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Original Contribution

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History of Recreational Physical Activity and Survival After Breast Cancer

The California Breast Cancer Survivorship Consortium

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Recent epidemiologic evidence suggests that prediagnosis physical activity is associated with survival in women diagnosed with breast cancer. However, few data exist for racial/ethnic groups other than non-Latina whites. To examine the association between prediagnosis recreational physical activity and mortality by race/ethnicity, we pooled data from the California Breast Cancer Survivorship Consortium for 3 population-based case-control studies of breast cancer patients (n = 4,608) diagnosed from 1994 to 2002 and followed up through 2010. Cox proportional hazards models provided estimates of the relative hazard ratio for mortality from all causes, breast cancer, and causes other than breast cancer associated with recent recreational physical activity (i.e., in the 10 years before diagnosis). Among 1,347 ascertained deaths, 826 (61%) were from breast cancer. Compared with women with the lowest level of recent recreational physical activity, those with the highest level had a marginally decreased risk of all-cause mortality from causes other than breast cancer (hazard ratio = 0.63, 95% confidence interval: 0.76, 1.01) and a statistically significant decreased risk of mortality from cardiovascular disease. No association was observed for breast cancer—specific mortality. These risk patterns did not differ by race/ethnicity (non-Latina white, African American, Latina, and Asian American). Our findings suggest that physical activity is beneficial for overall survival regardless of race/ethnicity.

breast cancer; mortality; race/ethnicity; recreational physical activity; survival

Abbreviations: AABCS, Asian American Breast Cancer Study; CARE, Contraceptive and Reproductive Experiences; CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; MET, metabolic equivalents of energy expenditure; PR, progesterone receptor; SEER, Surveillance, Epidemiology, and End Results; SFBCS, San Francisco Bay Area Breast Cancer Study.

Increasing evidence suggests that physical activity is associated with improved survival after breast cancer diagnosis (1, 2). Although prognosis has improved for all breast cancer patients, substantial survival differences by race/ethnicity still exist (3–5), and it is not known to what extent racial/ ethnic differences in physical activity contribute to this survival disparity. However, participants in previous studies were predominately non-Latina whites. No study has examined a diverse population of non-Latina white, African-American, Latina, and Asian-American women. Furthermore, few studies have assessed whether other risk factors modify the association between physical activity and mortality among breast cancer survivors, and these studies have produced inconsistent results (6–10). For example, 2 studies reported a decreased risk of all-cause mortality associated with high levels of physical activity among breast cancer patients with a body mass index (expressed as weight (kg)/height (m)²) <25 (7, 9), whereas others reported that the benefit of physical activity was limited to women with a body mass index ≥ 25 (6, 10). Here, we investigate whether prediagnosis recreational physical activity influences mortality risk in a racially and ethnically diverse cohort of breast cancer survivors using data from the California Breast Cancer Survivorship Consortium (11).

METHODS

Study design

A detailed description of the California Breast Cancer Survivorship Consortium has been published elsewhere (11). Three population-based case-control studies of invasive breast cancer that were part of the California Breast Cancer Survivorship Consortium used a common protocol and a similar approach for collecting histories of recreational physical activity before breast cancer diagnosis. These studies included 1,242 non-Latina whites and African Americans aged 35-64 years at diagnosis (between 1994 and 1998) from the Women's Contraceptive and Reproductive Experiences (CARE) Study, 1,144 Asian Americans aged 26-79 years at diagnosis (between 1995 and 2001) from the Asian American Breast Cancer Study (AABCS), and 2,258 non-Latina whites, African Americans, and Latinas aged 35-79 years at diagnosis (between 1995 and 2002) from the San Francisco Bay Area Breast Cancer Study (SFBCS). Among these participants, 36 women (3 from the Women's CARE Study, 18 from AABCS, and 15 from SFBCS) were excluded because they did not provide recreational physical activity information. Thus, 4,608 participants were included in this analysis. Participants in the Women's CARE Study and AABCS were Los Angeles County residents at diagnosis, and participants in SFBCS were from the San Francisco Bay Area. This study was approved by the institutional review boards at all participating institutions (City of Hope, University of Southern California, Cancer Prevention Institute of California, and Kaiser Permanente Northern California).

Each study collected detailed information on potential breast cancer risk factors/exposures during in-person interviews. Women in the Women's CARE Study were interviewed on average 5.1 months after breast cancer diagnosis; those in the AABCS were interviewed on average 18.5 months after diagnosis; and those in the SFBS were interviewed on average 17.2 months after diagnosis.

The 3 studies used almost identical questions to collect information on lifetime histories (from childhood or age 10 up to the age of breast cancer diagnosis) of regular recreational physical activity. In AABCS, women reported any activity in which they participated for at least 1 hour/week at any given age (12). In the Women's CARE Study, women reported activities lasting at least 2 hours/week for at least 4 months at any given age (13). In SFBCS, women reported activities lasting at least 1 hour/week for at least 4 months at any given age (14). To harmonize the levels of recreational physical activity across the 3 studies, we included only activities lasting at least 1 hour/week at any given age. Women with lower levels of activity were considered to be inactive at that age. For each activity episode, we collected information on the type of activity, the age at which the woman started and stopped the activity, the number of months per year of participation in the activity, and the average number of hours/week of participation in the activity.

We calculated the average number of hours of exercise activity per week for each year of age for each participant. We calculated several summary measures of activity represented as average hours/week for the 10 years before breast cancer diagnosis. We also estimated the metabolic equivalents of energy expenditure (MET)-hours per week for each age by multiplying the number of hours/week a woman spent in a particular activity, the proportion of the year spent in that activity, and the estimated MET score for the activity based on the Compendium of Physical Activities (15). Results using MET score measures were similar to those based on hours/week due to a high correlation between the 2 measurement scales (Web Table 1 available at http://aje.oxfordjournals.org/).

