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Behavioral risk factors and their relationship to tumor characteristics in Hispanic and non-Hispanic white long-term breast cancer survivors

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Abstract

Hispanics are more likely to be diagnosed with breast cancer at a younger age, with more advanced stage at diagnosis, hormone receptor-negative tumors, and worse prognosis than non-Hispanic whites (NHW). Little is known regarding the association between behavioral risk factors and breast tumor characteristics and whether these associations vary by race/ethnicity. We evaluated the association between several behavioral risk factors and tumor phenotype in a population-based study of Hispanics and NHWs. Participants are cases (846 Hispanic and 1,625 NHW women) diagnosed with breast cancer between 1999 and 2004 in Arizona, Colorado, New Mexico, or Utah. The association between breast cancer characteristics and obesity, physical activity, smoking, alcohol intake, and reproductive factors was examined. Logistic regression was used to compute the ethnic-specific odds ratios for the association between these risk factors and estrogen receptor (ER) status, tumor size, and histologic grade. Hispanics had more ER-negative tumors (28 vs. 20%), tumors >2 cm (39 vs. 27%), and poorly differentiated tumors (84 vs. 77%) than NHW. Among premenopausal women, obesity was associated with more ER-negative cancers among NHW [OR = 2.47 (95% CI: 1.08, 5.67)] but less ER-negative cancers among Hispanics [OR = 0.29 (0.13, 0.66)]. Obesity was associated with larger tumors among NHW [OR = 1.58 (1.09, 2.29)], but not among Hispanics. Never using mammography was associated with larger tumors in both ethnic groups. Moderate alcohol drinking and moderate and vigorous

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physical activity were weakly associated with smaller tumors in both ethnic groups. Our findings suggest that the association of obesity and other behavioral risk factors with breast cancer characteristics differ by ethnicity. We observed a divergent pattern between Hispanic and NHW cases in the association between obesity and ER status and tumor size. These observations suggest that a complex set of metabolic and hormonal factors related to estrogen and insulin pathways influence tumor characteristics.

Keywords

Breast cancer; Tumor phenotype; Behavioral risk factors; Ethnicity; Obesity

Introduction

Age-adjusted breast cancer incidence rates for Hispanic women are substantially lower than those for non-Hispanic white women (NHW), with 141 cases per 100,000 in NHW women and 90 in Hispanics [1]. Although incidence rates are lower, survival rates for Hispanic women are worse compared with NHW women. Hispanic women are also more likely to be diagnosed with breast cancer at a younger age, with more advanced disease stage, with hormone receptor-negative tumors and with worse prognosis [2, 3].

The reasons for these differences are not clear and are controversial [4]. Some have suggested that they stem from biological factors [5, 6], while others have suggested that socioeconomic and cultural factors [7] are the causes for the differences.

Behavioral factors associated with breast cancer are well documented and include the following: alcohol consumption (two or more drinks/day), recent exogenous hormone use (i.e., hormone replacement combined estrogen/progesterone therapy or oral contraceptives), low-level physical activity, nulliparity, late age at first birth (after age 30), lack of breast feeding, and obesity in the postmenopausal years [8–10]. Dietary factors such as high levels of fat or low levels of fruit and vegetable consumption do not appear to be consistently associated with risk of breast cancer [11].

The association between behavioral risk factors and their effect on tumor characteristics has not been elucidated fully. Colditz et al. [12] analyzed the role of selected breast cancer risk factors with breast cancer classified jointly by estrogen receptor (ER) and progesterone receptor (PR) status. There were statistically significant differences among the four ER/PR categories for several risk factors including age, menopausal status, body mass index (BMI) after menopause, the one-time adverse effect of first pregnancy, and past use of postmenopausal hormones, but not for others (benign breast disease, family history of breast cancer, alcohol use, and height).

Little is known regarding whether the effect of these factors on tumor characteristics varies by race/ethnicity as most studies did not include sufficient numbers of Hispanic women to evaluate these associations. We report associations between lifestyle factors and tumor characteristics such as tumor stage, ER status, tumor size, tumor grade, and nodal involvement. Our aim was to examine the associations of selected behavioral risk factors including obesity, physical inactivity, alcohol consumption, mammography use, and reproductive factors, on breast cancer characteristics in Hispanic and NHW women.

