
<High school	23.2	(11.5)		15.0	(8.9)		17.6	(10.6)	
High school	20.7	(10.5)		15.2	(8.6)		17.5	(9.8)	
>High school	21.5	(9.6)	0.56	16.2	(14.3)	0.90	18.2	(12.7)	0.97
Body mass index (kg/m^2)									
18.6–27.2	29.8	(12.9)		18.4	(10.0)		21.5	(11.9)	
27.3–29.8	24.4	(12.3)		14.7	(9.4)		19.4	(11.9)	
29.8–32.1	19.7	(9.5)		13.8	(8.7)		15.9	(9.4)	
32.2–35.4	22.9	(7.1)		14.3	(9.2)		16.9	(9.4)	
35.5–51.2	15.4	(7.4)	0.0008	14.0	(8.3)	0.14	14.5	(8.0)	0.002
Number of births									
0	25.4	(6.7)		18.0	(15.9)		21.0	(13.1)	
1–2	20.9	(12.6)		15.2	(9.9)		18.0	(11.6)	
3–4	24.6	(10.8)		15.3	(9.1)		18.9	(10.7)	
≥5	19.6	(9.2)	0.24	14.7	(8.6)	0.84	15.8	(8.9)	0.11
Age at first birth among parous women (yrs.)									
≤18	22.0	(11.2)		14.1	(7.7)		17.0	(9.9)	
19–21	23.5	(10.3)		15.8	(9.1)		17.9	(10.0)	
22–24	23.9	(12.1)		16.4	(12.3)		19.3	(12.6)	
≥25	20.4	(11.4)	0.72	14.4	(8.2)	0.60	16.8	(10.0)	0.60
Age at menarche (yrs.)[a]									
≤11	22.9	(12.5)		17.2	(10.3)		19.3	(11.4)	
12	25.4	(11.2)		14.3	(9.5)		18.5	(11.4)	
13	18.8	(8.8)		15.8	(9.3)		17.0	(9.2)	
14	23.5	(10.6)		14.3	(9.0)		17.3	(10.4)	
≥15	22.6	(13.0)	0.33	14.2	(8.4)	0.59	16.8	(10.7)	0.69
Age at menopause (yrs.)[b]									
22–42	–	–	–	15.3	(9.3)		–	–	–
43–46	–	–	–	15.5	(8.7)		–	–	–
47–50	–	–	–	14.2	(8.6)		–	–	–
51–59	–	–	–	15.2	(9.9)	0.88	–	–	–
Menopausal status									
Premenopausal	–	–	–	–	–	–	22.2	(11.0)	
Postmenopausal	–	–	–	–	–	–	15.1	(9.2)	< 0.0001
Use of hormone replacement therapy									
Never	21.9	(10.5)		14.0	(8.5)		17.6	(10.2)	
Past	22.1	(17.6)		14.0	(8.5)		15.2	(10.5)	
Current	29.2	(13.7)	0.35	18.2	(10.5)	0.02	19.2	(11.1)	0.22
Cigarette smoking									
Never	21.6	(10.4)		14.9	(9.1)		17.3	(10.1)	
Past	20.8	(14.2)		15.0	(10.0)		16.6	(11.4)	
Current	28.9	(10.0)	0.10	17.7	(9.7)	0.66	23.6	(11.2)	0.02
Alcohol intake									
Nondrinker	21.9	(11.4)		15.1	(9.1)		17.4	(10.4)	
<1 drink/week	21.9	(9.0)		13.9	(6.9)		17.8	(8.9)	
≥1 drink/week	27.4	(12.4)	0.50	17.7	(16.5)	0.65	22.2	(15.0)	0.27
First=degree family history of breast cancer[c]									
No	21.8	(11.3)		15.1	(9.4)		17.5	(10.6)	
Yes	29.0	(3.4)	0.37	14.5	(7.5)	0.83	16.4	(8.7)	0.70

[a] Excludes 1 premenopausal woman with missing data on age at menarche.
[b] Excludes 4 postmenopausal women who were missing data on age at menopause.
[c] Excludes 7 premenopausal and 8 postmenopausal women who did not know their family history of breast cancer.

both pre- and postmenopausal women (21). In a study of the relationships of various anthropometric factors with radiological features of the breast in premenopausal women, BMI was positively associated with total area and nondense area of the breast, and inversely associated with dense area (22). Our findings in Hispanic women are consistent with those of previous studies showing an inverse relationship between BMI and percentage of breast density. This is particularly noteworthy

Table 3 Multivariate associations of sociodemographic, reproductive, health and lifestyle factors with percentage of breast density among Hispanic women

Characteristic	Premenopausal (n = 105)			Postmenopausal (n = 191)			All (n = 296)		
	β	(SE)	P	β	(SE)	P	β	(SE)	P
Age (Δ 1 year)	−0.03	(0.30)	0.91	−0.21	(0.09)	0.03	−0.20	(0.09)	0.03
Postmenopausal *vs.* premenopausal				–	–	–	−5.19	(1.66)	0.002
Body mass index (Δ 1 kg/m^2)	−0.65	(0.18)	0.0006	−0.30	(0.12)	0.02	−0.43	(0.10)	<0.0001
Number of births (Δ 1)	−0.04	(0.51)	0.94	−0.10	(0.25)	0.68	−0.08	(0.23)	0.73
Current *vs.* never/past use of HRT[a]	4.80	(5.04)	0.34	3.50	(1.52)	0.02	3.34	(1.49)	0.03
Current *vs.* never/past cigarette smoking	6.23	(3.33)	0.06	0.10	(3.00)	0.97	3.34	(2.18)	0.13

[a] HRT, hormone replacement therapy.

because in the United States, a very high proportion of Hispanic women are overweight or obese (23). Therefore, measures of breast density could be useful markers in breast cancer risk reduction intervention studies focusing on weight loss in this ethnic group.

