Migration History, Acculturation, and Breast Cancer Risk in Hispanic Women

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Abstract

Background: **Migrant studies have shown that breast cancer risk increases in women who move from countries with low incidence rates to countries with high rates. We examined the influence of migration history and acculturation on breast cancer risk in Hispanic women ages 35 to 79 years.**
Methods: **In a population-based case-control study conducted in the San Francisco Bay Area, information on migration history, language usage, and other risk factors for breast cancer was collected through an in-person interview for 991 cases and 1,285 controls.**
Results: **Breast cancer risk was 50% lower in foreign-born Hispanics than U.S.-born Hispanics. Risk increased with increasing duration of residence in the United States, decreasing age at migration, and increasing acculturation. Among long-term foreign-born residents, risk was lower among Hispanics who moved to the United States at age ≥20 years and those who spoke mostly Spanish. The difference in risk between third-generation or higher-generation Hispanics and recent migrants from rural areas was ~6-fold in postmenopausal women and 4-fold in premenopausal women. Adjustment for differences in the distribution of breast cancer risk factors greatly attenuated the associations with migration patterns in premenopausal women; reduced risks remained only in those who resided in the United States for <10 years or migrated at age ≥30 years. In postmenopausal women, a 25% to 30% lower risk remained among long-term residents and those who migrated to the United States before age 20 years.**
Conclusions: **These findings suggest the importance of yet unidentified protective factors among both recent premenopausal migrants and postmenopausal migrants.** (Cancer Epidemiol Biomarkers Prev 2005;14(12):2905–13)

Introduction

Breast cancer incidence rates vary >10-fold worldwide and have increased in most countries in the past few decades (1, 2). Differences in the prevalence of hormonal and lifestyle factors are likely to explain some of the international variation in incidence. Migrant studies have shown that, over successive generations, incidence rates increase in women who migrate from low-incidence countries in Asia and Latin America to high-incidence countries, such as the United States, Australia, or other Western countries, approaching the incidence rates observed in the host country (3-5). These changing patterns of breast cancer incidence are well shown by the experience of Japanese American women living in Los Angeles and Hawaii who now have the same incidence rates as non-Hispanic White women (6, 7). There is also some evidence to suggest that breast cancer risk among first-generation migrants is higher among those who migrated at a young age (8, 9). Together, these observations suggest that changes in hormonal or lifestyle factors following migration, possibly at a young age, influence breast cancer risk.

Hispanic women constitute a large and rapidly growing migrant population in the United States, accounting for 12.5% of the U.S. population, with a major concentration in California (10). Originating mostly from Mexico and Central American countries, Hispanic women residing in California experience the lowest breast cancer incidence rate (84 per 100,000) compared with Asian Americans (92 per 100,000), African Americans (121 per 100,000), and non-Hispanic Whites (147 per 100,000; ref. 11). As noted for Asian immigrant populations (12), U.S.-born Hispanics have a higher incidence of breast cancer than foreign-born Hispanics (7, 13, 14), but few epidemiologic studies have examined breast cancer risk factors in this population (15, 16). We conducted a large population-based case-control study of breast cancer in >2,500 Hispanic women residing in the San Francisco Bay Area and report on the influence of migration patterns and acculturation on breast cancer risk. This is the largest population-based case-control of breast cancer conducted to date in Hispanic women residing in the United States.

Materials and Methods

Study Population

Cases. Women ages 35 to 79 years, residing in San Francisco, San Mateo, Alameda, Contra Costa, or Santa Clara counties, and newly diagnosed with a first primary invasive breast cancer were identified through the Greater Bay Area Cancer Registry, which ascertains all incident cancers as part of the Surveillance, Epidemiology, and End Results program and the California Cancer Registry. A total of 17,581 cases were identified, including Hispanic and non-Hispanic White cases diagnosed between April 1, 1995 and April 30, 2002 and African American cases diagnosed between April 1, 1995 and April 30, 1999. Of these, 508 (3%) were deceased, 174 (1%) could not be contacted due to physician-reported contraindications, 62 were not available due to another ongoing study, and 55 were not Hispanic, African American, or non-Hispanic White according to their physician. A brief telephone screening interview that assessed self-identified race/ethnicity and personal and family history of breast cancer was completed by 13,863 (83%) cases. Screening identified 1,253

Received 6/27/05; revised 9/9/05; accepted 9/26/05.

Grant support: National Cancer Institute grants CA63446 and CA77305 and California Breast Cancer Research Program grant 7PB-0068. Cancer incidence data used in this publication have been collected by the Northern California Cancer Center under contract N01-CN-65107 with the National Cancer Institute, NIH and with support of the California Cancer Registry, a project of the Cancer Surveillance Section, California Department of Health Services, under subcontract 050N-8701/8-S1522 with the Public Health Institute.

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doi:10.1158/1055-9965.EPI-05-0483

Hispanic cases of whom 1,119 (89%) completed an in-person interview in English (n = 731) or Spanish (n = 388).

Controls. Population controls were identified through random-digit dialing conducted between 1996 and 2001. A modification of the Waksberg method (17), described elsewhere (18), was used to generate 161,703 random telephone numbers. A household enumeration was obtained for 61,576 (84%) of 73,380 residential telephone numbers. From the pool of potentially eligible females, 3,757 controls were randomly selected by frequency matching on race/ethnicity and the expected 5-year age distribution of cases. The telephone screening interview, completed by 3,252 (87%) controls, identified 1,668 Hispanics of whom 1,462 (88%) completed the in-person interview in English (n = 604) or Spanish (n = 858).

Data Collection. Trained bilingual and bicultural professional interviewers administered a structured questionnaire in English or Spanish in the participant's home. Information was collected on race/ethnicity, family demographic background (country of birth for parents and grandparents, rural or urban type of residence before migration to the United States), language usage in five contexts (current language usage, first language learned, language used with spouse or partner, children living in the United States, and friends), residential history, physical activity, supplement use, body size, menstrual and reproductive history, hormone use, occupational history, and medical history. A food frequency questionnaire adapted from the Block Health History and Habits Questionnaire (19) was used to assess usual dietary intake and alcohol consumption during the reference year, defined as the calendar year before diagnosis (cases) or selection into the study (controls). The interviewers also took measurements of standing height and weight. Study participants provided written informed consent and the study was approved by the Northern California Cancer Center Institutional Review Board.

