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Original Contribution

Obesity and Mortality After Breast Cancer by Race/Ethnicity: The California Breast Cancer Survivorship Consortium

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We investigated body size and survival by race/ethnicity in 11,351 breast cancer patients diagnosed from 1993 to 2007 with follow-up through 2009 by using data from questionnaires and the California Cancer Registry. We calculated hazard ratios and 95% confidence intervals from multivariable Cox proportional hazard model–estimated associations of body size (body mass index (BMI) (weight (kg)/height (m)^2) and waist-hip ratio (WHR)) with breast cancer–specific and all-cause mortality. Among 2,744 ascertained deaths, 1,445 were related to breast cancer. Being underweight (BMI <18.5) was associated with increased risk of breast cancer mortality compared with being normal weight in non-Latina whites (hazard ratio (HR) = 1.91, 95% confidence interval (CI): 1.14, 3.20), whereas morbid obesity (BMI ≥40) was suggestive of increased risk (HR = 1.43, 95% CI: 0.84, 2.43). In Latinas, only the morbidly obese were at high risk of death (HR = 2.26, 95% CI: 1.23, 4.15). No BMI–mortality associations were apparent in African Americans and Asian Americans. High WHR (quartile 4 vs. quartile 1) was associated with breast cancer mortality in Asian Americans (HR = 2.21, 95% CI: 1.21, 4.03; *P* for trend = 0.01), whereas no associations were found in African Americans, Latinas, or non-Latina whites. For all-cause mortality, even stronger BMI and WHR associations were observed. The impact of obesity and body fat distribution on breast cancer patients' risk of death may vary across racial/ethnic groups.

adiposity; body mass index; breast cancer; mortality; obesity; race/ethnicity; survival; waist-hip ratio

Abbreviations: AABCS, Asian American Breast Cancer Study; BMI, body mass index; CARE, Women's Contraceptive and Reproductive Experiences Study; CBCSC, California Breast Cancer Survivorship Consortium; CCR, California Cancer Registry; CI, confidence interval; CTS, California Teachers Study; HR, hazard ratio; LACE, Life After Cancer Epidemiology; MEC, Multiethnic Cohort Study; SFBCS, San Francisco Bay Area Breast Cancer Study; WHR, waist-hip ratio.

Substantial evidence suggests that obese women have poorer survival after a breast cancer diagnosis compared with normal-weight women (1–3). However, most studies have assessed obesity by using body mass index (BMI) (weight (kg)/height (m)^2) and have been conducted primarily among non-Latina white women (4).

Racial/ethnic differences in body composition are well established (5–7). African American and Latina women have the highest average BMI values, whereas Asian American women have the lowest (8, 9). Compared with non-Latina whites, African Americans and Latinas are more obese (i.e., higher body weight, BMI, and percent body fat) (6–8, 10). African Americans also have greater average waist circumference and higher amounts of subcutaneous fat (11, 12). At the same BMI values, Asian Americans have a higher percent body fat and relatively more visceral fat than do non-Latina whites and African Americans (13, 14).

Differential effects of obesity on breast cancer–specific and all-cause mortality after breast cancer diagnosis might exist across racial/ethnic groups. In the California Breast

Cancer Survivorship Consortium (CBCSC), a multiethnic cohort of women diagnosed with invasive breast cancer pooled from 6 studies, we recently reported that African Americans had higher rates of breast cancer–specific mortality compared with non-Latina whites (hazard ratio (HR) = 1.13), but their overall mortality rates were similar (HR = 1.02) (15). In contrast, the breast cancer–specific mortality rates in Latinas (HR = 0.84) and Asian Americans (HR = 0.60) were lower than in non-Latina whites. To further explore these observed survival differences by race/ethnicity, we investigated the association between body size measurements and mortality in non-Latina white, African American, Asian American, and Latina women.

MATERIALS AND METHODS

California Breast Cancer Survivorship Consortium

The CBCSC represents 12,210 women diagnosed with primary invasive breast cancer between 1993 and 2007 from 6 California-based studies of breast cancer etiology or prognosis (15). It includes 3 population-based case-control studies (the Asian American Breast Cancer Study (AABCS) (16); the Los Angeles Component, Women's Contraceptive and Reproductive Experiences Study (CARE) (17); and the San Francisco Bay Area Breast Cancer Study (SFBCS) (18, 19)) and 3 prospective cohort studies (the California Teachers Study (CTS) (20), the Multiethnic Cohort Study (MEC) (21), and the Life After Cancer Epidemiology Study (LACE) (22)). The CTS and MEC identified newly diagnosed breast cancer cases through annual linkages with the California Cancer Registry (CCR) (20, 21). LACE is a breast cancer survivor cohort that recruited Kaiser Permanente Northern California patients for active follow-up after diagnosis (22). Each study collected data on reproductive, lifestyle, sociodemographic, and other breast cancer risk factors. Institutional review board approval was received from all participating institutions and the California Center for the Protection of Human Subjects. Patient data were obtained from in-person study interviews or mailed questionnaires and were harmonized and merged into a common data set.

Body size variables and prognostic factors

Weight and height. Data on weight before breast cancer diagnosis and on adult height were based on self-report at interview (in AABCS, CARE, and SFBCS), baseline survey (in LACE), or mailed questionnaires prior to breast cancer diagnosis (in CTS and MEC). In the AABCS and SFBCS, weight and height were also measured by an interviewer, and missing self-reported height data were supplemented by height measurements. For the AABCS, SFBCS, and LACE, the mean time for prediagnosis measurement was 1.0 (standard deviation (SD), 0.2) years, and for CARE, CTS, and MEC, the mean time was 5.1 (SD, 2.7) years.

Waist and hip circumference. Waist and hip circumferences, either prediagnosis or postdiagnosis, were measured by interviewers (in AABCS and SFBCS) or patients (in CTS and LACE) as described above for weight and height. These measurements were not collected in CARE and MEC, and LACE obtained only waist circumference measurements. For AABCS, SFBCS, and LACE, the mean time for postdiagnosis measurement was 1.7 (SD, 0.7) years; for CTS, the mean times were 3.8 (SD, 2.3) years prediagnosis (80% of the cohort) and 0.9 (SD, 0.6) years postdiagnosis (20% of the cohort).

Covariates. Variables based on self-report (categories shown in Table 1) included age at breast cancer diagnosis, race/ethnicity, education, birthplace, menopausal status, age at first birth, smoking history, alcohol intake, and comorbidities (diabetes, hypertension, and/or myocardial infarction). Information on marital status and a composite measurement of neighborhood socioeconomic status based on the distribution of census block groups within California was obtained from the CCR by using 2000 US Census data (23).