The characteristics of each woman's breast cancer diagnosis and treatment were obtained from the California Cancer Registry, which comprises 4 of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries. We abstracted data for age at breast cancer diagnosis, neighborhood socioeconomic status (a composite measurement based on education, income, occupation, and housing costs at the census block group level) (16), tumor stage (defined by the American Joint Committee on Cancer), estrogen receptor (ER) status, progesterone receptor (PR) status, tumor size, tumor grade, number of positive nodes, prior cancer history, type of surgery performed, and treatment by chemotherapy, hormonal therapy, or radiation therapy.

All patients were followed for vital status by the California Cancer Registry using standard SEER follow-up procedures with date of death and cause of death recorded. The date of last follow-up was December 31, 2010.

Statistical analysis

Multivariate Cox proportional hazards regression models were fit to provide estimates of the hazard ratio of death and its 95% confidence interval. The analytical endpoints were death from any cause, death from breast cancer (International Classification of Diseases, Ninth Revision, code(s) 174; International Classification of Diseases, Tenth Revision, code(s) C50), and death from causes other than breast cancer. Study-specific risk estimates were compared by using Cochrane's Q test (17). No evidence for heterogeneity was present in any of the analyses. Thus, we estimated the overall risk (across all studies). Age in days at interview and age in days at death or end of follow-up defined the time scale for analysis (11). In the analyses of breast cancer-specific mortality, women who died from other causes were censored on their dates of death. In the analyses of other causes of death, women who died from breast cancer were censored on their dates of death. All multivariate models were stratified by study and race/ethnicity (non-Latina white in CARE, non-Latina white in SFBCS, African American in CARE, African American in SFBCS, Latina in CARE and SFBCS, and Asian American in AABCS). Covariates in the final models were first selected on the basis of a priori determination from literature review, which included age in years at diagnosis (26-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-79 years); education (less than high school, high school graduate, some college/technical school, college graduate, unknown); neighborhood socioeconomic status (lowest,

	Recent 1) Years' Recrea	ational Physica	al Activity, %	Race/Ethnicity, %							
Characteristic	Overall (<i>n</i> = 4,608)	0–0.5 hours/week (<i>n</i> =2,386)	0.6–3.0 hours/week (<i>n</i> = 1,145)	>3.0 hours/week (<i>n</i> = 1,077)	Non-Latina White (<i>n</i> = 1,166)	African American (<i>n</i> =1,112)	Latina (<i>n</i> = 1,204)	Asian American (<i>n</i> = 1,126)				
Study and race/ethnicity												
CARE, non-Latina white	12.5	9.4	16.3	15.3								
SFBCS, non-Latina white	12.8	8.8	13.4	21.1								
CARE, African American	12.4	12.9	13.2	10.5								
SFBCS, African American	11.7	10.6	10.2	15.9								
Latina	26.1	28.7	24.2	22.6								
Asian American	24.4	29.7	22.7	14.7								
Age at diagnosis, years												
26–34	0.8	0.6	1.2	0.6	0.0	0.0	0.0	3.1				
35–39	9.1	8.8	9.3	9.6	11.8	9.6	9.4	5.5				
40–44	14.1	13.9	14.9	13.8	12.1	14.8	14.8	14.8				
45–49	16.6	17.1	16.2	15.9	13.8	16.9	16.7	19.0				
50–54	15.6	15.2	15.4	16.7	15.7	16.9	14.5	15.4				
55–59	13.9	13.3	14.7	14.5	14.7	15.4	13.0	12.7				
60–64	12.5	12.3	11.6	13.7	13.8	13.1	12.0	10.9				
65–79	17.5	18.8	16.7	15.3	18.2	13.2	19.7	18.6				
Level of education												
Less than high school	17.1	22.6	12.1	10.4	4.6	14.8	38.5	9.6				
High school graduate	20.2	21.1	20.1	18.5	20.4	25.9	23.1	11.4				
Some college/technical school	30.7	27.5	34.5	33.6	35.8	40.7	24.5	22.1				
College graduate	31.9	28.8	33.3	37.5	39.2	18.5	13.9	56.9				
Unknown	0.0	0.0	0.1	0.0	0.1	0.1	0.0	0.0				
BMI ^a												
<18.5	2.1	2.2	2.0	1.9	2.8	1.4	0.7	3.6				
18.5–24.9	43.5	38.5	47.0	50.8	54.1	31.4	29.6	59.3				
25–29.9	27.3	29.9	25.6	23.3	21.8	29.0	31.0	27.4				
≥30	21.0	23.8	19.6	16.3	14.1	30.9	31.0	7.6				
Unknown	6.2	5.6	5.9	7.8	7.2	7.4	7.8	2.1				

 Table 1.
 Distribution of Selected Characteristics According to Recreational Physical Activity During 10 Years Before Diagnosis and Race/

 Ethnicity, California Breast Cancer Survivorship Consortium, 1994–2010

Table continues

lower-middle, middle, higher-middle, highest, unknown); body mass index (<18.5, 18.5–24.9, 25–29.9, \geq 30); tumor stage (stage I, II, III, IV, unknown); type of surgery (no surgery, mastectomy, breast conserving, others); and chemotherapy (no, yes, unknown). Cancer registry data on endocrine treatment were not included because of 30%–40% underascertainment of this treatment when compared with prescription and selfreported data (S. L. Gomez, Cancer Prevention Institute of California, personal communication, 2014). Thus, we chose to use ER/PR status (ER+PR+, ER+PR–, ER–PR+, ER–PR–, ER/ PR unknown), with "+" indicating positive and "-" indicating negative, as a covariate instead of hormonal therapy.