Exposure Variables. Several migration-related variables were derived from the residential history, including age at migration to the United States, duration of residence in the United States, and type of residence before migration to the United States (rural, urban, mixed rural and urban). Women were classified as first generation if they were foreign-born, women born in the United States with at least one parent born outside the United States were considered second generation, and women born in the United States with both parents born in the United States were considered third generation. Each of the participant's residences as well as her country of birth and the country of birth of her parents and grandparents was classified as Western (United States, Canada, Europe, Australia, and New Zealand) or non-Western. As only eight cases and three controls were born in Western countries other than the United States, all Western-born women hereafter are called U.S.-born, and all non-Western-born women hereafter are called foreign-born. Similarly, as few women reported residences in Western countries other than the United States, all residences in Western countries hereafter are called U.S. residences. To measure the combined effect of various migration-related characteristics, a composite variable was created similar to the one developed by Ziegler et al. (12), grouping women according to the place of birth (U.S.-born, foreign-born), number of U.S.-born grandparents, type of residence before migration (rural, urban, mixed), and years of residence in the United States (<20, ≥20).

We created an acculturation index based on language usage and generational status that was adapted from other acculturation scales developed for Hispanics (20-22). For each of five contexts, language usage was assessed on a 5-point scale, ranging from 1 for use of Spanish only to 5 for use of English only. Language chosen for the interview and generational status were scaled to similarly fit a 5-point scale, with values of 1 and 5 assigned for interviews completed in Spanish and English, respectively, and values of 1, 3, and 5 assigned to first, second, and third generation, respectively. An acculturation index ranging from 1 (lowest) to 5 (highest) was calculated as the average score of the seven components.

Statistical Analysis. Unconditional logistic regression modeling was used to estimate age-adjusted odds ratios (OR) and 95% confidence intervals (95% CI) associated with migration history and acculturation, the exposures of primary interest. To account for differences in the distribution of various hormonal and lifestyle factors, multivariate-adjusted ORs were estimated, adjusting for age (continuous), education (some high school or less, high school graduate, some college, college graduate), family history of breast cancer in first-degree relatives (yes, no), biopsy-confirmed history of benign breast disease (yes, no), age at menarche (<12, 12, 13, 14, ≥15 years), number of full-term pregnancies (0, 1, 2, 3, 4, 5, ≥6), months of breast-feeding (0, ≤6, 7-12, 13-24, ≥25), use of postmenopausal hormone therapy (ever, never), height (quartiles among controls), body mass index (BMI; <25, 25.0-29.9, ≥30 kg/m^2), daily alcohol consumption (0, 0.1-4.9, 5-9.9, 10-19.9, ≥20 g), lifetime physical activity (quartiles among controls), daily energy intake (quintiles among controls), energy-adjusted fat intake (quintiles among controls), and energy-adjusted fiber intake (quintiles among controls). Linear trends were assessed across ordinal values of categorical variables. Characteristics of controls were compared across quartiles of the acculturation index. Means were age standardized to the 10-year age distribution of the combined control population, and linear trends across quartiles of the acculturation index were assessed.

Because associations with migration history differed by menopausal status, results are presented separately for premenopausal and postmenopausal women. Women were considered postmenopausal if their periods had stopped >1 year before diagnosis (cases) or selection into the study (controls) or if they had had a bilateral oophorectomy. Women ages ≥55 years at the time of diagnosis/selection were also classified as postmenopausal if they had started to use hormone therapy before the cessation of menses or had had a simple hysterectomy (without oophorectomy). Women ages <55 years at the time of diagnosis/selection were classified as having an undetermined menopausal status if they had had a simple hysterectomy or began using hormone therapy before the cessation of menses. The remaining women were considered premenopausal. BMI as a measure of adiposity was calculated as weight (kg) divided by height (m) squared and was based on measured height and self-reported weight in the reference year. When measured height was not available (4% of cases, 3% of controls), self-reported adult height was used; similarly, when self-reported weight in the reference year was not available (2% of cases, 4% of controls), measured weight was used. Average lifetime physical activity (hours per week) was estimated from lifetime histories of exercise and sports, walking for transportation, moderate to strenuous household and outdoor chores, and occupational physical activity (18). Energy-adjusted intake of fat and fiber was calculated using the residual method (23).

Analyses were based on 858 premenopausal women (376 cases, 482 controls) and 1,418 postmenopausal women (615 cases, 803 controls) after excluding 194 participants (83 cases, 111 controls) with undetermined menopausal status, 20 participants (7 cases, 13 controls) who spent <1 year in the United States before the reference year, 46 participants (13 cases, 33 controls) with missing information on risk factors included in the multivariate models, and 45 participants (25 cases, 20 controls) with a daily caloric intake that was considered unreliable (<600 or >5,000 kcal).

Results

Most study participants reported Mexican or Central American ancestry (82% of cases, 89% of controls), and large numbers were foreign-born (50% of cases, 67% of controls). Characteristics of U.S.-born and foreign-born women are presented in Table 1. Among foreign-born women, a family history of breast cancer, a personal history of benign breast disease, natural menopause, and use of postmenopausal hormone therapy were more frequently reported by cases than controls. Foreign-born cases also had a higher education, younger age at menarche, higher prevalence of surgical menopause, fewer full-term pregnancies, later age at first full-term pregnancy, shorter duration of breast-feeding, taller height, lower physical activity, higher alcohol consumption, higher fat intake, and lower fiber intake than controls. Differences between U.S.-born cases and controls were similar, although fewer were statistically significant.