Body size measures

Prediagnosis BMI was calculated for measurements at least 6 months before breast cancer diagnosis and categorized into 4- and 6-level BMI variables by using the World Health Organization international classifications (9, 24). The 4-level BMI variables are underweight (BMI <18.5), normal weight (BMI = 18.5–24.9; reference), overweight (BMI = 25.0–29.9), and obese (BMI ≥30.0). The 6-level variable further subdivides women with BMI values of 30 or more into categories of obese (BMI = 30.0–34.9), severely obese (BMI = 35.0–39.9), and morbidly obese (BMI ≥40). For analyses specific to race/ethnicity, we created a BMI variable based on deciles with the following values: <17.5, 17.5–19.9, 20.0–22.4, 22.5–24.9 (reference), 25.0–27.4, 27.5–29.9, 30.0–32.4, 32.5–34.9, 35.0–37.4, and ≥37.5 (25). The 6- and 10-level variables were used to explore nonlinear BMI associations.

Waist-hip ratio (WHR) was calculated as waist circumference (in cm) divided by hip circumference (in cm) as a measurement of fat distribution that reflects adipose tissue and muscle mass. Waist-height ratio was calculated as waist circumference (in cm) divided by height (in cm) as a measurement of abdominal fat alone (26). Waist circumference also estimates abdominal fat and is strongly correlated with BMI (27). WHR, waist-height ratio, and waist circumference were categorized into quartiles.

Clinicopathologic and treatment factors

Variables from the CCR (categories in Table 2) included cancer stage, estrogen receptor and progesterone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, and chemotherapy, hormonal therapy, and radiation therapy. Cancer stage was based on the staging system of the American Joint Committee on Cancer (Chicago, Illinois).

Study outcomes

Confirmation of vital status from the CCR was determined as of December 31, 2009. Cases were not presumed to be alive if there was no documentation of death. Breast cancer–specific deaths were ascertained from information

on the underlying cause of death on the death certificate based on *International Classification of Diseases, Ninth Revision,* codes 174–175 or *International Classification of Diseases, Tenth Revision,* code C50. Study endpoints included breast cancer–specific and all-cause mortality.

Analytical sample size

BMI analyses were based on 11,351 women, excluding those without information on prediagnosis weight or adult height ($n = 674$) or other covariates ($n = 185$). Waist circumference analyses included 7,191 women (from the AABCS, SFBCS, CTS, and LACE), excluding those with missing information ($n = 1,610$). WHR and waist-height ratio analyses included 5,720 and 7,180 women, respectively, excluding 3,081 and 1,621 women, respectively, with missing data. All missing covariate data were coded into "unknown" categories.

Statistical analysis

Before pooling data from the 3 case-control and 3 cohort studies, we conducted separate analyses by study design, and no systematic differences were found across studies. This was tested formally in our statistical models as an interaction term of race/ethnicity and study, and all likelihood ratio tests for this effect on mortality outcomes were $P > 0.15$ (11 df) (15).

Delayed entry Cox proportional hazards regression models with attained age as the time scale (28) and study as a stratification variable were used to estimate hazard ratios and 95% confidence intervals in overall and race/ethnicity–specific models. Although models were also run by using time from diagnosis as the time scale, attained age provided a slightly better model fit and was thus retained (15). The entry date into the risk set was the latter of the date of questionnaire completion or the date of breast cancer diagnosis. The exit date was the date of death (breast cancer–specific or all-cause mortality, depending on analysis) or the end of follow-up (the earlier of the last follow-up date in the CCR or December 31, 2009).

Covariates were selected on the basis of backward stepwise regression and a priori determination from literature review. The order of removal was determined by the Cox partial likelihood test for that variable, and removal continued until all remaining variables had a likelihood ratio with $P < 0.20$. Final models were adjusted for all variables in Tables 1 and 2, including treatment modalities of chemotherapy, radiation therapy, and hormonal therapy (no, yes, or unknown). For WHR, waist-height ratio, and waist circumference analyses, prediagnosis BMI and an indicator for prediagnosis or postdiagnosis WHR, waist-height ratio, or waist circumference measurement were also included.

Linear and nonlinear trends of BMI associated with each mortality outcome were obtained by modeling BMI as a continuous variable and using the partial likelihood test for linearity. To test whether the associations between each adiposity measure and mortality were modified by race/ethnicity, we constructed a likelihood ratio test for heterogeneity of trends comparing 2 multivariate Cox proportional hazard models (29). Effect modification was evaluated in the associations between BMI, WHR, and mortality outcomes by menopausal status and hormone receptor status, and statistical significance was determined by the Wald test.

For analyses of breast cancer–specific mortality, we considered competing risks from non–breast cancer deaths to test extreme model violations under the independence assumption. For subjects who were censored because of non–breast cancer deaths, they were 1) assumed to have died of breast cancer instead, and 2) assumed to have survived as long as the longest survival time observed in the cohort. All tests of statistical significance were 2-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

For BMI analyses, there were 1,445 breast cancer–specific deaths (2,744 deaths overall) after a mean follow-up of 11.0 (SD, 3.8) years. The mean time of weight and height measurements was 2.2 (SD, 0.5) years before diagnosis. For WHR analyses, there were 654 breast cancer–related deaths (1,284 deaths overall). The mean times of prediagnosis and postdiagnosis waist/hip measurement were 3.8 (SD, 2.3) years ($n = 2,187$) and 1.4 (SD, 0.7) years ($n = 3,533$), respectively.

Mean age at breast cancer diagnosis was 60.2 years, and two-thirds (66.4%) of cases were postmenopausal at diagnosis (Table 1). About half (53.3%) were non-Latina white, and the mean prediagnosis BMI was 26.3. Compared with normal-weight women, obese women were more likely to be African American or Latina, older at breast cancer diagnosis, current or past smokers, nondrinkers, less educated, and US born and were more likely to reside in a low socioeconomic status neighborhood and to have a comorbidity. In contrast, underweight women were more likely to be younger at diagnosis, nonsmokers, college educated, and foreign born and not to have a comorbidity and to live in a higher socioeconomic status neighborhood at diagnosis.

The distribution of all clinicopathological and treatment characteristics varied significantly across BMI categories, except for chemotherapy ($P = 0.16$) (Table 2). Compared with normal-weight women, obese women were more likely to be diagnosed with advanced stage, poorly differentiated, and larger tumors and less likely to have had breast cancer surgery or to receive hormonal therapy. In contrast, underweight women were more likely to be diagnosed with lower stage, well-differentiated, and smaller tumors, and not to receive hormonal therapy.

Although data are not shown, Asian Americans (44.7%) and Latinas (44.6%) were more likely to receive chemotherapy, followed by African Americans (40.4%) and non-Latina whites (38.8%). However, non-Latina whites were more likely to have radiation and hormonal therapy (56.4% and 44.2%, respectively) compared with the other groups. Asian Americans were least likely to have radiation (41.4%) and hormonal therapy (30.8%), followed by African Americans (radiation, 44.8%; hormonal therapy, 31.1%) and Latinas (radiation, 51.2%; hormonal therapy, 36.7%).