We assessed the influence of additional potential confounders on hazard ratio estimates, including first-degree family history of breast cancer (number of affected first-degree relatives, age at diagnosis of the affected relatives); pregnancies (number of livebirths, ages at first birth); menopause (type of menopause, age at menopause); smoking patterns (never, past ≤ 1 pack/day, past >1 pack/day, current ≤ 1 pack/day, current >1 pack/day, unknown); alcohol consumption levels (nondrinker, ≤ 2 drinks/week, >2 drinks/week, unknown); prior cancer history (no, yes, unknown); and history of comorbid conditions (i.e., diabetes, hypertension, and myocardial infarction history) at diagnosis (no, yes, unknown). None of these factors altered the hazard ratio for the association between recreational physical activity and outcome by as much as 5%; therefore, none was included in the final models.

We performed tests for trend for ordinal variables by fitting the ordinal value of each category as a continuous variable. To test whether the association between recent recreational physical activity and mortality was modified by race/ethnicity, we constructed a likelihood ratio test comparing 2 multivariate

Table 1. Continued

	Recent 10) Years' Recre	ational Physica	al Activity, %	Race/Ethnicity, %						
Characteristic	Overall (<i>n</i> = 4,608)	0–0.5 hours/week (<i>n</i> =2,386)	0.6–3.0 hours/week (<i>n</i> = 1,145)	>3.0 hours/week (<i>n</i> = 1,077)	Non-Latina White (<i>n</i> = 1,166)	African American (<i>n</i> = 1,112)	Latina (<i>n</i> = 1,204)	Asian American (<i>n</i> = 1,126)			
Neighborhood SES											
Lowest	10.2	12.5	8.0	7.2	2.7	23.0	4.8	10.9			
Lower middle	17.4	19.7	15.0	14.8	7.9	26.4	16.8	18.9			
Middle	19.2	20.2	19.3	16.8	14.4	21.4	21.9	19.1			
Higher middle	23.6	23.3	24.3	23.3	25.7	18.6	25.8	23.7			
Highest	28.2	22.8	32.1	36.0	47.9	9.8	28.8	25.3			
Unknown	1.5	1.5	1.2	2.0	1.4	0.8	1.8	2.0			
Tumor stage											
I	44.2	42.0	43.6	49.7	51.9	37.2	41.5	45.8			
II	44.4	46.1	45.5	39.7	38.5	48.1	47.8	43.3			
III	6.4	6.8	6.1	5.9	4.8	7.4	6.8	6.6			
IV	1.6	1.9	1.4	1.2	1.9	1.9	1.2	1.5			
Unknown	3.4	3.4	3.4	3.5	2.9	5.4	2.7	2.8			
ER and PR status ^b											
ER+PR+	52.2	52.3	52.8	51.4	57.1	43.2	55.7	52.5			
ER+PR-	8.8	8.6	8.5	9.7	9.4	8.1	10.1	7.6			
ER-PR+	3.2	2.9	3.2	4.0	2.9	4.4	2.7	2.9			
ER-PR-	18.6	18.9	19.0	17.7	16.1	23.7	21.8	12.8			
ER/PR unknown	17.1	17.4	16.5	17.2	14.5	20.7	9.7	24.2			
Type of surgery											
No surgery	1.6	2.0	1.1	1.2	1.2	2.6	1.3	1.2			
Mastectomy	45.8	48.7	42.4	42.8	38.5	42.5	47.3	55.0			
Breast conserving	52.6	49.2	56.5	55.9	60.0	54.9	51.4	43.8			
Others	0.1	0.1	0.1	0.1	0.3	0.1	0.0	0.1			
Chemotherapy											
No	50.0	49.4	49.9	51.4	55.9	48.5	44.2	51.5			
Yes	48.3	49.0	48.8	46.3	42.7	49.8	54.9	45.6			
Unknown	1.7	1.6	1.3	2.3	1.4	1.7	0.9	2.9			

Abbreviations: BMI, body mass index; CARE, Contraceptive and Reproductive Experiences; ER, estrogen receptor; PR, progesterone receptor; SES, socioeconomic status; SFBCS, San Francisco Bay Area Breast Cancer Study.

^a Body mass index: weight (kg)/height (m)².

^b ER and PR status: "+" indicates positive and "-" indicates negative.

Cox proportional hazards models. The base model, which included 1 variable for recent recreational physical activity, was compared with a model with 4 recent recreational physical activity variables (1 representing recent physical activity for each of the racial/ethnic groups: non-Latina white, African American, Latina, and Asian American), resulting in a likelihood ratio test for heterogeneity of trends with 3 df (18). We further examined the racial/ethnic-specific associations between recent recreational physical activity and mortality stratified by body mass index (<25 vs. \geq 25), ER status (ER+ vs. ER-), tumor stage (stage I–II vs. stage III–IV), and age at diagnosis (<50 vs. \geq 50 years). All statistical analyses were performed by using SAS, version 9.3, software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

The mean age at breast cancer diagnosis was 54 years. During a median follow-up of 9.9 years, 1,347 women died (360 non-Latina white, 475 African American, 286 Latina, and 226 Asian American), with 826 from breast cancer (194 non-Latina white, 310 African American, 171 Latina, and 151 Asian American). Among 521 women who died of causes other than breast cancer, 166 women died of cardiovascular disease and 160 women died of other types of cancer.