Among both premenopausal and postmenopausal women, foreign-born Hispanics had half the risk of developing breast cancer compared with U.S.-born Hispanics (Table 2), with the lowest age-adjusted ORs found in migrants born in Mexico or Central America. In postmenopausal women, risk varied little between migrants from urban and rural areas, whereas in premenopausal women the age-adjusted OR was 71% higher in migrants from urban areas (age-adjusted OR, 0.65) than those from rural areas (age-adjusted OR, 0.38).

In foreign-born Hispanics, risk increased with increasing duration of residence in the United States and decreasing age at migration (Table 2). In postmenopausal women, risk was thrice higher in U.S.-born Hispanics than in recent migrants who lived in the United States for <10 years (age-adjusted OR, 0.28), spent <25% of their life in the United States (age-adjusted OR, 0.31), or migrated to the United States at age ≥40 years (age-adjusted OR, 0.34). Compared with U.S.-born postmenopausal women, foreign-born women retained a lower risk of breast cancer even after 40 years of residence in the United States (age-adjusted OR, 0.66). Risks also remained lower in those who migrated in childhood (age-adjusted OR, 0.79) or adolescence (age-adjusted OR, 0.69). Risks were similar in women who migrated to the United States at age ≥20 years or who had spent <30 years in the United States. In premenopausal women, no risk reductions were noted in those who lived in the United States for ≥30 years or women who migrated before age 10 years. Given the inverse correlation between duration of residence in the United States and age at migration, we assessed the joint effect in all women combined. Compared with U.S.-born women, risk was highest among long-term residents (foreign-born with ≥20 years of U.S. residence) who migrated before age 20 years (age-adjusted OR, 0.75; 95% CI, 0.57-0.99), intermediate among long-term residents who migrated at age ≥20 years (age-adjusted OR, 0.48; 95% CI, 0.38-0.61), and lowest among short-term residents (foreign-born with <20 years of U.S. residence) who migrated at age ≥20 years (age-adjusted OR, 0.34; 95% CI, 0.27-0.44).

Associations with family migration characteristics are shown in Table 3. Increases in risk over successive generations were similar in premenopausal and postmenopausal women. Risk tended to be higher in women with U.S.-born parents or grandparents than those with foreign-born parents or grandparents. Classifying postmenopausal women by their country of birth (United States versus foreign), grandparents' country of birth (United States versus foreign), type of residence before migration (rural, urban, mixed), and years of residence in the United States (<20 versus ≥20) revealed an ~6-fold difference between third-generation or higher-generation Hispanics and recent migrants from rural areas (age-adjusted OR, 0.17). In premenopausal women, the difference in risk was ~4-fold (age-adjusted OR, 0.27).

Spanish language usage was strongly associated with reduced breast cancer risk (Table 4). The difference in risk between women who spoke Spanish only and those who spoke only English was 4-fold. Among both long-term and short-term residents, risk increased with increasing usage of English. Among long-term postmenopausal residents, age-adjusted ORs increased from 0.43 for mostly or exclusive Spanish speakers to 0.54 for women who spoke Spanish and English equally and 0.82 for mostly or exclusive English speakers.

Table 1. Characteristics of Hispanic women, by country of birth and case-control status

	U.S.-born Hispanics			Foreign-born Hispanics		
	Cases (n = 502)	Controls (n = 427)	P	Cases (n = 489)	Controls (n = 858)	P
Age (y)	56.3	56.8	0.48	54.4	53.9	0.39
Education (y)	12.1	12.0	0.75	9.5	7.8	<0.01
Family history of breast cancer (%)	17.2	14.1	0.19	11.7	5.5	<0.01
History of benign breast disease (%)	17.7	17.8	0.98	16.4	9.1	<0.01
Age at menarche	12.3	12.4	0.54	12.7	13.0	<0.01
No. full-term pregnancies	2.7	3.2	<0.01	3.1	3.9	<0.01
Age at first full-term pregnancy	23.2	22.5	0.06	24.1	23.1	<0.01
Lifetime breast-feeding (mo)	6.8	7.7	0.31	18.7	25.6	<0.01
Premenopausal (%)	35.1	34.2	0.78	40.9	39.2	0.53
Postmenopausal (%)						
Natural menopause	36.9	33.7	0.32	38.5	44.2	0.04
Surgical menopause*	14.5	17.1	0.29	12.1	8.7	0.05
Unknown†	13.6	15.0	0.53	8.6	7.9	0.67
Age at natural menopause (y)	49.4	48.8	0.30	48.4	47.6	0.09
Postmenopausal hormone therapy use (%)	61.0	66.6	0.16	58.8	48.5	<0.01
BMI (premenopausal women)	27.1	29.3	<0.01	27.6	29.3	<0.01
BMI (postmenopausal women)	29.2	30.3	0.03	29.4	29.6	0.57
Height (cm)	157.9	157.4	0.25	156.0	154.5	<0.01
Lifetime physical activity (h/wk)	16.9	17.9	0.31	17.0	19.9	<0.01
Alcohol consumption (g/d)‡	6.5	3.8	0.03	2.5	1.5	0.02
Caloric intake (kcal/d)‡	2154	2082	0.20	2311	2233	0.12
Fat intake (g/d) ‡	81.0	76.9	0.10	75.0	67.8	<0.01
Dietary fiber intake (g/d)‡	21.9	22.0	0.82	28.5	31.2	<0.01

*Bilateral oophorectomy (with or without hysterectomy) or hysterectomy with one-sided oophorectomy.
†Women ages ≥55 years who either began using hormone therapy before the cessation of menses or had a hysterectomy without oophorectomy.
‡During the reference year.