Materials and methods

Study population

The 4-Corners Breast Cancer Study is a population-based, case–control study of breast cancer designed to investigate diet, lifestyle, and genetic factors that contribute to disparities in breast cancer incidence between Hispanic and NHW women. Methods for selection, recruitment, and interview of subjects have been previously described in detail [13]. Briefly, women ages 25–79 at diagnosis of breast cancer (or date of selection for controls) were recruited from the Southwest United States (Arizona, Colorado, New Mexico, and Utah) between the years of 2000–2005. Cases of breast cancer diagnosed between October 1999 and May 2004 were identified through statewide cancer registries. All Hispanic cases and an age-matched sample of NHW cases were selected. Hispanic ethnicity was initially identified through the cancer registry or by surname using the GUESS (Generally Useful Ethnic Search System) algorithm [14]. Controls were frequency matched to cases on age and ethnicity. Control subjects less than 65 years of age were randomly selected from computerized drivers' license lists in New Mexico and Utah and from commercially available lists in Arizona and Colorado, while subjects aged 65 and older were selected from Center for Medicare Studies lists in all centers. Study participation has been reported on in detail elsewhere [15]. All aspects of the study were conducted in accordance with human subjects' research protocols approved at each institution. Subjects completed an in-person, computer-administered interview by trained personnel. The questionnaires included questions regarding diet, family history, reproductive history, menstrual history, physical activity, alcohol consumption, and body size. The study referent period was one year before diagnosis for cases and one year before selection for controls. For these analyses, we included 846 Hispanic and 1,625 non-Hispanic white women.

Tumor and exposure variables

Data describing tumor characteristics, such as stage, grade, histology, estrogen, and progesterone receptor status, were obtained through the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) cancer registry for New Mexico and Utah and from the state tumor registry database for Colorado and Arizona. Cases diagnosed prior to 2001 were coded according to the second edition of the *International Classification of Diseases for Oncology* (ICD-O-2), and cases diagnosed from 2001 were coded according to the ICD-O-3. The histological types were grouped accordingly as follows: ductal carcinoma (8230, 8500, 8521, 8523), lobular carcinoma (8520, 8524), ductal/lobular (8522), all others, and unknown. Tumor stage classifications were based on SEER summary stage codes according to the 1977 definitions for cases diagnosed prior to 2001 or the 2000 definitions for cases diagnosed from 2001 and on. ER and PR statuses were recorded as positive, negative, or unknown (test not done, borderline, or results not entered in chart) based on laboratory results from medical records at the time of data collection by the state tumor registry.

Coding of variables

Estrogen receptor status was coded as ER positive (irrespective of PR status) or negative; tumor stage was coded as localized (in situ or localized tumors without regional extension or nodal involvement) or non-localized; tumor size was coded small (≤2 cm) or 2 cm or more, and grade was coded as fair (well- + moderately differentiated tumors) or poor (poorly differentiated tumors).

Menopausal status was coded as pre/perimenopausal or postmenopausal; age as <50 years or ≥50 years; BMI during the reference year as normal (<25 kg/m^2), overweight (25 to <30 kg/m^2), or obese (≥30 kg/m^2); physical activity during the reference year as sedentary (<20

MET hours/week), moderate (≥20 to <45 MET hours/week), or vigorous (≥45 MET hours/week); alcohol intake during the reference year as none (0 gm/day), moderate (>0 to <3.49 gm/day), or high (≥3.49 gram/day); smoking as current, former, or never smoker; parity as none, low (1–2 children), or high (>2 children); age at first birth as young (<20 years), medium (20–25 years), or older (≥25 years); time since last pregnancy as short (<15 years), or long (≥15 years); mammography use as ever or never; HRT use as ever or never; and family history of breast cancer in first-degree relatives as yes or no. We also created a categorical variable representing the combined effect of BMI and HRT coded as "lean (BMI < 25 kg/m^2) and no HRT use," "lean and HRT use," "heavy (BMI ≥ 25 kg/m^2) and no HRT use," and "heavy and HRT use."

