Acculturation and Breast Density in Foreign-Born, U.S. Chinese Women

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Abstract

The role of acculturation in the breast cancer risk increase among U.S. Chinese women is unclear. We examined the association between acculturation and breast density in a sample of foreign-born, U.S. Chinese women and examined factors that may explain such an association. Between January 2002 and May 2003, 212 Chinese women were recruited from Philadelphia region screening programs. Cranial-caudal mammographic images were classified into one of four categories ranging from ''entirely fatty'' to ''extremely dense.'' Questionnaires assessed information on sociodemographic, cultural, reproductive, and lifestyle factors. An index of acculturation was created based on self-reported English proficiency and within- and cross-ethnicity social interactions. To estimate odds ratios (OR) for falling into a higher versus lower category for breast density, we conducted logistic regression analysis using proportional odds models for polychotomous outcomes. We found that women in the highest acculturation category had denser breasts [age-adjusted OR, 3.1; 95% confidence interval (95% CI), 1.6-6.0]. They also had fewer live births, higher age at first live birth, and higher dairy food intake, all factors associated with breast density. In 196 women with complete covariate data, only adjustment for number of live births and dairy food intake attenuated the estimate for acculturation by >10%. With adjustment for both simultaneously, the most acculturated women were still more likely to have denser breasts (age- and menopause-adjusted OR, 2.0; 95% CI, 1.0-4.2). These analyses are the first to show breast density differences by level of acculturation among foreign-born, U.S. Chinese women. Despite reproductive and lifestyle differences by level of acculturation, differences in these factors did not explain the acculturation-breast density association. Future longitudinal research will examine whether the association is due to early-life factors, postmigration lifestyle changes, or perimenopausal exposures. (Cancer Epidemiol Biomarkers Prev 2006;15(7):1301–5)

Introduction

Rates of breast cancer incidence range from <35 per 100,000 women in Asian countries to well >80 per 100,000 women in northern Europe and the United States (1). That rates in such low-risk populations as Chinese women increase after migration to the United States (2, 3) strongly suggests a role for environmental and behavioral factors (4), but the specific factors that might contribute to this increase in risk remain unclear. Among Asian Americans, attaining the same breast cancer risk as the host population may not occur until the second U.S.-born generation (1). Nevertheless, evidence that the increase begins as early as in the migrating generation would suggest that factors occurring in adulthood can affect risk. Such evidence is limited for U.S. Chinese women (2, 3, 5) because of the limited number of foreign-born women included in previous studies and because of the small number of breast cancer cases among such women.

Breast density, the percentage of total breast area with a mammographically dense appearance, is a useful surrogate marker for breast cancer risk in epidemiologic studies (6). It is strongly associated with breast cancer risk (7) in Asian women as well as in White women (8, 9). It may also be a useful marker for identifying factors contributing to increased breast cancer risk in Chinese immigrants to the United States. The objectives of this study were to examine whether a higher level of acculturation was associated with higher breast density in a sample of foreign-born U.S. Chinese women and to identify factors that might explain such an association.

Materials and Methods

Study Sample. A total of 250 participants were recruited between January 2002 and May 2003 from community organizations and contacts, mammography screening programs, and newspaper advertisements in the Philadelphia region. Women were eligible if they were of Chinese heritage, were at least 40 years old, and had received a mammogram within the previous 3 months. Exclusion criteria included history of breast augmentation or reduction; history of prophylactic mastectomy; history of any cancer, except nonmelanoma skin cancer; current breast-feeding or breast-feeding within last 9 months; and current pregnancy. Participants received $20 as reimbursement for their time. The study was approved by the Fox Chase Cancer Center Institutional Review Board.