Table 2. Birthplace, timing of migration to the United States, and breast cancer risk in Hispanic women, by menopausal status

	Premenopausal women			Postmenopausal women		
	Cases (n = 376)	Controls (n = 482)	Age-adjusted OR (95% CI)	Cases (n = 615)	Controls (n = 803)	Age-adjusted OR (95% CI)
Place of birth						
United States*	176	146	1.0	326	281	1.0
Foreign	200	336	0.50 (0.38-0.67)	289	522	0.48 (0.38-0.59)
Mexico	117	225	0.44 (0.32-0.60)	144	300	0.41 (0.32-0.53)
Central America	50	81	0.52 (0.34-0.78)	86	165	0.45 (0.33-0.61)
Cuba, Puerto Rico, Dominican Republic	8	11	0.61 (0.24-1.57)	20	18	0.96 (0.50-1.85)
South America	24	17	1.26 (0.65-2.45)	33	38	0.75 (0.46-1.22)
Other	1	2	0.44 (0.04-4.99)	6	1	5.16 (0.62-43.14)
Type of residence before migration						
U.S.-born	176	146	1.0	326	281	1.0
Urban	104	135	0.65 (0.46-0.91)	134	226	0.51 (0.39-0.67)
Mixed urban and rural	43	82	0.45 (0.29-0.69)	78	154	0.44 (0.32-0.60)
Rural	53	116	0.38 (0.26-0.56)	76	141	0.46 (0.34-0.64)
Years of residence in the United States *,†,‡						
U.S.-born	166	140	1.0	311	255	1.0
≥40	9	6	1.17 (0.41-3.38)	82	103	0.66 (0.47-0.92)
30-39	25	20	0.99 (0.52-1.87)	77	115	0.55 (0.39-0.76)
20-29	57	77	0.62 (0.41-0.94)	40	98	0.33 (0.22-0.50)
10-19	66	134	0.43 (0.30-0.62)	35	93	0.31 (0.20-0.47)
<10	25	65	0.34 (0.20-0.57)	23	68	0.28 (0.17-0.46)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$
% of Life spent in the United States *,†,‡						
100% (U.S.-born)	166	140	1.0	311	255	1.0
75-99%	21	14	1.27 (0.62-2.60)	37	41	0.74 (0.46-1.19)
50-74%	56	75	0.62 (0.41-0.94)	113	180	0.52 (0.39-0.69)
25-49%	72	141	0.45 (0.31-0.65)	65	143	0.37 (0.27-0.52)
<25%	33	72	0.39 (0.25-0.63)	42	113	0.31 (0.21-0.45)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$
Age at migration to the United States *,†						
U.S.-born	166	140	1.0	311	255	1.0
<10	17	13	1.14 (0.53-2.43)	19	20	0.79 (0.41-1.51)
10-19	47	58	0.72 (0.46-1.13)	48	58	0.69 (0.45-1.05)
20-29	64	121	0.48 (0.33-0.71)	74	141	0.44 (0.31-0.61)
30-39	44	90	0.40 (0.26-0.62)	48	96	0.42 (0.28-0.61)
≥40	10	20	0.35 (0.16-0.78)	68	162	0.34 (0.25-0.48)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$

*U.S.-born reference group includes women born in the United States or other Western countries (i.e., Canada, Europe, Australia, and New Zealand).
† Excludes women with two or more lifetime moves between the United States and foreign countries.
‡ Includes time spent in United States and other Western countries.

Among premenopausal women, long-term residents who spoke mostly English (age-adjusted OR, 1.36) or both English and Spanish equally (age-adjusted OR, 1.10) had similar risks as U.S.-born Hispanics who spoke mostly English. In postmenopausal women, risk increased with increasing acculturation and was thrice higher among women in the highest quartile of the acculturation index than those in the lowest quartile (age-adjusted OR, 0.33). Among premenopausal women, the risk gradient was 4-fold (age-adjusted OR, 0.25 for lowest versus highest quartile).

The distribution of known breast cancer risk factors among controls differed greatly by country of birth (Table 1) and by level of acculturation (Table 5). Among both premenopausal and postmenopausal women, education, family history of breast cancer, age at first full-term pregnancy, height, and alcohol consumption increased with increasing level of acculturation, whereas age at menarche, number of full-term pregnancies, duration of breast-feeding, physical activity, caloric intake, and fiber intake decreased. In postmenopausal women, personal history of benign breast disease, surgical menopause, age at natural menopause, use of hormone therapy, and dietary fat intake also increased significantly across increasing quartiles of the acculturation index.

Multivariate adjustment for differences in breast cancer risk factors greatly attenuated associations with the migration patterns in premenopausal women (Table 6). When adjusting for other risk factors individually, the biggest effects on the OR estimates were seen for education, parity, and breast-feeding. When comparing foreign-born with U.S.-born women, adjustment for these variables raised the OR (95% CI) from 0.50 (0.37-0.66) to 0.70 (0.51-0.97). After adjustment for additional risk factors, including dietary factors (Table 6), no difference in risk remained between foreign-born and U.S.-born women or between urban and rural migrants. Risk was reduced only in women who lived in the United States for <10 years (OR, 0.66) and women who migrated to the United States at age ≥30 years (OR, 0.79). The 4-fold difference in risk between third-generation or higher-generation Hispanics and recent migrants from rural areas was reduced to a 40% difference after adjustment for other risk factors. Strong inverse associations remained with language spoken now and the acculturation index; ORs were 0.44 for women who spoke only Spanish and 0.49 for women with the lowest acculturation index. Stratifying language usage by birthplace showed that adjustment for other risk factors greatly diminished the risk reduction associated with Spanish language usage among both short-term (OR, 0.69) and long-term (OR, 1.00) residents.