The categories of the above-described variables were chosen based on published cut points used by other researchers and/or the distributions of these variables in our study. We excluded 443 cases with missing information on ER status, 68 on stage, 362 on tumor size, and 319 on grade.

Statistical analyses

Descriptive statistics were first examined for selected behavioral breast cancer risk factors by ethnic group. Univariate and multivariate logistic regression models were then used to assess the relationship between selected behavioral risk factors and tumor characteristics (ER status, tumor size, stage, and histological grade). All analyses were conducted separately for Hispanic and NHW cases.

Model development was focused on determining the extent to which breast cancer risk factors accounted for differences in tumor characteristics. The initial set of models examined age-adjusted associations between each behavioral risk factor and breast cancer phenotype separately for Hispanic and NHW cases. Separate models were fit for each tumor characteristic (ER status, tumor size, stage, and grade). The final set of models evaluated the independent effect of each risk factor, adjusting for age and other risk factors (see below).

The variables included in the multivariate models include the following: BMI, physical activity, alcohol intake, smoking, age at first birth, years since last pregnancy, mammography use, HRT use (only in postmenopausal women), and family history of breast cancer. BMI was not included in the multivariate logistic regression models that examined the association between HRT use and tumor phenotype, and similarly, HRT use was not included in the models that examined the relationship between BMI and phenotype.

Other covariates including height, age at menarche, NSAIDS use, and parity were evaluated but did not alter the findings and were not included in the final models. All *P* values reported for the logistic regression analyses are for the Wald chi-squared statistic. Statistical analyses were performed using procedures of SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina) software.

Two-way interaction terms were used to test for interactions between ethnicity and risk factors on tumor characteristics. These risk factors were chosen a priori based on previous observations [16] and included obesity, physical activity, alcohol intake, family history of breast cancer, and age at first birth. This was done by including both independent variables (e.g., ethnicity and obesity) and their interaction/product (ethnicity × obesity) term in the logistic regression model.

Results

NHW cases were older, more likely to be overweight, and reported more HRT use than Hispanic cases. Hispanic cases were more likely to have ER- (28 vs 20%), larger (39 vs. 27%), less localized (35 vs. 26%), and poorly differentiated (84 vs. 77%) tumors than NHW cases (Table 1).

We found a significant statistical interaction between ethnicity and several key factors such as overweight ($P = 0.035$), obesity ($P = 0.0003$), and family history of breast cancer ($P = 0.01$). Among premenopausal women, obesity was significantly associated with reduced risk of ER-negative tumors in Hispanics [OR = 0.29 (95% CI: 0.13, 0.66)] and increased risk of ER-negative tumors in NHW [OR = 2.47 (95% CI: 1.08, 5.67)]. (Table 2) The same pattern was observed among postmenopausal cases although the association did not reach statistical significance. Moderate and vigorous physical activity were inversely associated with ER-negative tumors among premenopausal cases; however, this association was not independent of other risk factors. Similarly, an age at first pregnancy of ≥25 years was associated with reduced risk of ER-negative tumors in premenopausal Hispanic (OR = 0.51; 95% CI: 0.21, 1.24) and in NHW cases (OR = 0.25; 95% CI: 0.09, 0.65). A greater number of years since last pregnancy (≥15 years) was significantly associated with lower risk of ER-negative tumors among premenopausal non-Hispanics (OR = 0.46; 95% CI: 0.22, 0.94). The associations were observed in postmenopausal Hispanic and NHW cases, although they were not statistically significant.

Hispanic and NHW cases in the age groups 50–64 years and ≥65 years had significantly smaller tumors (<2 cm) than did younger cases (Table 3). Obesity was significantly associated with larger tumors in NHW cases (OR = 1.58; 95% CI: 1.09, 2.29). Similarly, older age at first pregnancy was significantly associated with small tumors in NHW cases only (OR = 0.58; 95% CI: 0.39, 0.86 and OR = 0.58; 95% CI: 0.38, 0.87 for the age categories 20–24 and ≥25 years respectively). A time interval of ≥15 years since last pregnancy was associated was tumors <2 cm; however, this association was not independent of other risk factors. As expected, never having a mammogram was associated with larger tumors in both Hispanics and NHW (OR = 2.04; 95% CI: 1.29, 3.23 and OR = 1.78; 95% CI: 1.10, 2.89, respectively). Moderate alcohol drinking and moderate and vigorous physical activity were weakly associated with smaller tumors in both ethnic groups.