Asian Americans reported the lowest level of recreational physical activity, and they were followed by Latinas (Table 1). Women with higher levels of education or neighborhood socioeconomic status or with lower levels of body mass index

Physical Activity,	D		All-Ca Dea	use th	Breast	Cance Dea	er–Specific th	Other Causes of Death				
hours/week	Person-Years	No. of Deaths	HRª	95% CI	No. of Deaths	HRª	95% CI	No. of Deaths	HR ^a	95% CI		
Overall		1,347			826			521				
0–0.5	21,151	728	1.00		425	1.00		303	1.00			
0.6–3.0	10,736	341	1.03	0.90, 1.17	211	1.07	0.90, 1.27	130	1.03	0.83, 1.27		
>3.0	10,301	278	0.88	0.76, 1.01	190	1.10	0.91, 1.31	88	0.63	0.49, 0.80		
P for trend				0.13			0.29			<0.01		
Non-Latina white		360			194			166				
0–0.5	4,314	153	1.00		78	1.00		75	1.00			
0.6–3.0	3,528	109	0.94	0.73, 1.20	63	0.99	0.71, 1.39	46	1.03	0.71, 1.50		
>3.0	4,110	98	0.80	0.62, 1.04	53	0.85	0.60, 1.22	45	0.80	0.55, 1.17		
P for trend				0.10			0.41			0.29		
African American		475			310			165				
0–0.5	5,080	252	1.00		156	1.00		96	1.00			
0.6–3.0	2,533	121	1.04	0.83, 1.29	76	1.00	0.75, 1.32	45	1.15	0.80, 1.64		
>3.0	2,670	102	0.85	0.67, 1.07	78	1.08	0.82, 1.44	24	0.49	0.31, 0.78		
P for trend				0.23			0.61			0.01		
Latina		286			171			115				
0–0.5	5,646	170	1.00		93	1.00		77	1.00			
0.6–3.0	2,413	62	1.03	0.76, 1.38	38	1.09	0.74, 1.59	24	0.91	0.57, 1.44		
>3.0	2,199	54	0.96	0.70, 1.31	40	1.37	0.94, 2.00	14	0.55	0.31, 0.98		
P for trend				0.85			0.11			0.05		
Asian American		226			151			75				
0–0.5	6,111	153	1.00		98	1.00		55	1.00			
0.6–3.0	2,262	49	1.16	0.84, 1.62	34	1.27	0.85, 1.89	15	1.00	0.56, 1.80		
>3.0	1,323	24	1.04	0.67, 1.61	19	1.25	0.76, 2.07	5	0.62	0.24, 1.57		
P for trend				0.61			0.23			0.41		
P for homogeneity of trends for race/ethnicity				0.55			0.30			0.61		

 Table 2.
 Hazard Ratio for Death and 95% Confidence Interval Among Breast Cancer Patients Associated With

 Recreational Physical Activity During 10 Years Before Diagnosis Overall and by Race/Ethnicity, California Breast

 Cancer Survivorship Consortium, 1994–2010

Abbreviations: AABCS, Asian American Breast Cancer Study; BMI, body mass index; CARE, Contraceptive and Reproductive Experiences; CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor; SFBCS, San Francisco Bay Area Breast Cancer Study.

^a Cox proportional hazards models use age (days) as the time metric, are stratified by combined variable of study site and race/ethnicity (non-Latina white in CARE, non-Latina white in SFBCS, African American in CARE, African American in SFBCS, Latina in CARE and SFBCS, and Asian American in AABCS), and include the following variables: age at diagnosis (26–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–79 years); level of education (less than high school, high school graduate, some college/technical school, college graduate, unknown); neighborhood socioeconomic status (lowest, lower middle, middle, higher middle, highest, unknown); BMI (<18.5, 18.5–24.9, 25–29.9, ≥30); tumor stage (I, II, III, IV, unknown); ER/PR status (ER+PR+, ER+PR−, ER−PR+, ER−PR−, ER/PR unknown), with "+" indicating positive and "–" indicating negative; type of surgery (no surgery, mastectomy, breast conserving, others); and chemotherapy (no, yes, unknown).

tended to have higher levels of recent recreational physical activity. Recent recreational physical activity levels did not differ by age at diagnosis, tumor stage, ER/PR status, type of surgery, or chemotherapy.

Women with the highest level of recent recreational physical activity (>3.0 hours/week) had marginally statistically significant decreased risk of all-cause mortality when compared with those with the lowest activity level (0–0.5 hours/ week) (hazard ratio (HR) = 0.88, 95% confidence interval (CI): 0.76, 1.01) (Table 2). The risk patterns were not statistically significantly different across racial/ethnic groups (*P* for homogeneity of trends = 0.55). No association was observed

		Overa	all	No	n-Latina	White	Afı	rican An	nerican		Latin	na	Asian American		
Physical Activity, hours/week	No. of Deaths	HRª	95% CI	No. of Deaths	HRª	95% CI	No. of Deaths	HRª	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI
BMI ^{b,c}															
BMI <25	551			184			160			75			132		
0–0.5	275	1.00		65	1.00		83	1.00		41	1.00		86	1.00	
0.6–3.0	143	0.99	0.80, 1.21	57	0.96	0.67, 1.40	39	0.99	0.67, 1.46	18	0.85	0.48, 1.51	29	1.19	0.77, 1.84
>3.0	133	0.91	0.74, 1.13	62	0.90	0.62, 1.31	38	0.96	0.64, 1.43	16	0.99	0.54, 1.79	17	1.10	0.64, 1.88
P for trend			0.42			0.58			0.83			0.58			0.58
BMI ≥25	745			168			295			192			90		
0–0.5	425	1.00		87	1.00		155	1.00		120	1.00		63	1.00	
0.6–3.0	187	1.06	0.89, 1.27	48	0.95	0.65, 1.38	80	1.06	0.80, 1.40	39	1.13	0.78, 1.64	20	1.46	0.87, 2.46
>3.0	133	0.87	0.71, 1.07	33	0.88	0.58, 1.35	60	0.76	0.56, 1.03	33	0.91	0.61, 1.36	7	1.21	0.54, 2.70
P for trend			0.31			0.56			0.13			0.83			0.27
P for homogeneity of trends			0.94			0.96			0.46			0.97			0.58
ER status ^d															
ER positive	780			227			249			171			133		
0–0.5	409	1.00		94	1.00		125	1.00		103	1.00		87	1.00	
0.6–3.0	202	1.10	0.93, 1.31	68	1.15	0.83, 1.59	60	1.13	0.82, 1.55	38	1.02	0.70, 1.49	36	1.53	1.02, 2.30
>3.0	169	0.91	0.76, 1.10	65	1.09	0.78, 1.53	64	0.96	0.70, 1.32	30	0.90	0.59, 1.38	10	0.71	0.36, 1.40
P for trend			0.51			0.56			0.92			0.70			0.97
ER negative	348			84			127			91			46		
0–0.5	199	1.00		36	1.00		78	1.00		53	1.00		32	1.00	
0.6–3.0	91	1.01	0.78, 1.30	32	0.87	0.53, 1.44	32	0.90	0.59, 1.37	20	1.27	0.74, 2.17	7	0.88	0.38, 2.05
>3.0	58	0.77	0.57, 1.05	16	0.48	0.26, 0.90	17	0.53	0.31, 0.92	18	0.94	0.54, 1.63	7	2.56	1.07, 6.17
P for trend			0.14			0.03			0.03			0.98			0.12
P for homogeneity of trends			0.36			0.02			0.07			0.83			0.20
Tumor stage ^e															
Stages I–II	1,057			288			373			225			171		
0–0.5	569	1.00		118	1.00		199	1.00		132	1.00		120	1.00	
0.6–3.0	268	1.01	0.87, 1.17	89	1.07	0.81, 1.43	95	1.04	0.81, 1.34	51	1.00	0.72, 1.39	33	0.88	0.59, 1.32
>3.0	220	0.86	0.73, 1.02	81	0.93	0.69, 1.25	79	0.77	0.59, 1.01	42	1.02	0.71, 1.46	18	0.96	0.57, 1.62
P for trend			0.11			0.66			0.10			0.97			0.73