In contrast, multivariate adjustment for other risk factors had a much smaller effect on OR estimates in postmenopausal women. For example, for the birthplace variable (age-adjusted OR, 0.50 for foreign-born versus U.S.-born women), only adjustment for breast-feeding changed the age-adjusted OR by >10% (OR, 0.58). Strong inverse associations remained in foreign-born postmenopausal women after adjustment for

Table 3. Family migration history and breast cancer risk in Hispanic women, by menopausal status

	Premenopausal women			Postmenopausal women		
	Cases (n = 376)	Controls (n = 482)	Age-adjusted OR (95% CI)	Cases (n = 615)	Controls (n = 803)	Age-adjusted OR (95% CI)
Generation						
Third or higher	101	75	1.0	133	102	1.0
Second	73	68	0.80 (0.51-1.24)	188	175	0.82 (0.59-1.14)
First	200	336	0.45 (0.32-0.64)	289	522	0.42 (0.32-0.57)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$
Birthplace of subject, birthplace of parents						
United States, 2 United States	101	75	1.0	133	102	1.0
United States, 1 United States	50	33	1.11 (0.65-1.90)	70	70	0.78 (0.50-1.17)
United States, 2 foreign	23	33	0.52 (0.28-0.96)	117	104	0.86 (0.59-1.26)
Foreign, 1-2 United States	6	12	0.35 (0.13-0.98)	22	23	0.73 (0.39-1.39)
Foreign, 2 foreign	194	324	0.45 (0.32-0.64)	264	498	0.41 (0.30-0.55)
Birthplace of subject, birthplace of grandparents						
United States, 3-4 United States	40	32	1.0	94	51	1.0
United States, 1-2 United States	51	31	1.32 (0.69-2.52)	62	45	0.75 (0.45-1.26)
United States, 4 foreign	55	54	0.79 (0.43-1.43)	132	135	0.53 (0.35-0.80)
Foreign, 1-4 United States	21	18	0.95 (0.43-2.08)	47	51	0.50 (0.30-0.85)
Foreign, 4 foreign	174	314	0.44 (0.27-0.73)	228	460	0.27 (0.19-0.39)
Birthplace of subject, birthplace of grandparents, type of residence before migration, years of U.S. residence*						
Foreign, 4 foreign, rural, <20 y	20	61	0.27 (0.14-0.54)	14	46	0.17 (0.09-0.34)
Foreign, 4 foreign, mixed, <20 y	25	56	0.38 (0.19-0.74)	18	50	0.20 (0.11-0.38)
Foreign, 4 foreign, urban, <20 y	39	70	0.46 (0.25-0.86)	18	53	0.19 (0.10-0.36)
Foreign, 4 foreign, rural, ≥20 y	26	38	0.53 (0.27-1.07)	52	84	0.34 (0.21-0.56)
Foreign, 4 foreign, mixed, ≥20 y	11	18	0.46 (0.19-1.12)	37	78	0.26 (0.16-0.45)
Foreign, 4 foreign, urban, ≥20 y	41	39	0.83 (0.44-1.59)	68	111	0.34 (0.22-0.54)
Foreign, <4 foreign	17	13	1.11 (0.46-2.63)	39	45	0.48 (0.28-0.84)
United States, 4 foreign	51	51	0.79 (0.43-1.46)	125	116	0.60 (0.39-0.92)
United States, 1-2 United States	50	30	1.36 (0.71-2.63)	59	42	0.78 (0.46-1.32)
United States, 3-4 United States	38	31	1.0	90	50	1.0

*Excludes women with multiple moves between United States and foreign countries.

breast-feeding and other known risk factors even in those who resided in the United States for ≥40 years (OR, 0.70) or migrated to the United States before age 10 years (OR, 0.75). As observed in the age-adjusted models, risk was similar in women with <30 years of residence in the United States (ORs ranging from 0.41 to 0.43) and increased only in those who lived for ≥30 years in the United States. Similarly, women who migrated to the United States at age ≥20 years had the same risk (ORs, 0.51-0.53), and risk increased only in those who migrated before age 20 years. There was little variation in risk between migrants from urban and rural areas. For the composite migration history variable, a 4-fold difference in risk remained between third-generation or higher-generation Hispanics and recent migrants from rural areas (OR, 0.26). Multivariate adjustment for other risk factors attenuated the inverse associations with language usage and acculturation index. Nevertheless, significantly reduced risks remained among Spanish-speaking migrants (OR, 0.56 for long-term residents and 0.39 for short-term residents).

Discussion

This population-based case-control study showed that breast cancer risk among Hispanic women is heterogeneous and is modified by country of birth, duration of residence in the United States, age at migration to the United States, family migration history, and language usage. Adjustment for differences in the distribution of hormonal and lifestyle factors attenuated the associations with migration patterns in premenopausal women but only partially explained differences in breast cancer risk in postmenopausal women.

This study is the first comprehensive examination of breast cancer risk in Hispanic women in relation to migration history and acculturation. The only previous case-control study of migration patterns and breast cancer risk was conducted in Asian American women ages 20 to 55 years (12). Most of the available data on breast cancer risk in migrant populations derive from migrant studies that relied on routinely collected incidence or mortality data and therefore have only limited information available on migration history and generally no information on other cancer risk factors. Studies, such as ours, which collected detailed information on family migration history, acculturation, and other risk factors, are valuable in providing new insights into breast cancer etiology, such as timing of exposures and migration-related changes in lifestyle and environmental factors.

Our finding of lower breast cancer risk in foreign-born Hispanics, depending on country of origin, parallels reports from migrant studies of Hispanic women who moved to the United States (7, 13, 14) and is consistent with incidence and mortality patterns described among Asian and European migrants who moved to the United States (14, 24-27), Australia (28-32), Israel (33-35), and other Western countries (36, 37). Consistent with migrant studies that had information available on length of residence in the host country (9, 28, 32, 34, 35), we found significant trends of increasing risk with increasing duration of residence in the United States and over successive generations, although risk in foreign-born postmenopausal Hispanics remained lower than in U.S.-born Hispanics even after ≥40 years of residence in the United States.

There is some evidence to suggest that breast cancer incidence rates are higher in women who migrated to Western countries at a young age (8, 9, 14). Unlike the findings in Asian Americans (12), where risks were similar in women who migrated before age 36 years, in our study, risk was higher among long-term residents who migrated before age 20 years than those who migrated at a later age. Furthermore, premenopausal women who migrated in childhood had the same risk as U.S.-born Hispanics. These findings suggest that timing of migration may be more

important in determining breast cancer risk than duration of residence in the host country, pointing toward the importance of early-life exposures.