Consistent with the effect of age on tumor size, older cases had significantly more localized tumors compared with younger cases (Table 4). This relationship was in the same direction in both ethnic groups. Never having had a mammogram was associated with more advanced tumors only in NHW; however, this relationship was not independent of other risk factors (OR = 1.42; 95% CI: 0.90, 2.24).

We examined the association between the above-mentioned risk factors and tumor grade and nodal involvement (data not shown). As with tumor size and stage, older age was significantly associated with a fair tumor grade among both Hispanic and NHW cases. Older age (≥65 years) was significantly associated with no lymph node involvement in both Hispanic and NHW cases, whereas positive family history of breast cancer was significantly associated with no lymph node involvement only in Hispanic cases.

Discussion

We conducted an investigation to assess the relationship between established behavioral risk factors for breast cancer and tumor characteristics (i.e., estrogen receptor status, disease stage, and tumor size). Potentially modifiable risk factors such as body size, physical activity, alcohol consumption, reproductive history, mammogram screening, and hormone

use were the focus of this analysis. Though the importance of these modifiable factors in breast cancer incidence is well-recognized, their association with tumor characteristics is not fully understood. Overall, our results suggest that several modifiable risk factors are associated with multiple tumor-related characteristics. Never having a mammogram prior to diagnosis was associated with increased risk of a large tumor (>2 cm), as expected. Reproductive history factors such as age at first pregnancy and time since last pregnancy were associated with both estrogen receptor status and tumor size. Older age at first pregnancy (>20 years) and increased length of time since last pregnancy (>15 years) were protective against large tumors and ER-negative tumors, respectively.

Obesity was associated with both ER status and tumor size. However, heterogeneity was observed in many of these associations by both menopausal status and ethnicity. It is important to note that few studies of weight and breast cancer characteristics are available among Hispanic women. However, similar to our findings, one published study from New Mexico found that Hispanic breast cancer patients had larger primary tumors that were more often ER-negative than those from the non-Hispanic white patients [17]. Access to care does not appear to explain this disparity. In a study by Watlington et al. [18], Hispanic and NHW women registered in Kaiser Permanente of Colorado Tumor Registry were compared with respect to tumor characteristics. Consistent with our findings, Hispanic women were more likely to have stage IV disease, poorly differentiated tumors, tumors >5 cm, and estrogen receptor– negative tumors.

We have previously demonstrated that the relationship between obesity and breast cancer risk differs by ethnicity [13]. Among premenopausal women, being obese at a young age reduced risk of breast cancer for both NHW and Hispanic women, as expected. Overweight and obesity were associated with increased breast cancer among postmenopausal NHW women who had not recently been exposed to hormones (HRT). However, this association was not observed among Hispanic women. In this same study, we also reported that estrogen receptor status of the tumor differs by ethnicity. Several measures of body size were associated with increased risk of ER tumors among NHW women, whereas these same factors were inversely associated with risk of ER tumors among Hispanic women. In the current report, we present the impact of ethnicity on additional tumor-related characteristics separately in preversus postmenopausal women. Among premenopausal NHW women, obesity was positively associated with a higher risk of ER-negative cancers (OR = 2.47; 95% CI: 1.08, 5.67) but was inversely associated with risk of ER-negative cancers among Hispanics (OR = 0.29; 95% CI: 0.13, 0.66). Although not statistically significant, a similar trend was observed among postmenopausal women. Similarly, obesity was significantly associated with larger tumors among NHW cases (OR = 1.58; 95% CI: 1.09, 2.29), but not among Hispanic cases (OR = 0.92; 95% CI: 0.60, 1.42).