 Table 3.
 Hazard Ratio for All-Cause Mortality and 95% Confidence Interval Among Breast Cancer Patients Associated With Recreational Physical Activity During 10 Years Before Diagnosis

 Overall and by Race/Ethnicity, Stratified by Other Factors, California Breast Cancer Survivorship Consortium, 1994–2010

Table continues

Table 3. Continued

		Overa	ıll	No	n-Latina	White	Afr	ican An	nerican		Latin	a	Δ	sian Ar	nerican
Physical Activity, hours/week	No. of Deaths	HR ^a	95% CI	No. of Deaths	HRª	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI
Stages III–IV	241			59			74			56			52		
0–0.5	133	1.00		28	1.00		39	1.00		35	1.00		31	1.00	
0.6–3.0	60	1.06	0.77, 1.46	16	0.52	0.25, 1.06	19	0.86	0.48, 1.55	10	1.49	0.70, 3.18	15	4.18	2.14, 8.19
>3.0	48	1.01	0.72, 1.42	15	0.72	0.36, 1.44	16	1.02	0.56, 1.86	11	0.72	0.34, 1.50	6	1.89	0.75, 4.75
P for trend			0.89			0.29			0.95			0.52			0.01
P for homogeneity of trends			0.41			0.41			0.55			0.56			0.02
Age at diagnosis, years ^f															
Age <50	487			118			186			101			82		
0–0.5	252	1.00		38	1.00		96	1.00		61	1.00		57	1.00	
0.6–3.0	126	0.98	0.80, 1.21	41	1.22	0.80, 1.86	46	0.88	0.62, 1.24	23	0.97	0.60, 1.57	16	1.11	0.63, 1.95
>3.0	109	1.01	0.81, 1.27	39	1.21	0.79, 1.86	44	0.93	0.65, 1.34	17	0.90	0.52, 1.54	9	1.23	0.60, 2.50
P for trend			0.98			0.36			0.56			0.69			0.55
Age ≥50	860			242			289			185			144		
0–0.5	476	1.00		115	1.00		156	1.00		109	1.00		96	1.00	
0.6–3.0	215	1.06	0.90, 1.25	68	0.91	0.67, 1.25	75	1.13	0.85, 1.50	39	1.08	0.74, 1.56	33	1.32	0.87, 1.98
>3.0	169	0.81	0.68, 0.97	59	0.78	0.56, 1.08	58	0.71	0.52, 0.96	37	0.95	0.65, 1.40	15	1.06	0.60, 1.85
P for trend			0.05			0.13			0.07			0.89			0.48
P for homogeneity of trend			0.23			0.08			0.47			0.80			0.96

Abbreviations: AABCS, Asian American Breast Cancer Study; BMI, body mass index; CARE, Contraceptive and Reproductive Experiences; CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor; SFBCS, San Francisco Bay Area Breast Cancer Study.

^a Cox proportional hazards models use age (days) as the time metric, are stratified by the combined variable of study site and race/ethnicity (non-Latina white in CARE, non-Latina white in SFBCS, African American in CARE, African American in SFBCS, Latina in CARE and SFBCS, and Asian American in AABCS), and include the following variables: age at diagnosis (26–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–79 years); level of education (less than high school, high school graduate, some college/technical school, college graduate, unknown); neighborhood socioeconomic status (lowest, lower middle, middle, higher middle, highest, unknown); BMI (<18.5, 18.5–24.9, 25–29.9, ≥30; tumor stage (I, II, III, IV, unknown); ER/PR status (ER+PR+, ER+PR−, ER−PR+, ER−PR−, ER/PR unknown), with "+" indicating positive and "–" indicating negative; type of surgery (no surgery, mastectomy, breast conserving, others); and chemotherapy (no, yes, unknown) in corresponding models. Total number of deaths may vary because of missing values in corresponding variables.

^b Body mass index: weight (kg)/height (m)².

^c P for homogeneity of trends across race/ethnicity is 0.91 for those with BMI <25 and is 0.63 for those with BMI ≥25.

^d P for homogeneity of trends across race/ethnicity is 0.99 for those with ER-positive tumors and is 0.13 for those with ER-negative tumors.

^e P for homogeneity of trends across race/ethnicity is 0.61 for those with stage I–II tumors and is 0.45 for those with stage III–IV tumors.