Data Collection. At enrollment, participants completed health history and dietary questionnaires that were either interviewer administered (n = 184) or self-administered (n = 66). Level of acculturation was quantified using two dimensions of acculturation: (a) adult English proficiency and (b) structural assimilation, or level of interaction with members of mainstream society (10). In work conducted among Mexican Americans, the two dimensions together seemed to reflect a ''higher-order construct'' that Hazuda et al. (10) termed ''adult functional integration with mainstream society.'' To assess adult English proficiency, participants gave one of five possible responses ranging from Chinese only to English only (coded 1-5) to three separate questions of what language they preferred to speak, read, and write (11). To assess structural assimilation, participants responded on a three-level scale

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(coded 1-3), ranging from mostly or all to few or none Chinese, when asked, as three separate questions, about the ethnicity of their neighbors, close friends, and coworkers. An acculturation score was then calculated as the sum of the scores for the six questions, with values ranging from 6 (representing the lowest level of acculturation) to 24 (representing the highest). We imputed values for each of the two dimensions separately for 2 of 7 women who responded to two of the three questions on English proficiency and for 72 of 74 women who responded to two of the three questions on structural assimilation by using the mean of the two nonmissing responses. Of the 72 women for whom we imputed a structural assimilation score, 56 were missing the response for coworkers' ethnicity because they were unemployed at the time. Estimates for level of acculturation were similar when we limited the sample to 156 women with complete data on all six questions.

Detailed residential histories were used to calculate length of U.S. residence and age at migration. Women also responded to questions on sociodemographic factors, breast cancer in first-degree or second-degree female relatives, pregnancy and breast-feeding history, menopausal status (no menstrual period in the last year), and birth control and female hormone pill use. Body mass index (BMI; in kg/m^2) was determined using self-reported weight and height. We calculated adult weight gain as the difference between their current weight and reported weight at age 18. Physical activity was assessed using a scale adapted from that used in the Framingham study (12, 13). Dietary intake was assessed using an 88-item food frequency questionnaire designed for the target population (14). Dietary factors of interest were calories, total and saturated fats, cholesterol, carbohydrates, protein, fiber, folic acid, and calcium as well as foods and food groups, including intake of red meat (beef and pork), vegetables, green leafy vegetables, dairy foods (milk, cheese, yogurt, and ice cream), and tofu.

Breast Density Assessment. We obtained mammographic images from the hospitals where participants had recently received their screening mammogram. The median time between mammogram and interview was 12 days. Breast density was assessed by the study radiologist (K.E.), who was blinded to the identity and other personal characteristics of study subjects. Breast images were classified as entirely fatty, having scattered fibroglandular tissue, heterogeneously dense, or extremely dense (15). Results presented below are based on radiological classifications for the cranial-caudal view of a randomly selected side. Consistent with previous work (16), however, left-side and right-side assessments were highly correlated (r = 0.99) in the 216 women with complete mammographic data, and assessments between left and right sides agreed in all but 4 (2%) women. Breast density assessments were highly reproducible when measured by the same radiologist in a separate study,[4] in which breast density was reassessed in a randomly selected set of 52 images (κ = 0.97 for left side and κ = 0.89 for right side).

Statistical Analyses. Analyses included 212 women not missing either acculturation score or breast density assessment. We created categories of approximately equal size to represent low, middle, and high levels of acculturation and then compared distributions of sociodemographic, lifestyle, reproductive, and dietary factors by acculturation category. Categorical variables were compared using the Cochran-Mantel-Haenszel test statistic. Continuous variables were compared using ANOVA.

To estimate odds ratios (OR), we did logistic regression analysis using proportional odds models for polychotomous outcomes (17). All log odds can be interpreted as having higher density versus lower density. Score test results (17) indicated that the assumption of proportional odds was not violated for any of the variables examined. All models were, at a minimum, adjusted for age as a continuous variable. Acculturation score was modeled as both continuous and categorical variables, with similar results. For ease of presentation, we show results for acculturation score modeled as a categorical variable. Models including dietary factors were additionally adjusted for caloric intake as a continuous variable. Nutrient values from dietary sources were energy-adjusted using the residual method (18). For dietary variables, we estimated ORs for tertiles of intake relative to the lowest tertile and estimated Ps for linear trend by including in the model an ordinal variable representing the scaled median value for each tertile. We examined the possibility of effect modification by menopausal status by examining Ps for interaction, estimated from a model with a variable × menopausal status interaction term. Dietary variables were divided at the median rather than into tertiles because of the limited sample size.