In fully-adjusted multivariate models, being underweight (HR = 1.41, 95% CI: 0.99, 2.02) or morbidly obese (HR = 1.42, 95% CI: 1.07, 1.88) was associated with an increased risk of breast cancer–specific mortality compared with being

Table 1. Sociodemographic and Body Size Characteristics by Prediagnosis BMI[a] of Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Characteristic	Total (n = 11,351)		BMI Category[a]							
			Underweight (n = 213)		Normal Weight (n = 5,332)		Overweight (n = 3,401)		Obese (n = 2,405)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Prediagnosis BMI[b]	26.3 (5.5)		17.7 (0.7)		22.2 (1.7)		27.2 (1.4)		34.6 (4.4)	
Race/ethnicity										
Non-Latina white	6,044	53.3	123	57.8	3,222	60.4	1,695	49.8	1,004	41.8
African American	1,886	16.6	23	10.8	546	10.2	634	18.6	683	28.4
Asian American	1,864	16.4	49	23.0	908	17.0	388	11.4	106	4.4
Latina	1,451	12.8	17	8.0	597	11.2	654	19.2	596	24.8
Other	106	0.9	1	0.5	59	1.1	30	0.9	16	0.7
Age at breast cancer diagnosis, years[b]	60.2 (12.2)		56.4 (13.7)		58.8 (12.7)		61.9 (11.8)		61.3 (11.1)	
<40	556	4.9	26	12.2	343	6.4	125	3.7	62	2.6
40–49	1,970	17.4	53	24.9	1,112	20.9	453	13.3	352	14.6
50–59	3,126	27.5	49	23.0	1,497	28.1	894	26.3	686	28.5
60–69	3,017	26.6	42	19.7	1,233	23.1	1,004	29.5	738	30.7
≥70	2,682	23.6	43	20.2	1,147	21.5	925	27.2	567	23.6
Education										
Less than high school	1,214	10.7	12	5.6	318	6.0	437	12.9	447	18.6
High school graduate	1,776	15.7	34	16.0	677	12.7	581	17.1	484	20.1
Some college	2,515	22.2	40	18.8	1,070	20.1	784	23.1	621	25.8
College graduate or higher	5,816	51.2	127	59.6	3,258	61.1	1,586	46.6	845	35.1
Unknown	30	0.3	0	0.0	9	0.2	13	0.4	8	0.3
Neighborhood (census block group) SES										
Low	4,894	43.1	79	37.1	1,895	35.5	1,574	46.3	1,346	56.0
High	6,133	54.0	125	59.2	3,298	61.9	1,721	50.6	988	41.1
Unknown	324	2.9	8	3.8	139	2.6	106	3.1	71	3.0
Place of birth										
United States	9,101	80.2	162	76.1	4,250	79.7	2,685	79.0	2,004	83.3
Outside United States	2,202	19.4	50	23.5	1,058	19.8	701	20.6	393	16.3
Missing/unknown	48	0.4	1	0.5	24	0.5	15	0.4	8	0.3
Marital status										
Married	6,780	59.7	117	54.9	3,383	63.5	1,993	58.6	1,287	53.5
Separated/widowed	3,062	25.5	52	24.4	1,196	22.4	920	27.1	714	29.7
Single/never married	1,442	12.7	44	20.7	649	12.2	411	12.1	338	14.1
Unknown	247	2.2	0	0.0	104	2.0	77	2.3	66	2.7
Menopausal status										
Premenopausal	3,097	27.3	85	39.9	1,749	32.8	746	21.9	517	21.5
Postmenopausal	7,542	66.4	113	53.1	3,198	60.0	2,471	72.7	1,760	73.2
Unknown	712	6.3	15	7.0	385	7.2	184	5.4	128	5.3
Age at first birth, years										
<20	1,752	15.4	20	9.4	543	10.2	593	17.4	596	24.8
20–29	5,746	50.6	91	42.7	2,740	51.4	1,730	50.9	1,185	49.3
≥30	1,542	13.6	26	12.2	852	16.0	458	13.5	206	8.5
Nulliparous	2,166	19.1	73	34.3	1,139	21.4	572	16.8	382	15.9
Unknown	145	1.3	3	1.4	58	1.1	48	1.4	36	1.5

Table continues

Table 1. Continued

Characteristic	Total (*n* = 11,351)		BMI Category[a]							
			Underweight (*n* = 213)		Normal Weight (*n* = 5,332)		Overweight (*n* = 3,401)		Obese (*n* = 2,405)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Smoking history										
Never	5,637	49.7	121	56.8	2,740	51.4	1,666	49.0	1,110	46.2
Current	1,004	8.8	28	13.2	482	9.0	301	8.9	193	8.0
Past	3,085	27.2	39	18.3	1,486	27.9	933	27.4	627	26.1
Unknown	1,625	14.3	25	11.7	624	11.7	501	14.7	475	19.8
Alcohol intake, drinks/week										
Nondrinker	5,347	47.1	103	48.4	2,174	40.8	1,632	48.0	1,438	59.8
≤2	2,032	17.9	33	15.5	943	17.7	642	18.9	414	17.2
>2	3,416	30.1	67	31.5	1,979	37.1	955	28.1	415	17.3
Unknown	556	4.9	10	4.7	236	4.4	172	5.1	138	5.7
Comorbidity (diabetes, hypertension, and/or myocardial infarction)										
Yes	3,615	31.9	31	14.6	1,169	21.9	1,213	35.7	1,202	50.0
No	6,087	53.6	160	75.1	3,533	66.3	1,667	48.8	733	30.5
Unknown	1,649	14.5	22	10.3	130	11.8	527	15.5	470	19.5
Waist-hip ratio, quartile[c]										
First	1,343	25.3	62	52.1	994	36.2	221	14.4	66	7.2
Second	1,349	25.4	33	27.7	818	29.8	351	22.8	147	16.1
Third	1,325	24.9	11	9.2	573	20.8	466	30.3	275	30.2
Fourth	1,300	24.4	13	10.9	364	13.2	499	32.5	424	46.5
Waist-height ratio, quartile[c]										
First	1,701	25.1	107	81.1	1,492	43.7	100	5.1	2	0.2
Second	1,712	25.3	18	13.6	1,222	35.8	434	22.0	38	3.0
Third	1,672	24.7	5	3.8	563	16.5	863	43.8	241	19.2
Fourth	1,683	24.9	2	1.5	134	3.9	575	29.2	972	77.6
Waist circumference, quartile[c]										
First	1,711	25.3	108	81.8	1,493	43.8	107	5.4	3	0.2
Second	1,787	26.4	15	11.4	1,243	36.4	480	24.3	49	3.9
Third	1,600	23.6	6	4.5	525	15.4	827	41.9	242	19.3
Fourth	1,670	24.7	3	2.3	150	4.4	558	28.3	959	76.5

Abbreviations: BMI, body mass index; SES, socioeconomic status.

[a] BMI (weight (kg)/height (m)^2) was calculated from self-reported or measured prediagnosis weight at least 6 months before breast cancer diagnosis and self-reported or measured height at the time of the baseline/first postdiagnosis interview and categorized by using the following World Health Organization international classifications: underweight (<18.5), normal weight (18.5–24.9; reference), overweight (25.0–29.9), and obese (≥30.0).

[b] Values are mean (standard deviation).