^f P for homogeneity of trends across race/ethnicity is 0.95 for those with stage I–II tumors and is 0.54 for those with stage III–IV tumors.

		Overa	1	Nor	n-Latina	White	Afri	can Am	erican		Latina	a	Asian American		
Physical Activity, hours/week	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI
BMI ^{b,c}															
BMI <25	369			109			112			58			90		
0–0.5	175	1.00		35	1.00		54	1.00		30	1.00		56	1.00	
0.6–3.0	99	1.05	0.81, 1.35	37	1.04	0.63, 1.70	27	0.97	0.60, 1.56	14	0.90	0.47, 1.73	21	1.29	0.76, 2.18
>3.0	95	1.13	0.87, 1.47	37	1.07	0.65, 1.78	31	1.23	0.78, 1.96	14	1.30	0.67, 2.53	13	1.31	0.70, 2.44
P for trend			0.37			0.79			0.43			0.54			0.30
BMI ≥25	432			81			187			105			59		
0–0.5	238	1.00		43	1.00		94	1.00		61	1.00		40	1.00	
0.6–3.0	106	1.08	0.85, 1.36	24	0.98	0.58, 1.67	49	1.04	0.73, 1.48	20	1.20	0.71, 2.01	13	1.59	0.83, 3.05
>3.0	88	1.08	0.84, 1.40	14	0.69	0.36, 1.31	44	0.98	0.68, 1.43	24	1.48	0.91, 2.40	6	1.45	0.60, 3.53
P for trend			0.48			0.31			0.97			0.11			0.19
P for homogeneity of trends			0.86			0.34			0.51			0.67			0.67
ER status ^d															
ER positive	447			110			154			94			89		
0–0.5	221	1.00		42	1.00		71	1.00		51	1.00		57	1.00	
0.6–3.0	114	1.15	0.91, 1.45	35	1.33	0.82, 2.14	35	1.13	0.74, 1.72	20	1.06	0.62, 1.81	24	1.54	0.93, 2.54
>3.0	112	1.15	0.91, 1.46	33	1.22	0.75, 1.99	48	1.27	0.86, 1.87	23	1.54	0.92, 2.56	8	0.79	0.37, 1.71
P for trend			0.20			0.41			0.22			0.13			0.85
ER negative	239			59			86			64			30		
0–0.5	131	1.00		24	1.00		52	1.00		36	1.00		19	1.00	
0.6–3.0	63	1.06	0.78, 1.45	22	0.87	0.46, 1.63	20	0.82	0.49, 1.40	15	1.41	0.74, 2.68	6	1.20	0.47, 3.09
>3.0	45	0.95	0.67, 1.35	13	0.57	0.28, 1.20	14	0.64	0.35, 1.19	13	1.15	0.59, 2.22	5	2.82	0.98, 8.08
P for trend			0.88			0.14			0.15			0.55			0.09
P for homogeneity of trends			0.38			0.09			0.05			0.61			0.17
Tumor stage ^e															
Stage I–II	589			136			229			119			105		
0–0.5	299	1.00		51	1.00		115	1.00		63	1.00		70	1.00	
0.6–3.0	150	0.99	0.81, 1.21	46	1.07	0.71, 1.62	55	0.96	0.69, 1.34	28	1.11	0.70, 1.75	21	0.92	0.56, 1.52
>3.0	140	1.06	0.86, 1.31	39	1.03	0.66, 1.59	59	1.00	0.72, 1.39	28	1.46	0.91, 2.32	14	1.24	0.68, 2.25
P for trend			0.64			0.89			0.97			0.13			0.63

 Table 4.
 Hazard Ratio for Breast Cancer–Specific Mortality and 95% Confidence Interval Among Breast Cancer Patients Associated With Recreational Physical Activity During 10 Years Before

 Diagnosis Overall and by Race/Ethnicity, Stratified by Other Factors, California Breast Cancer Survivorship Consortium, 1994–2010

Table continues

Table 4. Continued

		Overa	II	Nor	-Latina	White	Afri	can Am	erican		Latina	a	A	sian Am	nerican
Physical Activity, hours/week	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HR ^a	95% CI	No. of Deaths	HRª	95% CI	No. of Deaths	HR ^a	95% CI
Stage III–IV	213			53			69			47			44		
0–0.5	115	1.00		26	1.00		36	1.00		27	1.00		26	1.00	
0.6–3.0	54	1.28	0.92, 1.79	15	0.86	0.41, 1.79	17	0.83	0.45, 1.53	9	1.60	0.69, 3.70	13	4.25	2.03, 8.91
>3.0	44	1.23	0.85, 1.76	12	0.67	0.31, 1.46	16	1.10	0.59, 2.03	11	1.50	0.69, 2.27	5	1.79	0.64, 4.99
P for trend			0.17			0.31			0.91			0.25			0.02
P for homogeneity of trends			0.35			0.34			0.90			0.84			0.11
Age at diagnosis, years ^f															
<50	397			97			147			87			66		
0–0.5	201	1.00		33	1.00		75	1.00		48	1.00		45	1.00	
0.6–3.0	101	0.99	0.78, 1.26	34	1.15	0.71, 1.87	33	0.78	0.52, 1.18	22	1.25	0.75, 2.09	12	1.10	0.57, 2.12
>3.0	95	1.18	0.92, 1.51	30	1.14	0.69, 1.88	39	1.09	0.73, 1.63	17	1.25	0.71, 2.19	9	1.79	0.86, 3.73
P for trend			0.28			0.60			0.95			0.34			0.17
≥50	429			97			163			84			85		
0–0.5	224	1.00		45	1.00		81	1.00		45	1.00		53	1.00	
0.6–3.0	110	1.15	0.91, 1.44	29	0.98	0.61, 1.58	43	1.18	0.81, 1.72	16	1.03	0.58, 1.85	22	1.54	0.92, 2.56
>3.0	95	1.03	0.81, 1.31	23	0.79	0.47, 1.32	39	0.96	0.66, 1.41	23	1.57	0.94, 2.63	10	1.10	0.55, 2.21
P for trend			0.61			0.38			0.96			0.11			0.37
P for homogeneity of trends			0.64			0.29			0.99			0.67			0.64

Abbreviations: AABCS, Asian American Breast Cancer Study; BMI, body mass index; CARE, Contraceptive and Reproductive Experiences; CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor; SFBCS, San Francisco Bay Area Breast Cancer Study.