In premenopausal women, risk was higher in migrants from urban areas than those from rural areas, a finding that is similar to the one reported for Asian migrants (12). In postmenopausal women, risk varied little between urban and rural migrants. In both premenopausal and postmenopausal women, very low risks were noted in recent migrants from rural areas. Third-generation or higher-generation Hispanics had a 4- to 6-fold higher risk of breast cancer, which is similar to the 6-fold risk gradient reported for Asian migrants (12).

Increasing breast cancer incidence rates within one or two generations of migrants have generally been attributed to changes in environmental factors, including reproductive, menstrual, and lifestyle factors (3, 4). Our study found major differences in risk factors between foreign-born and U.S.-born Hispanics. The rate of increase in incidence or mortality, however, varies between migrant groups (29, 34) and is likely to reflect differences in education and related factors as well as differences in the rate of acculturation to the predominant culture in the host country. In our study, language usage, a widely used indicator of acculturation (20-22), was strongly associated with breast cancer risk in both premenopausal and postmenopausal women, with a 3- to 4-fold difference in risk found between women with the highest and lowest levels of acculturation. Importantly, we found that language usage influenced breast cancer risk even among long-term foreign-born residents, with an increase in risk with increasing English language usage. We are not aware of any other studies that examined breast cancer risk in Hispanics or other migrant groups in relation to language use.

Consistent with other reports (38-43), we found that hormonal and lifestyle factors varied significantly by acculturation level. Characteristics of a Western lifestyle (i.e., high education, early age at menarche, nulliparity or low parity, late age at first full-term pregnancy, no breast-feeding or short duration, hormone therapy use, tall height, sedentary lifestyle, and alcohol consumption) increased with increasing level of acculturation and therefore predict an increase in breast cancer risk. Thus, adoption of a Western lifestyle puts women from low-incidence countries at higher breast cancer risk either by greater exposure to risk factors that are more common in the host country or by decreased exposure to factors that used to protect them against the development of breast cancer.

Multivariate adjustment for differences in various hormonal and lifestyle factors had a major effect on the associations between migration history and breast cancer risk and revealed intriguing differences between premenopausal and postmenopausal women. After adjustment for known breast cancer risk factors, foreign-born premenopausal women had the same breast cancer risk as U.S.-born Hispanics; slightly lower risks were found only in recent migrants and women who migrated after age 30 years. In postmenopausal women, these same risk factors only partially accounted for the differences in risk seen between foreign-born and U.S.-born women; even women who migrated to the United States in childhood or adolescence remained at a 22% to 25% lower risk than U.S.-born women. Similarly, in the Multiethnic Cohort Study, estimated incidence rates in postmenopausal women that adjusted

Table 4. Language usage, acculturation, and breast cancer risk in Hispanic women, by menopausal status

	Premenopausal women			Postmenopausal women		
	Cases (n = 376)	Controls (n = 482)	Age-adjusted OR (95% CI)	Cases (n = 615)	Controls (n = 803)	Age-adjusted OR (95% CI)
Language chosen for interview						
English	250	201	1.0	391	335	1.0
Spanish	126	281	0.36 (0.27-0.48)	224	468	0.41 (0.33-0.51)
Language spoken now						
English only	57	38	1.0	61	30	1.0
More English than Spanish	123	99	0.79 (0.49-1.30)	201	179	0.54 (0.34-0.88)
English and Spanish equally	71	66	0.70 (0.41-1.19)	142	169	0.41 (0.25-0.66)
More Spanish than English	77	141	0.36 (0.22-0.60)	111	210	0.26 (0.16-0.42)
Spanish only	45	136	0.21 (0.13-0.37)	98	214	0.22 (0.14-0.37)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$
Language spoken with friends						
English only	135	95	1.0	175	119	1.0
More English than Spanish	55	58	0.68 (0.43-1.07)	121	108	0.75 (0.53-1.07)
English and Spanish equally	53	53	0.70 (0.44-1.12)	119	156	0.52 (0.37-0.72)
More Spanish than English	35	72	0.34 (0.21-0.55)	62	112	0.38 (0.25-0.55)
Spanish only	90	201	0.32 (0.22-0.46)	133	304	0.30 (0.22-0.41)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$
Birthplace, years of residence in the United States, language spoken						
U.S.-born, mostly English	150	117	1.0	223	172	1.0
U.S.-born, English and Spanish	23	22	0.82 (0.44-1.55)	83	88	0.73 (0.51-1.04)
U.S.-born, mostly Spanish	2	5	0.30 (0.06-1.59)	20	20	0.77 (0.40-1.48)
Foreign-born, ≥20 y, mostly English	23	13	1.36 (0.66-2.81)	37	35	0.82 (0.49-1.35)
Foreign-born, ≥20 y, English and Spanish	36	25	1.10 (0.63-1.94)	80	80	0.54 (0.36-0.80)
Foreign-born, ≥20 y, mostly Spanish	45	79	0.43 (0.27-0.66)	231	231	0.43 (0.32-0.58)
Foreign-born, <20 y, mostly English	7	7	0.84 (0.29-2.48)	2	2	0.77 (0.11-5.55)
Foreign-born, <20 y, English and Spanish	12	19	0.51 (0.24-1.10)	3	1	2.31 (0.24-22.4)
Foreign-born, <20 y, mostly Spanish	75	193	0.32 (0.22-0.46)	59	173	0.26 (0.18-0.38)
Acculturation index*						
4 (highest)	172	131	1.0	256	192	1.0
3	91	84	0.85 (0.58-1.23)	173	217	0.59 (0.45-0.78)
2	66	128	0.40 (0.28-0.58)	88	182	0.36 (0.27-0.50)
1 (lowest)	44	134	0.25 (0.17-0.38)	92	207	0.33 (0.25-0.45)
			$P_{trend} < 0.01$			$P_{trend} < 0.01$

*Categorized according to the approximate quartile distribution among premenopausal and postmenopausal controls combined.