A considerable amount of observational and clinical trial data support a modest increase in risk of breast cancer with use of combined HRT (*i.e.,* estrogen plus progestin) among recent or current users in particular (24–27). In addition, use of HRT has been associated with higher percentage of breast density in most studies (3). For example, the initiation of HRT use has been associated with increased density, whereas discontinuation has been associated with decreased breast density (9). Moreover, data from the Postmenopausal Estrogen/Progestin Intervention Trial were used to study the effects of CEE, CEE plus cyclic or continuous medroxy progesterone acetate, and CEE plus micronized progesterone on changes in radiographic breast density (5). In that study, the percentage of women with increased breast density was >2-fold greater for those randomized to CEE plus medroxy progesterone acetate or micronized progesterone (>18%) compared with those randomized to CEE alone (8%) or placebo (2%). Unfortunately, most women in our study who reported taking HRT did not know the composition of the preparations used; therefore, we could not examine differences in percentage of density according to type of HRT.

Results from epidemiological studies of the associations between cigarette smoking and breast cancer risk are inconsistent with some showing higher, lower, or no risk (28, 29), and few studies have assessed the relationship of cigarette smoking with breast density. Our finding of a higher density among current smokers compared with nonsmokers is consistent with the hypothesis that cigarette smoking increases risk of breast cancer. Conversely, Vachon *et al.* (8) found an inverse relationship of smoking with percentage of density for premenopausal women and no association for postmenopausal women. The nature of the relationship between cigarette smoking and breast cancer risk (or breast density) is unclear. There are data from experimental models showing that the carcinogens present in tobacco smoke induce mammary tumorigenesis and form DNA adducts in breast epithelial cells, which could lead to genetic alterations involved in neoplastic transformations (29). Alternatively, it has been proposed that smoking could have antiestrogenic effects (30), which would support the findings of Vachon *et al.* (8). Clearly, additional research is needed to better understand whether cigarette smoking affects breast structure and breast cancer risk.

The associations of other established breast cancer risk factors such as younger age at menarche, older age at menopause and first birth, and nulliparity with percentage of breast density have been explored in many studies. In most previous studies, nulliparous women have a higher density than parous women, and older age at first birth have been associated with lower density (3). Similarly, positive association between alcohol consumption and risk of breast cancer has been noted in most epidemiological studies (31), and there is some evidence of a positive association between alcohol intake and percentage of breast density (32, 33). In our study of Hispanic women, we observed no relationships of parity, age at first birth, or alcohol intake with percentage of density. The lack of such relationships may be attributed to the very low proportion of women who were nulliparous (≤4%), the very high proportion of women whose age at first birth was ≤21 years (>60%), or the high proportion of nondrinkers in this study, which results in limited power to observe potential associations of these variables with percentage of breast density.

A primary strength of the CBHP is the use of full-field digital mammography in which the images are acquired directly by a computer and percentage of breast density is determined quantitatively, whereas most studies of the factors associated with breast density have relied on qualitative classifications of density. In particular, in the three previous studies that included Hispanic women (10, 13, 14) assessment of breast density was based on either the Wolfe system (34) or on the American College of Radiology Breast Imaging Reporting and Data System (35), which are discrete density classifications and do not provide a continuous scale for quantitative evaluation of density. Although the average percentage of breast density among the participants in this study was low, this level of density is consistent with national data showing a lower incidence of breast cancer for Hispanic than for non-Hispanic white or black women (12). Moreover, in our sample of women there was a very high prevalence of overweight/obesity (>80%) and a very high prevalence of parity (97%), which could result in a low average percentage of breast density. Finally, we recognized that the ethnic category Hispanic contains significant diversity and represents individuals from different cultural backgrounds (*e.g.,* Mexican, Puerto Rican, Cuban, and so forth). However, the small sample size of women according to country of origin precludes a meaningful stratified analysis of the factors associated with breast density.

In summary, CBHP was uniquely designed to examine the factors associated with mammographically assessed breast density among Hispanic women. Our results are consistent with those of previously published studies for primarily non-Hispanic white women showing that significant associations of age, BMI, menopausal status, and current use of HRT were associated with the extent of density. We also found evidence, for the first time that we are aware of, that cigarette smoking might increase percentage of breast density. Additional research among Hispanic women focusing on the relationships of other, potentially modifiable factors, as well as related endogenous hormonal factors, with the extent of breast density is warranted to develop targeted interventions that are culturally competent.

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