Subsequent analyses were limited to 196 women not missing values for any of the potential explanatory factors of interest. To evaluate the extent to which selected factors could explain the association between acculturation and breast density, we included each factor individually in the model containing acculturation, age, and menopausal status because of its close association with age and possibly independent association with breast density. We then compared OR estimates for acculturation in the models with and without each potential explanatory factor. We arbitrarily selected a change of 10% in the estimate for the acculturation variable as our criterion for identifying potentially important explanatory variables.

Results

Among 212 women with information on breast density and level of acculturation, mean (SD) age was 53.2 (10.4) years, mean length of residence in the United States was 11.8 (8.6) years (range, <1-45 years), and mean age at migration to the United States was 41.3 (13.2) years (range, 11-69 years). Most women (81%) were born in China or Hong Kong; the others were born in Southeast Asia (10%) or Taiwan (8%). Level of acculturation in general was low [mean (SD), 9.5 (2.8); range, 6-20]. Education level of participants showed greater variability, with 40% having less than a high school education, 35% high school graduates, and 25% having at least a college degree. With respect to breast density, over half of the women fell into the extremely (38%) or heterogeneously (28%) dense categories, 27% were classified as having scattered fibroglandular tissue, and only 7% of women fell into the least dense (entirely fatty) category.

We found a significant association between level of acculturation and breast density (Table 1). Women in the highest category of acculturation had a 3-fold greater odds of

Table 1. Age-adjusted ORs and corresponding 95% CIs for acculturation category and higher breast density (n = 212)

Breast density category	Acculturation category		
	6-8 (n = 84)	>8-10 (n = 69)	>10 (n = 59)
Entirely fatty	6	7	7
Scattered fibroglandular tissue	31	29	17
Heterogeneously dense	32	30	20
Extremely dense	31	33	56
Age-adjusted OR (95% CI)	1.0	1.8 (1.0-3.4)	3.1 (1.6-6.0)

[4] Unpublished data.

having denser breasts (OR, 3.1; 95% CI, 1.6-6.0) relative to women in the lowest category.

To investigate potential explanatory factors for this association, we compared lifestyle and reproductive factors across categories of acculturation (Table 2). More acculturated women had a higher level of education, were less likely to have been born in China, had longer U.S. residence, and migrated at a slightly younger age. They also tended to have a lower age at menarche, fewer live births, higher age at their first live birth, and shorter duration of breast-feeding, and among postmenopausal women, they were more likely to have used hormone therapy. With respect to dietary intake, more acculturated women were more frequent consumers of dairy foods, vegetables, and tofu but less frequent consumers of green leafy vegetables. They also had higher intake of energy and total fat but lower intake of carbohydrates and folic acid (data not shown).

More acculturated women were more likely to have a first-degree relative with breast cancer and to have used hormonal contraceptives, but the differences were not statistically significant across acculturation categories. We observed no differences in mean BMI by level of acculturation or in weight change or physical activity (data not shown).

Associations of lifestyle and reproductive factors with breast density are also shown in Table 2. Higher breast density was significantly associated with having a first-degree relative with breast cancer and with higher age at first live birth. It was significantly inversely associated with BMI, number of live births, and number of months of breast-feeding. With adjustment for age only, adult weight change was also inversely associated with breast density (OR, 0.7; 95% CI, 0.5-0.9 per 10 kg weight gain) but not after additional adjustment for BMI (OR, 1.4; 95% CI, 0.6-3.2), which was strongly correlated with weight change (r = 0.7). We observed suggestive associations with breast density for level of education, birthplace, nulliparity, and hormonal contraceptive and hormone therapy use as well as a suggestive inverse association for postmenopausal status, but these were not statistically significant. Length of U.S. residence, age at migration, and age at menarche were not related to breast density in this sample.