Obesity has also been associated with poor tumor characteristics such as larger tumor size, more extensive lymph node involvement, and more aggressive so-called triple negative tumors that lack receptors for estrogen, progesterone, and Her2neu [19, 20]. A limitation of our study is that we were not able to study the relationship between Her2neu and obesity because this marker was not routinely recorded in tumor registry records during the eligibility timeframe of our case ascertainment. Other limitations to our study are the inability to study the influence of other known predictors of breast cancer phenotype such as genetic factors (BRCA1/2 and other genes). Strengths of our study are the population-based study design, significant representation from Hispanic women, a varied and adequate number of women across various stages and ages of breast cancer, and well-measured behavioral risk factors.

Similar to the results of Colditz et al. [12], our findings suggest that risk factors differ according to tumor-related characteristics including estrogen receptor status of the tumor. Further, our results suggest that these relationships are different by ethnicity. These observations support the results of other studies and suggest that a complex set of metabolic and hormonal factors related to estrogen and insulin pathways influence not only breast cancer risk but breast cancer characteristics.

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Table 1

Distribution of breast cancer risk factors among cases by ethnicity

Characteristics	Hispanics *N* (%)	Non-Hispanics *N* (%)
Age (years)		
<50	375 (52)	555 (51)
50–64	335 (50)	694 (55)
≥65	136 (36)	376 (44)
BMI (kg/m^2)		
Normal (<25)	277 (52)	772 (51)
Overweight (25 to <30)	289 (46)	475 (51)
Obese (≥30)	277 (46)	375 (47)
Physical activity		
Sedentary	289 (49)	564 (51)
Moderate	249 (48)	526 (49)
Vigorous	308 (47)	535 (51)
Alcohol (gm/day)		
None	462 (49)	645 (47)
Low-Moderate (>0–3.49)	61 (54)	199 (51)
High (>3.49)	61 (42)	257 (54)
Mammogram		
Ever	704 (48)	1476 (51)
Never	142 (46)	149 (45)
HRT (postmenopausal only)		
Ever	270 (43)	795 (50)
Never	188 (48)	247 (50)
Age, first birth (years)		
<20	186 (44)	212 (49)
20–24	343 (48)	566 (48)
≥25	230 (50)	568 (51)
Time since last pregnancy (years)		
<15	253 (55)	315 (50)
≥15	527 (45)	1109 (50)
Estrogen receptor status		
Positive	395 (72)	844 (80)
Negative	151 (28)	216 (20)
Size (cm)		
Less than 2	432 (61)	965 (73)
≥2	271 (39)	363 (27)
Stage		
Localized	521 (65)	1140 (74)
Non-localized	284 (35)	406 (26)
Grade		

Characteristics	Hispanics *N* (%)	Non-Hispanics *N* (%)
Well differentiated	118 (16)	323 (23)
Poorly differentiated	604 (84)	1080 (77)

Table 2

Factors associated with estrogen receptor status among breast cancer cases (event = ER negative)