[c] A subset of women with BMI measurements had waist-related measurements. There were 403 women with waist-hip ratio measurements but no BMI measurements, 412 with waist-height ratio measurements but no BMI measurements, and 423 with waist circumference measurements but no BMI measurements (all not shown in table).

normal weight (Table 3). Stronger results were found for all-cause mortality (for underweight, HR = 1.47, 95% CI: 1.14, 1.91; for morbidly obese, HR = 1.41, 95% CI: 1.14, 1.75; *P* for trend = 0.04; *P* for departure from linearity = 0.004). When assessing the impact of competing risks for breast cancer–specific mortality, we found that the hazard ratios were similar to the main hazard ratios above when making the following 2 assumptions about deaths not due to breast cancer: 1) subjects died of breast cancer, or 2) subjects survived for the longest time observed in the cohort (data not shown).

Table 2. Clinicopathological and Treatment Characteristics by Prediagnosis BMI[a] in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Characteristic	Total (*n* = 11,351)		BMI Category[a]							
			Underweight (*n* = 213)		Normal Weight (*n* = 5,332)		Overweight (*n* = 3,401)		Obese (*n* = 2,405)	
	No.	%	No.	%	No.	%	No.	%	No.	%
AJCC stage										
I	5,537	48.8	117	54.9	2,752	51.6	1,636	48.1	1,032	42.9
II	4,601	40.5	81	38.0	2,058	38.6	1,414	41.6	1,048	43.6
III	648	5.7	5	2.4	277	5.2	175	5.2	191	7.9
IV	196	1.7	4	1.9	78	1.5	63	1.9	51	2.1
Unknown	369	3.3	6	2.8	167	3.1	113	3.3	83	3.5
Hormone receptor status										
ER and/or PR+	7,865	69.3	143	67.1	3,756	70.4	2,313	68.0	1,653	68.0
ER– and PR–	1,811	16.0	29	13.6	781	14.7	579	17.0	422	17.0
Unknown	1,675	14.8	41	19.3	795	14.9	509	15.0	330	15.0
Nodal positivity										
No nodes	7,304	64.4	153	71.8	3,517	66.0	2,192	64.5	1,442	60.0
Positive nodes	3,686	32.5	54	25.4	1,682	31.6	1,097	32.3	853	35.5
Unknown	361	3.2	6	2.8	133	2.5	112	3.3	110	4.6
Tumor grade										
Grade 1 (well-differentiated)	2,188	19.3	46	21.6	1,107	20.8	630	18.5	405	16.8
Grade 2	4,282	37.7	70	32.9	2,051	38.5	1,268	37.3	893	37.1
Grade 3 (poorly differentiated)	3,705	32.6	67	31.5	1,629	30.6	1,157	34.0	852	35.4
Unknown	1,176	10.4	30	14.1	545	10.2	346	10.2	255	10.6
Tumor size, cm										
<2	6,258	55.1	132	62.0	3,108	58.3	1,833	53.9	1,185	49.3
2–5	4,029	35.5	63	29.6	1,743	32.7	1,274	37.5	949	39.5
≥5	510	4.5	7	3.3	225	4.2	137	4.0	141	5.9
Unknown	554	4.9	11	5.2	256	4.8	157	4.6	130	5.4

Table continues

Women in the highest WHR quartile compared with those in the lowest quartile had an increased risk of breast cancer–specific mortality in the fully-adjusted model (HR = 1.27, 95% CI: 0.98, 1.65; *P* for trend = 0.04) (Table 3). For all-cause mortality, the association with high WHR was stronger (HR = 1.30, 95% CI: 1.07, 1.57; *P* for trend = 0.001). Waist-height ratio and waist circumference were not associated with mortality outcomes. Again, when assessing the impact of competing risks, we found that the hazard ratios under both scenarios were similar to the main hazard ratios above (data not shown).

Similar to the overall cohort, non-Latina whites (for underweight, HR = 1.91, 95% CI: 1.14, 3.20; for morbidly obese, HR = 1.43, 95% CI: 0.84, 2.43) and Latinas (for underweight, HR = 1.40, 95% CI: 0.33, 5.92; for morbidly obese, HR = 2.26, 95% CI: 1.23, 4.15) had U-shaped associations of BMI with breast cancer–specific mortality, yet *P* for trends and departures from linearity were not statistically significant (Table 4). When categorizing BMI into deciles, we found that the U-shaped associations among non-Latina whites and Latinas were less consistent with results based on the 6-level BMI categories for BMI of 30.0 or more. Overall, there were no BMI associations with breast cancer mortality in African Americans and Asian Americans. For all-cause mortality, statistically significant, increased risks in both the underweight and morbidly obese groups of non-Latina whites (for underweight, HR = 1.72, 95% CI: 1.22, 2.44; for morbidly obese, HR = 1.61, 95% CI: 1.12, 2.31; *P* for trend = 0.08; *P* for departure from linearity = 0.009) and Latinas (for underweight, HR=1.82, 95% CI: 0.72, 4.63; for morbidly obese, HR = 1.93, 95% CI: 1.21, 3.10; *P* for trend = 0.02; *P* for departure from linearity = 0.27) were found (Table 5). However, no such associations were observed among Asian Americans and African Americans. Furthermore, after additional adjustment for WHR in a subset of women, all BMI–mortality associations remained consistent (data not shown).

Similar to the total cohort, high WHR was associated with increased risk of breast cancer–specific mortality in Asian Americans (HR = 2.21, 95% CI: 1.21, 4.03) with a significant linear trend (*P* = 0.01) (Table 6). No WHR associations were apparent among African Americans, Latinas, and non-Latina whites. For all-cause mortality, although similar associations were observed for Asian Americans (HR = 1.64,

Table 2. Continued

Characteristic	Total ($n = 11,351$)		BMI Category[a]							
			Underweight ($n = 213$)		Normal Weight ($n = 5,332$)		Overweight ($n = 3,401$)		Obese ($n = 2,405$)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Prior cancer history										
No	10,542	92.9	188	88.3	4,952	92.9	3,169	93.2	2,233	92.9
Yes	809	7.1	25	11.7	380	7.1	232	6.8	172	7.2
Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Surgery type										
Breast conserving	6,302	55.5	112	52.6	2,973	55.8	1,918	56.4	1,299	54.0
Mastectomy	4,780	42.1	95	44.6	2,258	42.4	1,410	41.5	1,017	42.3
No surgery	251	2.2	5	2.4	92	1.7	69	2.0	85	3.5
Other	18	0.2	1	0.5	9	0.2	4	0.1	4	0.2
Chemotherapy										
No	6,532	57.6	130	61.0	3,023	56.7	2,014	59.2	1,365	56.8
Yes	4,634	40.8	78	36.6	2,215	41.5	1,336	39.3	1,005	41.8
Unknown	185	1.6	5	2.4	94	1.8	51	1.5	35	1.5
Hormonal therapy										
No	6,638	58.5	147	69.0	3,137	58.5	2,007	59.0	1,347	56.0
Yes	4,439	39.1	61	28.6	2,054	38.5	1,314	38.6	1,010	42.0
Unknown	274	2.4	5	2.4	141	2.6	80	2.4	48	2.0
Radiation therapy										
No	5,480	48.3	123	57.8	2,547	47.8	1,632	48.0	1,178	49.0
Yes	5,871	51.7	90	42.3	2,785	52.2	1,769	52.0	1,227	51.0

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor.