With respect to dietary factors, intake of dairy foods was positively associated with breast density, whereas vegetable intake was inversely associated. Among nutrients of interest, the association of calcium intake with breast density differed by menopausal status ($P_{interaction}$ = 0.01): calcium intake was significantly associated with higher breast density among 97 premenopausal women (OR, 3.8; 95% CI, 1.5-9.8, above versus below median) but not among 115 postmenopausal women (OR, 0.7; 95% CI, 0.4-1.4, above versus below median). In premenopausal women, including calcium and dairy intake in the same model attenuated the OR (95% CI) for calcium to 2.7 (0.9-8.5) and for dairy intake from (above versus below median) OR (95% CI) of 3.4 (1.3-9.1) to 1.8 (0.6-6.1). In

Table 2. Distributions of demographic characteristics and potential predictors of breast density by acculturation category and age-adjusted ORs and corresponding 95% CIs for higher breast density (n = 212)

Characteristics	Distribution by acculturation category*				Age-adjusted OR for higher vs lower breast density	
	6-8 (n = 84)	>8-10 (n = 69)	>10 (n = 59)	P		
Age (y)	51.7 ± 9.2	56.2 ± 11.5	51.7 ± 10.1	0.01	0.6 (0.5-0.6)†	
Postmenopausal	50	61	53	0.39	0.5 (0.2-1.1)	
Length of U.S. residence (y)‡	9.6 ± 7.5	10.9 ± 8.5	15.9 ± 9.0	<0.0001	1.0 (0.8-1.1)†	
Age at migration (y)‡	42.1 ± 12.4	44.9 ± 13.3	35.9 ± 12.6	0.0005	1.0 (0.9-1.2)†	
Level of education						
Less than high school	68	36	5	<0.0001	1.0	
High school graduate to less than college	26	45	37		1.6 (0.9-2.9)	
College graduate or more	6	19	58		1.7 (0.9-3.4)	
Place of birth						
China	93	80	66	0.0003	1.0	
Southeast Asia	5	14	14		1.4 (0.6-3.4)	
Taiwan	2	6	20		1.8 (0.7-4.8)	
BMI (kg/m^2)‡	24.3 ± 3.6	23.9 ± 3.3	24.1 ± 3.4	0.78	0.8 (0.8-0.9)	
First-degree relative with breast cancer	5	3	10	0.19	4.7 (1.4-16.4)	
Age at menarche (y)	15.0 ± 2.0	14.3 ± 1.7	13.8 ± 1.4	<0.0001	1.0 (0.5-2.1)†	
Nulliparity	4	9	12	0.17	1.7 (0.6-4.8)	
No. live births§	2.4 ± 1.3	2.5 ± 1.3	1.9 ± 0.8	0.008	0.6 (0.5-0.8)	
Age at first birth (y)§	25.6 ± 5.1	26.2 ± 5.1	28.9 ± 4.4	0.0008	1.5 (1.1-2.0)†	
No. months breast-fed§	15.9 ± 24.0	9.8 ± 15.1	5.7 ± 7.8	0.006	0.9 (0.9-1.0)	
Ever used hormonal contraceptives‡	10	9	20	0.12	1.5 (0.7-3.5)	
Ever used hormone therapy‖	10	21	32	0.06	1.6 (0.7-3.8)	
					Tertile 2 vs tertile 1	Tertile 3 vs tertile 1
Dietary intake (servings/wk)						
Red meat	6.8 ± 5.7	7.3 ± 4.6	7.0 ± 6.0	0.85	0.6 (0.3-1.2)	0.6 (0.3-1.2) P_{trend} = 0.19
Dairy	4.6 ± 4.4	6.3 ± 4.9	6.4 ± 5.5	0.03	1.3 (0.7-2.5)	2.3 (1.1-4.8) P_{trend} = 0.05
Vegetables	22.5 ± 9.9	28.0 ± 12.7	26.9 ± 14.6	0.02	1.0 (0.5-2.0)	0.5 (0.2-1.0) P_{trend} = 0.05
Greens	7.6 ± 5.0	5.8 ± 3.7	5.2 ± 3.7	0.002	0.5 (0.3-0.9)	0.7 (0.3-1.5) P_{trend} = 0.35
Tofu	1.4 ± 1.5	2.2 ± 2.0	2.2 ± 2.0	0.007	1.0 (0.5-2.0)	0.7 (0.3-1.3) P_{trend} = 0.18