^a Cox proportional hazards models use age (days) as the time metric, are stratified by the combined variable of study site and race/ethnicity (non-Latina white in CARE, non-Latina white in SFBCS, African American in CARE, African American in SFBCS, Latina in CARE and SFBCS, and Asian American in AABCS), and include the following variables: age at diagnosis (26–34, 35– 39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–79 years); level of education (less than high school, high school graduate, some college/technical school, college graduate, unknown); neighborhood socioeconomic status (lowest, lower middle, higher middle, highest, unknown); BMI (<18.5, 18.5–24.9, 25–29.9, ≥30); tumor stage (I, II, III, IV, unknown); ER/PR status (ER+PR+, ER+PR−, ER−PR+, ER−PR−, ER/PR unknown), with "+" indicating positive and "–" indicating negative; type of surgery (no surgery, mastectomy, breast conserving, others); and chemotherapy (no, yes, unknown) in corresponding models. The total number of deaths may vary because of missing values in corresponding variables.

^b Body mass index: weight (kg)/height (m)².

^c P for homogeneity of trends across race/ethnicity is 0.83 for those with BMI <25 and is 0.46 for those with BMI ≥25.

^d P for homogeneity of trends across race/ethnicity is 0.79 for those with ER-positive tumors and is 0.27 for those with ER-negative tumors.

^e P for homogeneity of trends across race/ethnicity is 0.50 for those with stage I–II tumors and is 0.56 for those with stage III–IV tumors.

^f P for homogeneity of trends across race/ethnicity is 0.82 for those with stage I–II tumors and is 0.34 for those with stage III–IV tumors.

for breast cancer-specific mortality (HR = 1.10, 95% CI: 0.91, 1.31 for the highest vs. lowest activity level), but an inverse association was observed for mortality from causes other than breast cancer (HR = 0.63, 95% CI: 0.49, 0.80; *P* for trend < 0.01). The decreased risk of death from causes other than breast cancer was driven mostly by the inverse association between recent recreational physical activity and mortality from cardiovascular diseases (HR = 0.49, 95%CI: 0.31, 0.79; *P* for trend = 0.01) (data not shown). Even though the risk patterns for deaths from breast cancer and deaths from causes other than breast cancer were not statistically significantly different across racial/ethnic groups (P for homogeneity of trends = 0.30 and 0.61, respectively), a statistically significant decreased risk of mortality from causes other than breast cancer was observed for African Americans (HR = 0.49, 95% CI: 0.31, 0.78) and Latinas (HR = 0.55, 95% CI: 0.31, 0.98).

We further examined whether the associations between recent recreational physical activity and all-cause mortality (Table 3), breast cancer-specific mortality (Table 4), and mortality from other causes (Web Table 2) were modified by body mass index, ER status, tumor stage, or age at diagnosis. The risk patterns were not statistically significantly different across racial/ethnic groups for all-cause mortality or for breast cancer-specific mortality (P's for homogeneity of trends were all >0.05). For deaths from all causes, inverse associations were observed among non-Latina whites (P for trend = 0.03) and African Americans (P for trend = 0.03) with ER-negative tumors, whereas no associations were observed for their counterparts with ER-positive tumors (both *P*'s for trend > 0.05) (*P*'s for homogeneity of trends = 0.02and 0.07, respectively). Among Asian Americans with ERnegative tumors, a positive association between all-cause mortality and level of recent recreational physical activity was observed for those with the highest level of recent recreational physical activity (HR = 2.56, 95% CI: 1.07, 6.17). However, the number of deaths in this group was small (n =7), and no linear trend was noted (*P* for trend = 0.12).

Among women with stage I-II cancers, we observed decreased risk of all-cause mortality among those in the highest recreational physical activity group (HR = 0.86, 95% CI: 0.73, 1.02), especially among African Americans (HR = 0.77, 95% CI: 0.59, 1.01); however, the confidence intervals did not exclude 1.0. The association between recreational physical activity and all-cause mortality differed by tumor stage among Asian Americans (P for homogeneity of trends = 0.02), with a 4-fold increased risk observed among those with tumor stage III-IV cancers. Similar risk patterns were observed for breast cancer-specific mortality, although the test for homogeneity of trends was not statistically significant. The numbers of deaths among Asian Americans were small (n = 15 for all-cause mortality; n = 13 for breast cancer– specific mortality). The association between recreational physical activity and all-cause mortality was not modified by body mass index or age at diagnosis for women overall or for any specific race/ethnicity (all P's for homogeneity of trends > 0.05). A decreased risk of all-cause mortality was observed among women aged 50 years or more who had the highest level of recreational physical activity (HR = 0.81, 95% CI: 0.68, 0.97), especially among African Americans (HR = 0.71, 95% CI: 0.52, 0.96). Although several *P*'s for homogeneity of trends were statistically significant in the stratified analysis for mortality from other causes, the results were based on small numbers (Web Table 2).

DISCUSSION

In this large, pooled, population-based multiethnic study of women diagnosed with invasive breast cancer, we found that women with high levels of recent recreational physical activity had a decreased risk of death that was marginally statistically significant. Although no association was observed for breast cancer–specific mortality, recent recreational physical activity was associated with lower risk of death from causes other than breast cancer, especially from cardiovascular diseases. These results did not differ by race/ethnicity.