[a] BMI (weight (kg)/height $(m)^2$) was calculated from self-reported or measured prediagnosis weight at least 6 months before breast cancer diagnosis and self-reported or measured height at the time of the baseline/first postdiagnosis interview and categorized by using the following World Health Organization international classifications: underweight (<18.5), normal weight (18.5–24.9; reference), overweight (25.0–29.9), and obese (≥30.0).

95% CI: 1.02, 2.63; P for trend = 0.02), high WHR was associated with elevated risk in African Americans (HR = 2.19, 95% CI: 1.15, 4.19; P for trend = 0.01) (Table 7). The effects by prediagnosis versus postdiagnosis measurements in Asian Americans and African Americans could not be determined because of limited numbers (data not shown). Consistent with the overall cohort results, waist-height ratio and waist circumference were not associated with mortality in any racial/ethnic group.

No significant interactions of BMI, WHR, and breast cancer–specific mortality with hormone receptor status were observed (Table 8). The BMI associations were also similar among premenopausal and postmenopausal women (data not shown). When these stratified analyses of hormone receptor and menopausal status were conducted within each racial/ethnic group, no significant interactions were found (data not shown).

DISCUSSION

In this large, multiethnic study of 11,351 breast cancer patients, we found that those with very high or very low prediagnosis BMI or high WHR had the highest risk of death. Compared with normal-weight women, both underweight and morbidly obese women had 1.4-fold greater risk of breast cancer–specific mortality, and women in the highest quartile of abdominal obesity had 1.3-fold greater risk of breast cancer–specific mortality. Our results suggest that the associations of obesity with mortality vary by measurement and degree of obesity, as well as by race/ethnicity. The U-shaped associations of BMI with breast cancer–specific mortality were suggestive among non-Latina whites and Latinas and were not observed in African Americans and Asian Americans. In contrast, high WHR was associated with elevated breast cancer–specific mortality after BMI adjustment among Asian Americans, but not African Americans, Latinas, or non-Latina whites. The results were stronger for all-cause mortality. Investigating these adiposity associations within the CBCSC allowed us to examine effects across 4 racial/ethnic groups, as well as by hormone receptor and menopausal status.

Reviews of BMI and breast cancer prognosis (4, 30, 31) report that roughly two-thirds of the studies conducted in the last decade have reported higher BMI at diagnosis as a significant risk factor for disease recurrence and mortality. Two meta-analyses have confirmed that obesity (BMI ≥30) preceding breast cancer diagnosis is related to breast

Table 3. Associations of Body Size Measurements and Mortality in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Measurement by Mortality Type	No. of Exposed	No. of Outcomes	Person-years	Rate per 1,000 Person-years	Fully Adjusted HR[a,b]	95% CI
Breast cancer–specific mortality						
Prediagnosis BMI category[c]						
Underweight	213	34	2,328	14.61	1.41	0.99, 2.02
Normal weight	5,332	602	59,094	10.19	1.00	Referent
Overweight	3,401	429	37,687	11.38	1.02	0.89, 1.16
Obese	1,576	238	16,832	14.14	1.11	0.94, 1.31
Severely obese	553	81	5,789	13.99	0.99	0.78, 1.27
Morbidly obese	276	61	2,768	22.04	1.42	1.07, 1.88
P for trend					0.21	
P for linearity					0.12	
Waist-hip ratio, quartile[d,e]						
First	1,430	149	16,410	9.08	1.00	Referent
Second	1,437	149	15,536	9.59	1.04	0.81, 1.33
Third	1,422	165	14,640	11.27	0.99	0.77, 1.27
Fourth	1,431	191	14,650	13.04	1.27	0.98, 1.65
P for trend					0.04	
Waist-height ratio, quartile[d,f]						
First	1,795	157	19,977	7.86	1.00	Referent
Second	1,795	165	18,844	8.76	1.00	0.79, 1.27
Third	1,786	191	17,764	10.75	0.96	0.74, 1.23
Fourth	1,804	242	16,810	14.4	1.17	0.86, 1.59
P for trend					0.16	
Waist circumference, quartile[d,g]						
First	1,798	152	19,572	7.77	1.00	Referent
Second	1,887	181	19,786	9.15	1.11	0.88, 1.41
Third	1,709	188	16,999	11.06	1.11	0.86, 1.42
Fourth	1,797	236	17,155	13.76	1.20	0.88, 1.63
P for trend					0.12	
All-cause mortality						
Prediagnosis BMI category[c]						
Underweight	213	63	2,328	27.06	1.47	1.14, 1.91
Normal weight	5,332	1,130	59,094	19.12	1.00	Referent
Overweight	3,401	820	37,687	21.76	0.98	0.89, 1.07
Obese	1,576	467	16,832	27.75	1.09	0.97, 1.22
Severely obese	553	162	5,789	27.98	1.10	0.93, 1.31
Morbidly obese	276	102	2,768	36.85	1.41	1.14, 1.75
P for trend					0.04	
P for linearity					0.004	

Table continues

cancer–specific mortality (HR range = 1.26–1.43) and all-cause mortality (HR range = 1.19–1.33) (2, 32), and that the associations may be U- or J-shaped (33). However, finer categories of obesity were not examined in these analyses. In a 2011 pooled analysis of 14,948 breast cancer survivors (34), both underweight women (HR = 1.33, 95% CI: 0.92, 1.92) and morbidly obese women (HR = 1.40, 95% CI: 1.00, 1.96) had the greatest risks of breast cancer–specific mortality compared with normal-weight women, and the associations with all-cause mortality were even stronger.

We know of only 3 studies to date that have examined BMI and mortality after breast cancer diagnosis by race/ethnicity (35–37), 2 of which are included in our analyses (35, 36). No significant racial/ethnic differences of BMI and mortality were found in the MEC, which included an equal number of women from sites in Hawaii and California. However,

Table 3. Continued

Measurement by Mortality Type	No. of Exposed	No. of Outcomes	Person-years	Rate per 1,000 Person-years	Fully Adjusted HR[a,b]	95% CI
Waist-hip ratio, quartile[d]						
First (<0.763)	1,430	240	16,410	14.63	1.00	Referent
Second (0.763–<0.814)	1,437	267	15,536	17.19	1.00	0.83, 1.21
Third (0.814–<0.867)	1,422	331	14,640	22.61	1.06	0.88, 1.28
Fourth (≥0.867)	1,431	446	14,650	30.44	1.30	1.07, 1.57
P for trend					0.001	
Waist-height ratio, quartile[d]						
First (<0.467)	1,795	289	19,977	14.47	1.00	Referent
Second (0.467–<0.521)	1,795	348	18,844	18.47	0.99	0.83, 1.17
Third (0.521–<0.587)	1,786	397	17,764	22.35	0.98	0.81, 1.17
Fourth (≥0.587)	1,804	490	16,810	29.15	1.00	0.81, 1.25
P for trend					0.08	
Waist circumference, quartile[d]						
First (<29.8 cm)	1,798	293	19,572	14.97	1.00	Referent
Second (29.8–<33.0 cm)	1,887	361	19,786	18.25	1.05	0.89, 1.24
Third (33.0–<37.1 cm)	1,709	402	16,999	23.65	1.06	0.88, 1.27
Fourth (≥37.1 cm)	1,797	475	17,155	27.69	1.06	0.86, 1.32
P for trend					0.09	

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.