*Categorical variables are expressed as percent distribution within each acculturation category. Continuous variables are expressed as mean (SD). Ps were determined by Cochran-Mantel-Haenszel test statistic for categorical variables or by ANOVA for continuous variables.
†OR for 5-year increment.
‡Due to missing data, n differed for the following variables: length of U.S. residence and age at migration (n = 209), BMI (n = 208) and hormonal contraceptive use (n = 208).
§Conducted among 196 parous women; for age at first live birth, n = 194 due to missing data.
‖Conducted among 115 postmenopausal women.

postmenopausal women, in contrast, including calcium and dairy intake in the same model strengthened the OR (95% CI) for calcium intake to 0.3 (0.1-0.7) and for dairy intake from (above versus below median) OR (95% CI) of 2.0 (0.9-4.2) to 5.2 (1.9-14.6). We observed a suggestive but statistically nonsignificant inverse association for folic acid intake (OR, 0.6; 95% CI, 0.3-1.1, tertile 3 versus tertile 1, $P_{trend} = 0.09$). Other dietary factors were not associated with breast density in our sample (data not shown).

In analyses restricted to the 196 women with complete covariate data, we adjusted for each potential explanatory factor to determine the extent to which they might explain the association between acculturation and breast density. Adjustment for only two variables (number of live births and dairy food intake) attenuated the estimate for level of acculturation by >10%. Among the 196 women, the OR (95% CI) for the highest level of acculturation was attenuated from 2.7 (1.3-5.4) to 2.2 (1.1-4.4) with adjustment for number of live births and to 2.4 (1.2-4.9) with adjustment for dairy food intake. Simultaneous adjustment for both number of live births and dairy food intake attenuated the OR (95% CI) to 2.0 (1.0-4.1). Adjustment for tofu intake, on the other hand, increased the OR (95% CI) for the highest level of acculturation to 3.0 (1.5-6.2). In a model that included all potentially important explanatory variables (age, menopausal status, BMI, first-degree relative with breast cancer, number of live births, age at first live birth, months of breast-feeding, and intake of calories, dairy, vegetables, and tofu), the OR (95% CI) for the highest level of acculturation was 2.3 (1.1-5.1). We conducted similar analyses for hormone therapy among 108 postmenopausal women only and for calcium intake among 88 premenopausal women, but neither factor explained the association for level of acculturation in either group (data not shown).

Discussion

These analyses are the first to show differences in breast density by level of acculturation within the migrating generation of Chinese women to the United States, suggesting substantial differences in breast cancer risk among foreign-born, U.S. Chinese women. That breast cancer risk increases with migration to the United States is well recognized even beginning in the migrating generation (3). How breast cancer risk varies within the migrating generation is less clear. Ziegler et al. (2) observed significant differences in risk among Asia-born women by years of residence in the United States. Shimizu et al. (5) found a gradient in risk among U.S. Japanese women, with the lowest rates in most recent immigrants, highest rates in the U.S.-born, and intermediate rates in women who had immigrated early in life. They concluded that early-life factors are important contributors to breast cancer development.

The extent to which risk changes within the migrating generation of Chinese women to the United States may shed light on whether acculturation-related lifestyle changes in adulthood affect breast cancer risk. Indicators of acculturation are generally interpreted as the extent to which individuals in a minority group adopt the host population's lifestyle characteristics, such as dietary intake and physical activity. An association between acculturation and breast density may also be the result of social or cultural differences established before migration. That the more acculturated women in our sample had a higher level of education, lower age at menarche, and stronger family history of breast cancer, for example, suggests that early-life or other premigration factors also contributed to the observed differences in breast density by level of acculturation.

Higher breast density has been associated with lower BMI, less physical activity, nulliparity, and, among parous women, later age at first birth and fewer live births (7, 19). In our sample, we observed substantial differences in the distributions of several hormone-related risk factors for higher breast density and breast cancer across levels of acculturation, but adjustment only for number of live births resulted in a meaningful attenuation of the estimate for acculturation. Even with adjustment, however, the association between level of acculturation and breast density persisted, similar to the findings of previous studies on reproductive factors and breast cancer risk in Asian American women (20-22). Despite consistent findings of associations of adult weight gain with postmenopausal breast cancer (23) and recent weight gain with breast cancer risk in Asian American women in their 50s (24), we observed no difference in self-reported weight gain with either level of acculturation or breast density when BMI was also considered.