Risk factors	Hispanics				Non-Hispanics			
	ER$^+$*N* (%)	**ER$^-$*N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**	**ER$^+$*N* (%)**	**ER$^-$*N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**
Women <50 years								
BMI (kg/m^2)								
<25	58 (57)	43 (43)	Ref	Ref	167 (82)	36 (18)	Ref	Ref
25–29.9	49 (58)	36 (42)	1.11	0.88 (0.44, 1.74)	63 (65)	34 (35)	**2.93**	**2.70** (1.32, 5.51)
≥30	54 (77)	16 (23)	**0.41**	**0.29** (0.13, 0.66)	44 (68)	21 (32)	**2.58**	**2.47** (1.08, 5.67)
P. activity								
Sedentary	46 (60)	31 (40)	Ref	Ref	85 (73)	31 (27)	Ref	Ref
Moderate	52 (66)	27 (34)	0.80	0.53 (0.24, 1.16)	101 (78)	28 (22)	0.67	0.61 (0.30, 1.25)
Vigorous	63 (63)	37 (37)	0.98	0.55 (0.27, 1.13)	88 (73)	32 (27)	0.72	0.63 (0.32, 1.60)
Alcohol (gm/day)								
None	97 (64)	55 (36)	Ref	Ref	136 (75)	46 (25)	Ref	Ref
Moderate (>0–3.49)	33 (69)	15 (31)	0.80	0.84 (0.38, 1.87)	40 (71)	16 (29)	1.18	1.60 (0.68, 3.76)
High (≥3.49)	31 (55)	25 (45)	1.42	1.26 (0.59, 2.71)	98 (77)	29 (23)	0.87	0.75 (0.35, 1.63)
Age, first pregnancy (years)								
<20	33 (59)	23 (41)	Ref	Ref	24 (59)	17 (41)	Ref	Ref
20–24	50 (57)	38 (43)	1.05	1.02 (0.47, 2.21)	56 (72)	22 (28)	0.54	0.54 (0.22, 1.34)
≥25	59 (71)	24 (29)	0.62	0.51 (0.21, 1.24)	129 (82)	28 (18)	**0.30**	**0.25** (0.09, 0.65)
Time since last pregnancy (years)								
<15	94 (62)	58 (38)	Ref	Ref	132 (73)	48 (27)	Ref	Ref
≥15	53 (63)	31 (37)	1.56	1.004 (0.50, 2.0)	98 (77)	29 (23)	0.81	**0.46** (0.22, 0.94)
Women ≥50 years								
BMI (kg/m^2)								
<25	62 (79)	16 (21)	Ref	Ref	231 (83)	47 (17)	Ref	Ref
25–29.9	80 (78)	23 (22)	1.11	1.32 (0.59, 2.94)	170 (82)	37 (18)	1.10	1.06 (0.63, 1.79)
≥30	90 (84)	17 (16)	0.73	0.68 (0.29, 1.60)	166 (80)	41 (20)	1.23	1.36 (0.80, 2.31)
P. activity								

Risk factors	Hispanics				Non-Hispanics			
	ER$^+$*N* (%)	**ER$^-$*N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**	**ER$^+$*N* (%)**	**ER$^-$*N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**
Sedentary	85 (83)	18 (17)	Ref	Ref	212 (80)	54 (20)	Ref	Ref
Moderate	67 (80)	17 (20)	1.20	1.09 (0.49, 2.39)	184 (85)	32 (15)	0.69	0.69 (0.41, 1.15)
Vigorous	82 (80)	21 (20)	1.21	1.21 (0.55, 2.65)	174 (82)	39 (18)	0.91	0.98 (0.59, 1.61)
Alcohol (gm/day)								
None	164 (80)	40 (20)	Ref	Ref	312 (80)	77 (20)	Ref	Ref
Moderate (>0–3.49)	32 (80)	8 (20)	1.02	0.71 (0.24, 2.08)	96 (82)	21 (18)	0.87	0.85 (0.47, 1.54)
High (≥3.49)	38 (83)	8 (17)	0.86	0.77 (0.30, 1.94)	162 (86)	27 (14)	0.67	0.61 (0.35, 1.06)
Age, first pregnancy (years)								
<20	51 (76)	16 (24)	Ref	Ref	85 (81)	20 (19)	Ref	Ref
20–24	97 (80)	24 (20)	0.79	0.80 (0.37, 1.76)	236 (83)	50 (17)	0.92	0.87 (0.48, 1.56)
≥25	58 (82)	13 (18)	0.71	0.86 (0.34, 2.16)	167 (79)	45 (21)	1.12	1.13 (0.61, 2.11)
Time since last pregnancy (years)								
<15	13 (76)	4 (24)	Ref	Ref	16 (76)	5 (24)	Ref	Ref
≥15	198 (80)	50 (20)	0.78	0.74 (0.21, 2.65)	495 (82)	111 (18)	0.72	0.79 (0.27, 2.35)
HRT[b]								
Ever	132 (84)	26 (16)	Ref	Ref	418 (81)	96 (19)	Ref	Ref
Never	96 (77)	29 (23)	1.54	1.62 (0.85, 3.11)	137 (85)	25 (15)	0.79	0.80 (0.46, 1.38)

BMI and HRT are not adjusted for each other, but adjusted for all other variables

[a]Adjusted for all the variables listed in the table in addition to parity, mammography use, family history of breast cancer, and smoking

[b]Postmenopausal women only

Bold values indicate $P < 0.05$

Table 3

Factors associated with tumor size among breast cancer cases (event = tumors >2 cms)