[a] Cox models with attained age as time scale and study as a stratification variable. Minimally adjusted models included age at breast cancer diagnosis, log of age at breast cancer diagnosis, and American Joint Committee on Cancer stage. Fully adjusted models also included race/ethnicity, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, hormone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity.

[b] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

[c] Prediagnosis BMI (weight (kg)/height $(m)^2$) is in the following World Health Organization BMI categories: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), severely obese (35.0–39.9), and morbidly obese (≥40).

[d] Includes only women with waist, hip, and/or height measurements. Models also adjusted for prediagnosis BMI and indicator of prediagnosis versus postdiagnosis waist-hip ratio, weight-height ratio, or waist circumference measurement.

consistent with our results, a suggestive elevated risk of breast cancer–specific mortality among obese Asian Americans was noted (HR = 1.51, 95% CI: 0.52, 4.44). In the expanded CARE Study (based on all 5 study sites, not just Los Angeles County, California), an elevated risk of all-cause mortality was found among non-Latina white women (HR = 1.54, 95% CI: 1.21, 1.96) but not among African American women (HR = 1.03, 95% CI: 0.81, 1.29; *P* for homogeneity of trends = 0.03) (36).

BMI reflects the relationship of weight to height and does not completely capture the between-individual variation in total adiposity (38). Few studies have examined the association of body fat distribution as measured by WHR with breast cancer survival in racial/ethnic minority populations. Three studies found an association of greater WHR with worse survival in primarily white premenopausal (39, 40) or postmenopausal (41) patients, whereas another study in Shanghai, China, found no association of WHR or waist circumference with survival (42).

Ours is one of the first studies to report differences in the association between BMI, WHR, and mortality in the major US racial/ethnic groups. These findings most likely reflect the underlying heterogeneity of body composition for each racial/ethnic group. When considering differences in body composition for survival studies, BMI might not be the most accurate adiposity measure in Asian Americans and perhaps in African Americans. Indeed, our observation of higher breast cancer–specific and/or all-cause mortality associated with high WHR in only these 2 racial/ethnic groups supports this notion and underscores the importance of using the most appropriate measurement to assess weight and adiposity by race/ethnicity.

Several biological mechanisms have been proposed to underlie the effects of obesity on breast cancer outcomes (43, 44), including higher circulating estrogens in obese (compared with nonobese) postmenopausal women (45, 46), increases in insulin and insulinlike growth factors involved in the regulation of normal and malignant growth of epithelial breast cells (47, 48), and adipose tissue as an important endocrine organ that secretes obesity-related regulatory proteins (adipokines) (49–51). It is unclear why our analysis suggests a possible threshold effect by obesity level. We hypothesize that larger amounts of adipose tissue in the morbidly obese

Table 4. Associations of BMI[a] and Breast Cancer–Specific Mortality by Race/Ethnicity[b] in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

BMI Measurement	Non-Latina White			African American			Asian American			Latina		
	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI
Prediagnosis BMI (WHO category)[e]												
Underweight	16	1.91	1.14, 3.20	6	0.70	0.28, 1.74	10	1.87	0.85, 4.10	2	1.40	0.33, 5.92
Normal weight	292	1.00	Referent	139	1.00	Referent	88	1.00	Referent	78	1.00	Referent
Overweight	181	1.12	0.92, 1.35	125	0.82	0.63, 1.06	45	1.31	0.87, 1.98	75	0.90	0.64, 1.27
Obese	81	1.34	1.03, 1.75	94	0.86	0.65, 1.16	14[f]	1.53	0.81, 2.89	49	1.01	0.68, 1.52
Severely obese	31	1.09	0.73, 1.61	32	0.81	0.53, 1.24				17	0.94	0.53, 1.68
Morbidly obese	16	1.43	0.84, 2.43	28	1.06	0.67, 1.66				17	2.26	1.23, 4.15
P for trend			0.21			0.76			0.14			0.34
P for linearity			0.10			0.48			0.25			0.19
Prediagnosis BMI decile												
First (<17.5)	8	3.37	1.59, 7.15	2	1.09	0.24, 4.94	4	1.14	0.25, 5.15	1	2.17	0.27, 17.39
Second (17.5–19.9)	44	1.05	0.73, 1.50	13	0.71	0.38, 1.34	15	0.99	0.52, 1.89	8	1.49	0.66, 3.36
Third (20.0–22.4)	122	1.00	0.77, 1.28	53	1.17	0.80, 1.72	37	0.88	0.54, 1.43	27	1.22	0.72, 2.04
Fourth (22.5–24.9)	134	1.00	Referent	77	1.00	Referent	42	1.00	Referent	44	1.00	Referent
Fifth (25.0–27.4)	112	1.20	0.92, 1.55	78	0.90	0.65, 1.26	25	0.91	0.53, 1.56	48	1.04	0.67, 1.61
Sixth (27.5–29.9)	69	1.00	0.74, 1.36	47	0.77	0.52, 1.13	20	2.11	1.15, 3.88	27	0.88	0.53, 1.47
Seventh (30.0–32.4)	54	1.34	0.96, 1.87	51	0.78	0.54, 1.15	14[f]	1.47	0.74, 2.89	35	1.19	0.73, 1.96
Eighth (32.5–34.9)	27	1.33	0.87, 2.04	43	1.06	0.70, 1.58				14	0.93	0.49, 1.76
Ninth (35.0–37.4)	18	1.05	0.63, 1.75	20	1.03	0.60, 1.75				11	1.10	0.53, 2.27
Tenth (≥37.5)	29	1.27	0.83, 1.93	40	0.89	0.58, 1.35				23	1.71	0.97, 3.00
P for trend			0.21			0.76			0.14			0.34
P for linearity			0.15			0.53			0.22			0.65

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; WHO, World Health Organization.

[a] Weight (kg)/height $(m)^2$.

[b] *P* for homogeneity of BMI trend across racial/ethnic groups <0.001.

[c] Cox models with attained age as the time scale and study as a stratification variable. Adjusted for age at breast cancer diagnosis, log of age at breast cancer diagnosis, American Joint Committee on Cancer stage, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, hormone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity.

[d] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

[e] Prediagnosis BMI is in the following WHO BMI categories: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), severely obese (35.0–39.9), and morbidly obese (≥40).

[f] For Asian Americans, the categories of obese, severely obese, and morbidly obese were combined into 1 category representing BMI of 30 or more.