Increasing evidence from observational epidemiologic studies has suggested that recreational physical activity decreases the risk of all-cause mortality, but its association with breast cancer-specific mortality is not consistent. A meta-analysis that included 6 studies with 12,108 breast cancer patients reported that prediagnosis recreational physical activity reduced all-cause mortality by 18% (HR = 0.82, 95% CI: 0.67, 0.99), but no association was observed for breast cancer mortality (HR = 0.93, 95% CI: 0.72, 1.21) (2), which is consistent with the pooled analysis results from our study. Among the 9 studies reporting prediagnosis recreational physical activity results for all-cause mortality that were published after publication of this meta-analysis, 3 studies (8, 19, 20) reported no association, 2 studies (7, 21) observed nonstatistically significant decreased risks (HR = 0.82, 95% CI: 0.67, 1.01 and HR = 0.74, 95% CI: 0.51, 1.08, respectively) when comparing the highest with the lowest activity categories, and 4 studies (9, 10, 22, 23) observed statistically significant decreased risks of all-cause mortality that ranged from 23% to 43%. With regard to breast cancer-specific mortality, 1 study (20) reported null findings; 4 studies (7, 9, 19, 21) reported nonstatistically significant reduced risks, and 3 (10, 22, 23) studies reported statistically significant risk reductions that ranged from 34% to 47%.

Few studies have examined whether certain subgroups of breast cancer patients might benefit more from prediagnosis recreational physical activity than others, and the results are inconsistent. One previous study reported a stronger inverse association among women with early stage tumors (10), which is in agreement with our results, especially those for African Americans. The stratified analysis by ER status in our study showed stronger inverse associations among women with ER-negative than among those with ER-positive tumors, and especially among non-Latina whites and African Americans. Results from other studies are mixed, with 1 study (8) reporting a stronger inverse association for ERpositive breast cancer and another (10) showing no difference by ER status. Interestingly, a recent study (9) following 3.393 women (367 deaths) with breast cancer reported that higher levels of prediagnosis recreational physical activity reduced the risk of recurrence of ER-negative/PR-negative breast tumors. We unexpectedly observed positive associations for all-cause mortality and breast cancer-specific mortality among Asian American subgroups (ER+ tumors, ER- tumors, and women with stage III-IV tumors). However, the analyses

for Asian Americans were based on few deaths, and the risk patterns were not consistent.

We observed a statistically significant inverse association between recent recreational physical activity and overall mortality for women aged 50 years or more and a null association for women younger than 50 years, although the interaction was not statistically significant. One previous study (7) reported a stronger inverse association for women older than 55 years at diagnosis than for younger women. The association between recreational physical activity and all-cause mortality did not differ by body mass index in our study, whereas previous studies have produced mixed results, showing no difference by body mass index (8), a stronger reduction in risk among women with high levels of body mass index (6, 10), or a lower risk only among those with low-to-normal levels of body mass index (7, 9).

To our knowledge, our study is the first to examine whether prediagnosis recreational physical activity and mortality associations differ among non-Latina whites, African Americans, Latinas, and Asian Americans with invasive breast cancer. A major strength of this pooled analysis is that the 3 contributing studies used almost identical questionnaires to assess recreational physical activity histories, allowing consistent estimates across time periods of recreational physical activity. Another strength is that detailed information was available on a large number of prognostic factors, including tumor characteristics and treatment, enabling us to assess many potential confounders, build appropriate multivariate models, and evaluate possible effect modifiers. Nevertheless, the treatment information from SEER may not be completely accurate. A recent study compared SEER data with Medicare data among patients aged 65 years or more. The authors reported that the overall sensitivity of SEER breast cancer data to capture chemotherapy and radiation therapy was moderate (69% and 80%, respectively). The overall positive predictive value was 91.2% and 97.5%, respectively (24). Because the choice of treatment is unlikely to be related to the level of recreational physical activity during 10 years before breast cancer diagnosis, it is likely to be a nondifferential error and will bias the results toward the null. Finally, our study had large numbers of events for both allcause mortality (n = 1,347) and breast cancer-specific mortality (n = 826) because of the long follow-up (mean = 9.9 years).

Our study also has several limitations. First, self-reports of recreational physical activity may be inaccurate. However, this measurement error would be expected to be nondifferential with respect to mortality, and any reporting bias would be expected to attenuate the true underlying associations. Further, our main analyses were based on activity in the 10 years prior to diagnosis, which should lessen the magnitude of errors in reporting. Second, we did not collect any physical activity information after breast cancer diagnosis; physical activity patterns after diagnosis may differ from activity patterns before diagnosis. One prior study, however, collected physical activity information from 20 years prior to breast cancer diagnosis to 9 years following diagnosis and reported that 33% were active both prior to and following diagnosis, 28% were both inactive, and more subjects began exercising (23%) than quit exercising (16%) once being diagnosed (25). Finally, we did not have information on nonrecreational physical activity for all 3 studies that may have introduced exposure misclassification.

The Women's CARE Study collected only recreational physical activity. AABCS collected information on occupational physical activity, but this was limited to the 3 longest held jobs. Only SFBCS collected lifetime history of occupational physical activity, as well as activity related to household chores and transportation, and showed that different types of activities varied across racial/ethnic groups, with Latinas having lower levels of recreational physical activity than African Americans and non-Latina whites (14). In the current analysis, we also observed substantial differences in the distribution of recreational physical activity across the racial/ethnic groups. Asian American women had high levels of other types of physical activity but were less likely to be involved in recreational physical activity. If all types of physical activity similarly influence mortality, then our reference group of inactive Asian American women may not have truly reflected their total activity level, and thus the results could be biased.

In summary, we found that recreational physical activity levels varied substantially across racial/ethnic groups in this pooled analysis; however, the benefit of recreational physical activity on overall survival remains consistent across different races/ethnicities. Additional research is warranted to clarify the associations between recreational physical activity and disease outcomes among different subgroups of patients (e.g., ER status, tumor stage, and so on) within each race/ethnicity group.

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