Risk factors	Hispanics				Non-Hispanics			
	Small *N* (%)	Big *N* (%)	Age adjusted OR	Fully adjusted OR (95% CI)[a]	Small *N* (%)	Big *N* (%)	Age adjusted OR	Fully adjusted OR (95% CI)[a]
Age (years)								
Young (<50)	163 (52)	148 (48)	Ref	Ref	291 (66)	150 (34)	Ref	Ref
Middle (50–64)	194 (71)	81 (29)	**0.46**	**0.49** (0.30, 0.78)	421 (74)	150 (26)	**0.69**	0.95 (0.63, 1.44)
Old (≥65)	75 (64)	42 (36)	**0.62**	0.58 (0.32, 1.05)	253 (80)	63 (20)	**0.48**	**0.56** (0.34, 0.92)
BMI (kg/m^2)								
<25	143 (61)	92 (39)	Ref	Ref	444 (74)	157 (26)	Ref	Ref
25–29.9	151 (64)	85 (36)	0.98	0.90 (0.59, 1.37)	301 (75)	102 (25)	1.05	1.06 (0.76, 1.48)
≥30	138 (60)	91 (40)	1.17	0.92 (0.60, 1.42)	219 (68)	102 (32)	1.48	**1.58 (1.09, 2.29)**
P. activity								
Sedentary	140 (58)	102 (42)	Ref	Ref	340 (72)	132 (28)	Ref	Ref
Moderate	136 (63)	79 (37)	0.77	0.80 (0.52, 1.22)	309 (73)	117 (27)	0.94	0.97 (0.69, 1.35)
Vigorous	156 (63)	90 (37)	0.76	0.71 (0.47, 1.08)	316 (73)	114 (27)	0.91	0.86 (0.61, 1.22)
Alcohol (gm/day)								
None	281 (61)	177 (39)	Ref	Ref	506 (72)	197 (28)	Ref	Ref
Moderate (>0–3.49)	78 (63)	45 (37)	0.78	0.77 (0.48, 1.25)	168 (74)	58 (26)	0.87	0.99 (0.67, 1.48)
High (≥3.49)	73 (60)	49 (40)	0.93	1.12 (0.70, 1.79)	291 (73)	108 (27)	0.91	0.95 (0.67, 1.34)
Age, first pregnancy (years)								
<20	100 (62)	62 (38)	Ref	Ref	116 (65)	63 (35)	Ref	Ref
20–24	179 (66)	93 (34)	0.82	0.84 (0.54, 1.29)	352 (76)	109 (24)	**0.60**	**0.58** (0.39, 0.86)
≥25	112 (59)	79 (41)	1.06	1.16 (0.71, 1.89)	339 (74)	120 (26)	**0.57**	**0.58** (0.38, 0.87)
Time since last pregnancy (years)								
<15	112 (53)	99 (47)	Ref	Ref	160 (65)	88 (35)	Ref	Ref
≥15	287 (66)	145 (34)	0.96	1.04 (0.65, 1.68)	228 (25)	687 (75)	1.01	0.67 (0.42, 1.06)
Mammogram								
Ever	377 (65)	203 (35)	Ref	Ref	893 (74)	312 (26)	Ref	Ref
Never	55 (45)	68 (55)	**1.83**	**2.04** (1.29, 3.23)	72 (59)	51 (41)	**1.54**	**1.78** (1.10, 2.89)

Risk factors	Hispanics				Non-Hispanics			
	Small *N* (%)	**Big *N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**	**Small *N* (%)**	**Big *N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**
HRT[b]								
Ever	153 (70)	65 (30)	Ref	Ref	506 (77)	149 (23)	Ref	Ref
Never	110 (68)	51 (32)	1.09	0.78 (0.47, 1.31)	156 (74)	55 (26)	1.20	1.17 (0.77, 1.77)

BMI and HRT are not adjusted for each other, but adjusted for all other variables

[a]Adjusted for all the variables listed in the table in addition to parity, family history of breast cancer, and smoking

[b]Postmenopausal women only

Bold values indicate $P < 0.05$

Table 4

Factors associated with tumor stage among breast cancer cases (event = non-localized tumors)