Table 5. Associations of BMI[a] and All-Cause Mortality by Race/Ethnicity[b] in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

BMI Measurement	Non-Latina White			African American			Asian American			Latina		
	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI	No. of Outcomes	HR[c,d]	95% CI
Prediagnosis BMI (WHO category)[e]												
Underweight	35	1.72	1.22, 2.44	11	1.06	0.55, 2.04	12	1.36	0.71, 2.61	5	1.82	0.72, 4.63
Normal weight	643	1.00	Referent	214	1.00	Referent	147	1.00	Referent	113	1.00	Referent
Overweight	382	1.00	0.88, 1.14	227	0.87	0.72, 1.07	72	1.12	0.82, 1.54	134	0.97	0.74, 1.26
Obese	186	1.21	1.01, 1.43	160	0.88	0.70, 1.10	23[f]	1.37	0.85, 2.21	99	1.08	0.80, 1.46
Severely obese	64	1.13	0.86, 1.48	62	0.95	0.70, 1.29				35	1.29	0.86, 1.94
Morbidly obese	33	1.61	1.12, 2.31	41	1.02	0.71, 1.47				27	1.93	1.21, 3.10
P for trend			0.08			0.83			0.50			0.02
P for linearity			0.009			0.61			0.27			0.27
Prediagnosis BMI decile												
First (<17.5)	11	2.04	1.10, 3.79	4	1.47	0.52, 4.19	6	1.68	0.61, 4.61	1	1.48	0.19, 11.30
Second (17.5–19.9)	99	1.15	0.91, 1.45	23	0.87	0.54, 1.39	28	1.18	0.73, 1.91	14	1.75	0.95, 3.26
Third (20.0–22.4)	263	0.99	0.84, 1.17	78	1.10	0.81, 1.49	59	0.94	0.64, 1.37	38	1.00	0.66, 1.52
Fourth (22.5–24.9)	305	1.00	Referent	120	1.00	Referent	66	1.00	Referent	65	1.00	Referent
Fifth (25.0–27.4)	240	1.00	0.84, 1.19	129	0.88	0.68, 1.14	44	0.96	0.64, 1.45	77	1.01	0.71, 1.43
Sixth (27.5–29.9)	142	1.01	0.82, 1.24	98	0.90	0.68, 1.20	28	1.58	0.97, 2.58	57	0.98	0.67, 1.42
Seventh (30.0–32.4)	118	1.15	0.92, 1.44	87	0.80	0.60, 1.07	23[f]	1.38	0.82, 2.30	66	1.12	0.78, 1.63
Eighth (32.5–34.9)	68	1.32	1.00, 1.73	73	1.03	0.75, 1.40				33	1.09	0.70, 1.69
Ninth (35.0–37.4)	35	1.00	0.70, 1.43	40	1.10	0.75, 1.61				20	1.27	0.74, 2.16
Tenth (≥37.5)	62	1.47	1.11, 1.95	63	0.93	0.67, 1.29				42	1.73	1.13, 2.64
P for trend			0.08			0.83			0.50			0.02
P for linearity			0.12			0.56			0.31			0.49

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; WHO, World Health Organization.

[a] Weight (kg)/height (m)2.

[b] *P* for homogeneity of BMI trend across racial/ethnic groups <0.001.

[c] Cox models with attained age as the time scale and study as a stratification variable. Adjusted for age at breast cancer diagnosis, log of age at breast cancer diagnosis, American Joint Committee on Cancer stage, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, hormone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity.

[d] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

[e] Prediagnosis BMI is in the following WHO BMI categories: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), severely obese (35.0–39.9), and morbidly obese (≥40).

[f] For Asian Americans, the categories of obese, severely obese, and morbidly obese were combined into 1 category representing BMI of 30 or more.

Table 6. Associations of Central Adiposity Measurements and Breast Cancer–Specific Mortality by Race/Ethnicity in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Central Adiposity Measurement	Non-Latina White			African American			Asian American			Latina		
	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI
Waist-hip ratio, quartile												
First (<0.763)	89	1.00	Referent	14	1.00	Referent	28	1.00	Referent	18	1.00	Referent
Second (0.763–<0.814)	61	0.73	0.50, 1.05	16	0.87	0.34, 2.23	40	1.63	0.94, 2.83	31	1.84	0.92, 3.68
Third (0.814–<0.867)	56	0.64	0.43, 0.96	33	1.20	0.50, 2.86	35	1.09	0.62, 1.93	41	1.43	0.72, 2.81
Fourth (≥0.867)	72	0.89	0.59, 1.33	40	1.59	0.69, 3.66	37	2.21	1.21, 4.03	42	1.50	0.73, 3.09
P for trend		0.69			0.40			0.01			0.21	
P for homogeneity						<0.001						
Waist-height ratio, quartile												
First (<0.467)	94	1.00	Referent	8	1.00	Referent	36	1.00	Referent	17	1.00	Referent
Second (0.467–<0.521)	92	1.00	0.72, 1.38	10	0.37	0.10, 1.34	41	0.97	0.58, 1.63	20	0.94	0.45, 1.99
Third (0.521–<0.587)	81	0.74	0.51, 1.08	39	0.91	0.29, 2.83	43	1.47	0.81, 2.68	27	0.64	0.29, 1.39
Fourth (≥0.587)	98	0.93	0.59, 1.47	53	1.10	0.33, 3.71	22	1.64	0.71, 3.80	68	0.95	0.42, 2.15
Waist circumference, quartile												
First (<29.8 cm)	78	1.00	Referent	8	1.00	Referent	46	1.00	Referent	19	1.00	Referent
Second (29.8–<33.0 cm)	93	1.07	0.77, 1.50	12	0.31	0.08, 1.16	48	1.37	0.84, 2.23	25	0.97	0.47, 2.01
Third (33.0–<37.1 cm)	94	0.98	0.68, 1.41	30	0.53	0.17, 1.73	34	1.68	0.91, 3.12	30	0.87	0.41, 1.82
Fourth (≥37.1 cm)	102	1.01	0.65, 1.56	60	0.69	0.20, 2.41	14	1.63	0.67, 3.97	58	0.98	0.44, 2.21

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Cox models with attained age as the time scale and study as a stratification variable. Adjusted for age at breast cancer diagnosis, log of age at breast cancer diagnosis, American Joint Committee on Cancer stage, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, hormone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity, prediagnosis body mass index (weight (kg)/height $(m)^2$), and indicator of prediagnosis versus postdiagnosis waist-hip ratio, waist-height ratio, or waist circumference measurement.