Dietary intake differed substantially by level of acculturation, but most dietary factors that we examined were not associated with breast density in our sample. Soy food intake is thought to protect against breast cancer (25-27); however, in our sample, controlling for tofu intake increased rather than attenuated the estimate for acculturation. Of the dietary factors, only dairy food intake emerged as a potentially important explanatory variable. Milk intake has been linked to higher levels of insulin-like growth factor-I (28, 29), a predictor of both higher breast density (30) and increased breast cancer risk (31-33) in premenopausal women. Of two studies that have previously examined milk intake in relation to breast density, one (34) found a nonsignificant positive association, whereas the other (35) found an inverse association among postmenopausal women only. Findings regarding dairy intake in relation to breast cancer risk are mixed (36), although ecologic studies (37) and one meta-analysis (38) support a positive association. On the other hand, dairy intake is often thought to protect against breast cancer through its calcium and vitamin D content (36). We observed a protective effect for calcium only among postmenopausal women and only when dairy intake was also controlled for. Disparate effects for dairy and calcium in postmenopausal women suggest the possibility that dairy affects breast density through a calcium-independent pathway in these women. The link between milk intake and insulin-like growth factor-I level is one possibility, but insulin-like growth factor-I has been associated with breast density and breast cancer risk only among premenopausal women (30-33). Contrary to previous findings (39, 40), dietary calcium was associated with higher breast density among premenopausal women in our sample, and it seemed to explain much of the association between dairy intake and breast density in these women as well.

The association between acculturation and breast density may persist with adjustment for several potential explanatory factors because they were incompletely controlled. For example, more accurate measures of dietary intake or of weight gain may have yielded stronger associations. In addition, the relevant time window of exposure for influencing breast density is unclear. For factors such as dietary intake, information was available only on recent ''exposure,'' and the relevant time window of exposure may be earlier in life or during the perimenopausal period. Nevertheless, our findings for dairy intake suggest that even recent diet is worth investigating further as an explanatory factor. It further suggests the importance of examining changes that might have occurred because of migration in a prospective design to examine how specific postmigration lifestyle changes, such as changes in diet, might affect breast density.

Lower breast density among less acculturated women may also reflect the continued influence of health determinants related to living in Asia, including health-related influences that occurred prenatally or during childhood or adolescence.

Indeed, several of the variables we considered were established primarily before migration, such as level of education, age at menarche, number of live births, and age at first live birth; only 42 of the 250 women in our complete sample migrated before giving birth to their first child, so most women arrived during or after their childbearing years. Mechanisms by which health status earlier in life might influence breast density or breast cancer risk later have yet to be explored.

The relatively small sample size of the study may have limited our ability to detect significant associations. In addition, quantitative estimates of percent breast density and size of dense area would have given us greater precision in our analyses than a qualitative four-category assessment of breast density. Indeed, indirect evidence suggests that quantitative estimates of dense breast area may be more relevant to breast cancer risk in Asian American women than estimates of percent density: Despite being at lower risk for breast cancer, Asian American women have higher percent breast density than White women in the United States (41-43) most likely because of their generally lower BMI. Nevertheless, breast density on a relative scale remains a significant predictor of breast cancer risk in Asian American women as it does in White women (8, 9).

In summary, in our sample of foreign-born Chinese women in the United States, we found an association between acculturation and higher breast density. Despite differences in the distribution of known and potential risk factors for higher breast density and breast cancer risk by level of acculturation, however, the association remained largely unexplained. Whether differences in breast density and hence breast cancer risk reflect early-life factors, postmigration lifestyle changes, or factors occurring within a narrow window of time, such as the perimenopausal period, are possibilities not easily determined from a cross-sectional study and deserve attention in future longitudinal research with detailed assessments of earlier-life factors.

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