Table 5. Age-standardized mean values of breast cancer risk factors among controls, by acculturation index and menopausal status

	Premenopausal controls					Postmenopausal controls				
	Q1	Q2	Q3	Q4	*P**	Q1	Q2	Q3	Q4	*P**
Education (y)	5.4	8.7	12.9	13.4	<0.01	4.0	7.8	10.8	12.4	<0.01
Family history of breast cancer (%)	3.7	2.3	4.8	11.5	<0.01	4.3	6.0	12.9	15.1	<0.01
History of benign breast disease (%)	3.0	9.4	3.6	9.2	0.19	6.3	13.7	17.1	24.5	<0.01
Age at menarche	13.2	12.9	12.8	12.2	<0.01	13.2	13.2	12.7	12.4	<0.01
No. full-term pregnancies	3.9	3.2	2.2	2.4	<0.01	6.1	3.7	3.4	3.2	<0.01
Age at first full-term pregnancy	22.0	22.4	24.3	24.0	<0.01	22.3	22.9	24.0	22.8	0.05
Lifetime breast-feeding (mo)	27.9	20.6	11.4	7.6	<0.01	37.9	19.6	9.8	6.1	<0.01
Postmenopausal (%)										
Natural menopause						83.6	68.7	54.8	53.6	<0.01
Surgical menopause†						5.8	17.0	22.1	29.2	<0.01
Unknown‡						10.6	14.3	23.0	17.2	0.02
Age at natural menopause (y)						47.6	47.3	48.4	48.8	0.03
Use of hormone therapy (%)						32.9	54.4	63.1	68.8	<0.01
BMI (kg/m^2)	29.9	29.4	28.7	29.1	0.16	30.5	29.5	29.2	30.1	0.45
Adult height (cm)	155.3	155.6	156.2	159.5	<0.01	152.8	154.2	155.1	156.9	<0.01
Lifetime physical activity (h/wk)	22.8	20.1	19.5	14.7	<0.01	21.9	19.6	17.5	17.9	<0.01
Alcohol consumption (g/d)§	1.3	1.5	1.8	5.9	<0.01	0.4	1.0	3.1	3.4	<0.01
Caloric intake (kcal/d)§	2,670	2,351	2,116	2,231	<0.01	2,075	2,275	1,998	1,976	0.03
Fat intake (g/d)§	80.2	72.1	68.2	84.8	0.46	61.2	69.3	64.7	73.6	<0.01
Fiber intake (g/d)§	38.8	31.8	24.8	20.4	<0.01	31.5	31.7	25.8	21.1	<0.01

NOTE: Acculturation index is age standardized to 10-year age distribution of the combined control population.
*P for test of linear trend.
†Bilateral oophorectomy (with or without hysterectomy) or hysterectomy with one-sided oophorectomy.
‡Women ages ≥55 years who either began using hormone therapy before the cessation of menses or had a hysterectomy without oophorectomy.
§During the reference year.

for differences in the distribution of the major breast cancer risk factors (i.e., age at menarche, age at first birth, parity, age and type of menopause, weight, use of hormone replacement therapy, and alcohol consumption) remained lower in foreign-born Hispanic women compared with non-Hispanic White women, whereas U.S.-born Hispanic women had the same adjusted incidence rate as non-Hispanic Whites (7). These findings underline the importance of other yet unidentified factors. A recent report of the Women's Health Initiative also found that breast cancer incidence rates in Hispanic women did not differ from rates in non-Hispanic White women after adjustment for known risk factors; that report, however, did not assess breast cancer incidence in foreign-born versus U.S.-born Hispanic women (44).

Multivariate adjustment for other risk factors also attenuated the OR estimates associated with variables related to language usage. Nevertheless, risks remained reduced among recent Spanish-speaking migrants, regardless of menopausal status (OR, 0.69 in premenopausal women and 0.39 in postmenopausal women), and among long-term Spanish-speaking postmenopausal migrants (OR, 0.56). These findings suggest that Spanish language usage among foreign-born Hispanics reflects some protective factor(s) not considered in this analysis.

The findings from our large case-control study and those from the Multiethnic Cohort Study suggest the importance of additional factors in explaining differences in risk by birthplace in postmenopausal Hispanic women. Recent increases in incidence rates in countries becoming more westernized parallel changes in various hormonal and lifestyle factors, including diet (2). These factors also affect endogenous sex hormone levels (45) and mammographic breast density (46), both of which are associated with breast cancer risk (46, 47). Some data also suggest that diet early in life may influence breast cancer risk (48). No information on these exposures was available in this study.

Our study is the largest case-control study of breast cancer conducted to date in Hispanics residing in the United States. The study has several strengths, including a population-based study design; screening of >17,000 cases to identify those who self-identify as Hispanic rather than relying on cancer registry records, which would have missed some Hispanic cases listed as non-Hispanic White (49); detailed assessment of migration history and acculturation; and assessment of a wide range of currently known breast cancer risk factors. As in every case-control study, potential selection and information bias need to be considered when interpreting the results. It has been shown that more acculturated Hispanics are more likely to see a physician about breast health, to receive a mammogram, and to perform breast self-examination (50-53). Larger breast tumors have been found in first-generation Hispanics compared with U.S.-born Hispanics, although the proportion of women with advanced disease stage did not differ between the two migrant groups (50). These observations raise the concern whether controls in our study were less likely to be diagnosed with breast cancer due to delays in the timeliness of cancer diagnosis. The inclusion of undiagnosed breast cancer cases in the control group would tend to overestimate the associations with migration history and acculturation. Our questionnaire did not inquire about breast cancer screening behaviors. It is reassuring that the proportion of cases diagnosed with regional or distant stage of disease did not significantly vary by migration history or acculturation. To ensure the collection of high-quality data, particularly of potentially sensitive topics, such as migration history, the questionnaire was administered in-person in Spanish or English by bilingual and bicultural interviewers. Response rates were similarly high in cases and controls and exceeded those achieved for African American and non-Hispanic White women who participated in this multiethnic case-control study (18).