Risk factors	Hispanics				Non-Hispanics			
	Local. *N* (%)	Non-local *N* (%)	Age adjusted OR	Fully adjusted OR (95% CI)[a]	Local. *N* (%)	Non-local *N* (%)	Age adjusted OR	Fully adjusted OR (95% CI)[a]
Age (years)								
Young (<50)	197 (55)	160 (45)	Ref	Ref	349 (67)	175 (33)	Ref	Ref
Middle (50–64)	224 (71)	93 (29)	**0.51**	**0.57** (0.37, 0.88)	492 (74)	172 (26)	**0.70**	0.84 (0.57, 1.22)
Old (≥65)	100 (76)	31 (24)	**0.38**	**0.37** (0.21, 0.67)	299 (84)	59 (16)	**0.39**	**0.47** (0.30, 0.74)
BMI (kg/m^2)								
<25	168 (64)	95 (36)	Ref	Ref	549 (75)	183 (25)	Ref	Ref
25–29.9	177 (65)	97 (35)	1.10	1.14 (0.77, 1.69)	331 (73)	123 (27)	1.26	1.28 (0.94, 1.74)
≥30	175 (66)	90 (34)	1.06	0.89 (0.59, 1.34)	259 (73)	98 (27)	1.29	1.38 (0.98, 1.96)
P. activity								
Sedentary	180 (67)	89 (33)	Ref	Ref	392 (73)	145 (27)	Ref	Ref
Moderate	154 (63)	89 (37)	1.12	1.13 (0.76, 1.69)	370 (74)	127 (26)	0.90	0.87 (0.63, 1.19)
Vigorous	187 (64)	106 (36)	1.09	1.11 (0.75, 1.64)	378 (74)	134 (26)	0.95	1.02 (0.74, 1.40)
Alcohol (gm/day)								
None	343 (65)	186 (35)	Ref	Ref	592 (74)	206 (26)	Ref	Ref
Moderate (>0–3.49)	87 (64)	49 (36)	0.85	0.85 (0.54, 1.32)	199 (73)	74 (27)	1.07	1.09 (0.76, 1.56)
High (≥3.49)	91 (65)	49 (35)	0.84	0.81 (0.52, 1.27)	349 (73)	126 (27)	0.98	1.02 (0.74, 1.39)
Age, first pregnancy (years)								
<20	111 (63)	65 (37)	Ref	Ref	145 (72)	57 (28)	Ref	Ref
20–24	212 (66)	111 (34)	0.84	0.86 (0.57, 1.29)	401 (75)	135 (25)	0.89	0.91 (0.62, 1.32)
≥25	145 (65)	77 (35)	0.82	0.83 (0.52, 1.32)	396 (73)	145 (27)	0.83	0.88 (0.59, 1.32)
Time since last pregnancy (years)								
<15	131 (55)	109 (45)	Ref	Ref	193 (65)	103 (35)	Ref	Ref
≥15	349 (70)	153 (30)	0.99	0.89 (0.58, 1.39)	804 (76)	253 (24)	0.71	0.76 (0.50, 1.15)
Mammogram								
Ever	443 (66)	228 (34)	Ref	Ref	1,057 (75)	350 (25)	Ref	Ref
Never	78 (58)	56 (42)	0.96	1.06 (0.68, 1.64)	83 (60)	56 (40)	1.48	1.42 (0.90, 2.24)

Risk factors	Hispanics				Non-Hispanics			
	Local. *N* (%)	**Non-local *N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**	**Local. *N* (%)**	**Non-local *N* (%)**	**Age adjusted OR**	**Fully adjusted OR (95% CI)[a]**
HRT[b]								
Ever	187 (73)	68 (27)	Ref	Ref	590 (78)	170 (22)	Ref	Ref
Never	132 (73)	48 (27)	1.02	0.92 (0.57, 1.48)	178 (75)	58 (25)	1.18	1.11 (0.75, 1.65)

BMI and HRT are not adjusted for each other, but adjusted for all other variables

[a]Adjusted for all the variables listed in the table in addition to parity, family history of breast cancer, mammography use, and smoking

[b]Postmenopausal women only

Bold values indicate $P < 0.05$