[b] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

Table 7. Associations of Central Adiposity Measurements and All-Cause Mortality by Race/Ethnicity in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Central Adiposity Measurement	Non-Latina White			African American			Asian American			Latina		
	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI	No. of Outcomes	HR[a,b]	95% CI
Waist-hip ratio, quartile												
First (<0.763)	156	1.00	Referent	17	1.00	Referent	42	1.00	Referent	25	1.00	Referent
Second (0.763–<0.814)	140	0.96	0.75, 1.24	28	0.99	0.47, 2.08	54	1.07	0.69, 1.67	43	1.21	0.69, 2.13
Third (0.814–<0.867)	153	0.96	0.74, 1.25	51	1.18	0.60, 2.33	60	0.99	0.63, 1.55	67	1.06	0.61, 1.81
Fourth (≥0.867)	214	1.08	0.83, 1.41	85	2.19	1.15, 4.19	58	1.64	1.02, 2.63	86	1.25	0.72, 2.17
P for trend		0.24			0.01			0.02			0.21	
P for homogeneity						<0.001						
Waist-height ratio, quartile												
First (<0.467)	196	1.00	Referent	14	1.00	Referent	55	1.00	Referent	21	1.00	Referent
Second (0.467–<0.521)	230	1.04	0.84, 1.30	20	0.47	0.20, 1.12	62	0.87	0.58, 1.32	33	0.80	0.43, 1.51
Third (0.521–<0.587)	214	0.96	0.76, 1.22	64	0.77	0.35, 1,70	68	1.18	0.73, 1.90	47	0.53	0.28, 1.00
Fourth (≥0.587)	236	1.01	0.76, 1.36	92	0.76	0.32, 1.80	36	1.04	0.54, 2.01	125	0.65	0.33, 1.28
Waist circumference, quartile												
First (<29.8 cm)	177	1.00	Referent	14	1.00	Referent	74	1.00	Referent	26	1.00	Referent
Second (29.8–<33.0 cm)	231	1.09	0.88, 1.36	21	0.48	0.20, 1.16	66	1.01	0.69, 1.49	39	0.73	0.40, 1.32
Third (33.0–<37.1 cm)	236	1.14	0.90, 1.44	50	0.50	0.22, 1.14	59	1.28	0.80, 2.06	54	0.60	0.33, 1.09
Fourth (≥37.1 cm)	239	1.07	0.81, 1.43	105	0.64	0.27, 1.53	22	1.01	0.50, 2.02	107	0.72	0.38, 1.36

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Cox models with attained age as the time scale and study as a stratification variable. Adjusted for age at breast cancer diagnosis, log of age at breast cancer diagnosis, American Joint Committee on Cancer stage, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, hormone receptor status, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity, prediagnosis body mass index (weight (kg)/height $(m)^2$), and indicator of prediagnosis versus postdiagnosis waist-hip ratio, waist-height ratio, or waist circumference measurement.

[b] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

Table 8. Associations of Body Size Measurements and Breast Cancer Mortality by ER/PR Status in Women in the California Breast Cancer Survivorship Consortium, 1993–2009

Body Size Measurement	ER+ and PR+			ER+ or PR+			ER− and PR−		
	No. of Deaths	HR[a,b]	95% CI	No. of Deaths	HR[a,b]	95% CI	No. of Deaths	HR[a,b]	95% CI
Prediagnosis BMI[c]									
Underweight	18	1.46	0.85, 2.49	5	1.89	0.69. 5.13	5	1.26	0.50, 3.17
Normal weight	253	1.00	Referent	79	1.00	Referent	159	1.00	Referent
Overweight	176	1.12	0.92, 1.38	58	1.18	0.80, 1.76	121	0.91	0.70, 1.17
Obese	94	1.04	0.80, 1.35	35	2.03	1.24, 3.33	66	0.97	0.70, 1.35
Severely obese	42	1.26	0.89, 1.80	10	1.84	0.87, 3.91	14	0.71	0.40, 1.26
Morbidly obese	25	1.18	0.76, 1.84	8	3.24	1.30, 8.08	16	1.37	0.77, 2.41
P for interaction					0.30				
Waist-hip ratio, quartile[d]									
First (<0.763)	66	1.00	Referent	29	1.00	Referent	36	1.00	Referent
Second (0.763–<0.814)	63	0.96	0.65, 1.40	23	0.85	0.42, 1.75	43	1.27	0.75, 2.16
Third (0.814–<0.867)	81	1.23	0.84, 1.78	23	0.48	0.22, 1.03	35	0.71	0.39, 1.28
Fourth (≥0.867)	89	1.48	1.00, 2.20	28	0.52	0.23, 1.19	44	1.09	0.60, 1.99
P for interaction					0.22				

Abbreviations: CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor.

[a] Cox models with attained age as the time scale and study as a stratification variable. Adjusted for age at breast cancer diagnosis, log of age at breast cancer diagnosis, American Joint Committee on Cancer stage, education, neighborhood socioeconomic status, place of birth, marital status, menopausal status, age at first birth, smoking history, alcohol intake, nodal positivity, tumor grade, tumor size, prior cancer history, surgery type, chemotherapy, radiation therapy, hormonal therapy, and comorbidity.

[b] Follow-up to death or end of follow-up (the earlier of the last follow-up date in the California Cancer Registry or December 31, 2009), whichever occurred first.

[c] Prediagnosis body mass index (weight (kg)/height $(m)^2$) is in the following World Health Organization body mass index categories: underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), severely obese (35.0–39.9), and morbidly obese (≥40).

[d] Includes only women with waist and hip measurements. Models also adjusted for prediagnosis body mass index and indicator of prediagnosis versus postdiagnosis waist-hip ratio, waist-height ratio, or waist circumference measurement.

compared with the moderately obese might create a more heightened, constant imbalance in obesity-related regulatory proteins and inflammatory cytokines. Furthermore, from the treatment perspective, obese women may be underdosed for chemotherapy because of toxicity-related concerns, resulting in reduced therapeutic response and worse outcomes (52–54). Although we did observe treatment differences by race/ethnicity and BMI in our cohort, adjustment for treatment modalities in our survival models did not substantially change the hazard ratios and 95% confidence intervals. A recent Surveillance Epidemiology and End Results–Medicare study also found that treatment differences explained few of the survival differences between non-Latina white and African American breast cancer patients aged 65 years and older, yet, similar to a limitation of our study, details of chemotherapy administration and hormonal therapy were not incorporated (55, 56). Thus, further investigation of treatment differences is warranted.

Few studies have considered the biological mechanisms underlying associations of being underweight and having worse breast cancer outcomes. Underweight could be an indicator of preexisting comorbid conditions that have already placed these women at greater risk of poor outcomes (4). Although we adjusted for 3 common comorbid conditions (diabetes, hypertension, and myocardial infarction) and our mortality estimates did not differ by comorbidity, residual confounding by other unmeasured comorbidities is possible. In a sensitivity analysis, we excluded deaths that occurred during the first 2 years after study enrollment, and elevated mortality risks remained in the underweight group for breast cancer–specific and all-cause mortality (HR = 1.4).

Strengths of this study include being the largest to date of racially and ethnically diverse breast cancer survivors, resulting in adequate power to examine potential associations of adiposity with mortality while adjusting for most known prognostic and treatment-related factors. Limitations were self-reported prediagnosis weight (yet substantial agreement between self-reported and measured weight has been shown (57)) and a lack of information on recurrent disease and associated treatments.

In conclusion, this large, multiethnic study confirms the overall association of obesity with mortality after breast cancer diagnosis, but the degree of obesity and body fat distribution at breast cancer diagnosis appear to have differential effects on mortality across racial/ethnic groups. BMI as a function of weight and height might better reflect a relationship to survival among non-Latina whites and Latinas, whereas WHR, a measure of central adiposity, may be a better index of obesity in relationship to survival among Asian Americans and perhaps African Americans. Future studies of racial/ethnic minorities and survival in breast cancer patients should incorporate multiple measurements of obesity to tease apart racial/ethnic differences in body composition and mortality.

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