Hispanics are the fastest-growing racial/ethnic group in the United States. Despite its large size, few large-scale epidemiologic studies of breast cancer have been conducted in this migrant population (16). Our results support the findings from other studies that migration-related changes in hormonal and lifestyle factors have a major influence on breast cancer risk. Many of these factors are potentially

Table 6. Migration history, acculturation, and breast cancer risk in Hispanic women, by menopausal status—multivariate-adjusted analyses

	Premenopausal women, OR (95% CI)*	Postmenopausal women, OR (95% CI)*
Type of residence before migration		
U.S.-born†	1.0	1.0
Foreign-born	1.11 (0.74-1.64)	0.61 (0.47-0.80)
Urban	1.19 (0.77-1.83)	0.57 (0.42-0.78)
Mixed urban and rural	1.07 (0.62-1.85)	0.63 (0.43-0.91)
Rural	1.03 (0.60-1.76)	0.73 (0.50-1.08)
Years of residence in the United States†,‡,§		
U.S.-born	1.0	1.0
≥40	1.42 (0.42-4.75)	0.70 (0.49-1.01)
30-39	1.70 (0.82-3.52)	0.64 (0.43-0.93)
20-29	1.25 (0.72-2.15)	0.43 (0.27-0.70)
10-19	0.92 (0.56-1.54)	0.41 (0.25-0.68)
<10	0.66 (0.34-1.28)	0.43 (0.23-0.77
	P_{trend} = 0.43	P_{trend} < 0.01
Age at migration to the United States†,‡		
U.S.-born	1.0	1.0
<10	1.70 (0.71-4.02)	0.75 (0.38-1.48)
10-19	1.26 (0.72-2.21)	0.78 (0.50-1.22)
20-29	1.07 (0.63-1.79)	0.53 (0.36-0.77)
30-39	0.79 (0.45-1.40)	0.51 (0.33-0.80)
≥40	0.78 (0.30-2.06)	0.51 (0.33-0.78)
	P_{trend} = 0.47	P_{trend} < 0.01
Generation		
Third	1.0	1.0
Second	0.83 (0.51-1.36)	0.91 (0.64-1.30)
First	1.01 (0.64-1.59)	0.59 (0.42-0.83)
	P_{trend} = 0.97	P_{trend} < 0.01
Birthplace of subject, birthplace of grandparents, type of residence before migration, years of U.S. residence‖		
Foreign, 4 foreign, rural, <20 y	0.71 (0.30-1.66)	0.26 (0.12-0.58)
Foreign, 4 foreign, mixed, <20 y	0.83 (0.38-1.83)	0.30 (0.14-0.62)
Foreign, 4 foreign, urban, <20 y	0.83 (0.40-1.73)	0.27 (0.13-0.54)
Foreign, 4 foreign, rural, ≥20 y	1.13 (0.50-2.55)	0.51 (0.29-0.88)
Foreign, 4 foreign, mixed, ≥20 y	0.91 (0.32-2.57)	0.35 (0.20-0.64)
Foreign, 4 foreign, urban, ≥20 y	1.43 (0.68-3.02)	0.37 (0.22-0.61)
Foreign, <4 foreign	1.29 (0.48-3.45)	0.53 (0.29-0.95)
United States, 4 foreign	0.71 (0.36-1.38)	0.66 (0.42-1.04)
United States, 1-2 United States	1.39 (0.67-2.89)	0.83 (0.48-1.44)
United States, 3-4 United States	1.0	1.0
Language spoken now		
English only	1.0	1.0
More English than Spanish	0.85 (0.50-1.44)	0.62 (0.37-1.03)
English and Spanish equally	0.95 (0.52-1.74)	0.49 (0.29-0.84)
More Spanish than English	0.67 (0.36-1.24)	0.36 (0.21-0.64)
Spanish only	0.44 (0.22-0.89)	0.37 (0.20-0.67)
	P_{trend} = 0.03	P_{trend} < 0.01
Birthplace, years in the United States, language spoken		
U.S.-born, mostly English	1.0	1.0
U.S.-born, English and Spanish	1.13 (0.56-2.27)	0.83 (0.56-1.22)
U.S.-born, mostly Spanish	0.32 (0.05-1.99)	0.91 (0.45-1.84)
Foreign-born, ≥20 y, mostly English	2.08 (0.94-4.60)	0.84 (0.50-1.44)
Foreign-born, ≥20 y, English and Spanish	1.59 (0.81-3.12)	0.58 (0.37-0.88)
Foreign-born, ≥20 y, mostly Spanish	1.00 (0.55-1.81)	0.56 (0.39-0.81)
Foreign-born, <20 y, mostly English	1.11 (0.32-3.80)	1.02 (0.13-8.20)
Foreign-born, <20 y, English and Spanish	0.80 (0.33-1.92)	1.88 (0.18-19.39)
Foreign-born, <20 y, mostly Spanish	0.69 (0.40-1.18)	0.39 (0.25-0.61)
Acculturation index¶		
4 (highest)	1.0	1.0
3	1.20 (0.77-1.88)	0.68 (0.50-0.92)
2	0.68 (0.41-1.13)	0.45 (0.31-0.67)
1 (lowest)	0.49 (0.27-0.89)	0.48 (0.31-0.73)
	P_{trend} = 0.02	P_{trend} < 0.01

*Adjusted for age, education, family history of breast cancer, history of benign breast disease, age at menarche, number of full-term pregnancies, breast-feeding, use of postmenopausal hormone therapy, height, BMI, lifetime physical activity, alcohol consumption, caloric intake, energy-adjusted fat intake, and energy-adjusted fiber intake.

†Includes women born in the United States or other Western countries.

‡Excludes women with two or more moves between United States and foreign countries.

§Includes time spent in United States and other Western countries.

‖Excludes women with multiple moves between United States and foreign countries.

¶Categorized according to the approximate quartile distribution among premenopausal and postmenopausal controls combined.

modifiable, thus offering avenues toward primary prevention and risk reduction. However, differences in hormonal and lifestyle factors only partially explain the lower breast cancer risk observed in foreign-born postmenopausal women, suggesting the importance of other factors. Further studies in this understudied population could have important implications for prevention and intervention that apply to women of all racial/ethnic backgrounds.

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