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Central adiposity after breast cancer diagnosis is related to mortality in the Health, Eating, Activity, and Lifestyle study

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Abstract

We examined whether waist circumference (WC) and waist-to-hip ratio (WHR) after breast cancer diagnosis are associated with all-cause or breast cancer-specific mortality and explored potential biological pathways mediating these relationships. Our analysis included 621 women diagnosed with local or regional breast cancer who participated in the Health, Eating, Activity, and Lifestyle study. At 30 (± 4) months postdiagnosis, trained staff measured participants' waist and hip circumferences and obtained fasting serum samples for biomarker assays for assays of insulin, glucose, C-peptide, insulin growth factor-1 and binding protein-3, C-reactive protein (CRP), and adiponectin. We estimated multivariate hazard ratios (HR) and 95 % confidence intervals (CI) for death over ~ 9.5 years of follow-up. After adjustment for measured body mass index, treatment,

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comorbidities, race/ethnicity, diet quality, and postdiagnosis physical activity, WC was positively associated with all-cause mortality ($HR_{q4:q1}$: 2.99, 95 % CI 1.14, 7.86) but its positive association with breast cancer-specific mortality was not statistically significant ($HR_{q4:q1}$: 2.69, 95 % CI 0.69, 12.01). WHR was positively associated with all-cause mortality ($HR_{q4:q1}$: 2.10, 95 % CI 1.08, 4.05) and breast cancer-specific mortality ($HR_{q4:q1}$: 4.02, 95 % CI 1.31, 12.31). After adjustment for homeostatic model assessment (HOMA) score and C-reactive protein, risk estimates were attenuated and not statistically significant. In this diverse breast cancer survivor cohort, postdiagnosis WC and WHR were associated with all-cause mortality. Insulin resistance and inflammation may mediate the effects of central adiposity on mortality among breast cancer patients.

Keywords

Central obesity; Breast cancer; Mortality; Insulin resistance; Inflammation

Introduction

It is estimated that 232,670 women will be newly diagnosed with invasive breast cancer in 2014 in the United States (US) [1], adding to the 2.5 million women already living with a personal history of breast cancer, and making this group of cancer survivors the largest and fastest growing in the country [2, 3]. Obesity presents an additional clinical and public health challenge for breast cancer survivors; accumulating evidence has shown that obesity may influence the course of breast cancer, as well as morbidity and mortality after treatment concludes [4]. In clinical practice and epidemiological studies, obesity is most commonly assessed using body mass index (BMI), defined as weight in kilograms divided by height in meters squared. However, while importantly linked to adverse outcomes after cancer, such as mortality [5], BMI does not discriminate abdominal obesity (e.g., central or visceral adiposity) from overall obesity [6]. Waist circumference (WC) and waist-to-hip ratio (WHR) are the most common clinical measures of body fat distribution [7]. Abdominal fat has been shown to vary considerably within a narrow range of body mass index [7] has been independently associated with mortality in the general population [8], and its study among breast cancer survivors could inform our understanding further of the health consequences of obesity.

However, it is difficult to synthesize the mixed results from the few population studies of breast cancer survivors that have examined the relationship between central adiposity and survival after breast cancer, because timing (prediagnosis, at diagnosis, or postdiagnosis) and assessment method (self, trained staff) have varied among studies, and none of these studies have controlled for postdiagnosis BMI to best separate out the independent contribution of the location of body fat on mortality risk. Further, to our knowledge among breast cancer survivors, no studies have controlled for physical activity, which may be a strong confounder of the relationship between obesity and survival. To inform the design of weight loss programs in breast cancer survivors, systematic research is needed to examine how and if abdominal obesity after diagnosis independently predicts survival.

Thus, in the Health, Eating, Activity, and Lifestyle (HEAL) study, we investigated the associations of WC and WHR and all-cause and breast cancer-specific mortality. In a subsample (90 %), we also examined potential biological pathways [4] through which central adiposity might be related to survival.

Methods

The HEAL study is a multiethnic prospective cohort study that has enrolled 1,183 women with first primary breast cancer drawn from Surveillance, Epidemiology, and End Results (SEER) population-based cancer registries in New Mexico, Los Angeles County, and Western Washington. The study was designed to determine whether lifestyle, hormones, or other exposures affect breast cancer prognosis. Details of the study have been published [9–11]. Written informed consent was obtained from all study participants at each assessment, and the study was approved by the institutional review board at each participating center, in accord with assurances filed with and approved by the US Department of Health and Human Services.

Briefly, in New Mexico, we recruited 615 women aged 18 years or older, diagnosed with in situ to regional breast cancer between July 1996 and March 1999, and living in Bernalillo, Santa Fe, Sandoval, Valencia, or Taos counties. In Western Washington, we recruited 202 women between ages 40 and 64 years, diagnosed with in situ to regional breast cancer between September 1997 and September 1998, and living in King, Pierce, or Snohomish counties. The age range for the Washington patients was restricted due to other ongoing breast cancer studies. In Los Angeles County, we recruited 366 black women diagnosed with in situ to regional breast cancer between May 1995 and May 1998 who had participated in the Los Angeles portion of the Women's Contraceptive and Reproductive Experiences (CARE) study or who had participated in a parallel case-control study of in situ breast cancer. The women's CARE study restricted eligibility to women ages 35–64 years at diagnosis.

Of the 1183 women in the HEAL study, 944 were alive at the time of the in—person anthropometric assessment at study centers, and we excluded women who had a second primary or recurrent breast cancer before this assessment ($n = 57$). We further excluded those with in situ breast cancer ($n = 197$) due to their low risk for mortality [12], those missing any anthropometric measurement ($n = 56$), missing diet data ($n = 10$), and those lost to follow-up at the time of the anthropometric assessment ($n = 3$). Our final sample included 621 women.

Outcome assessment

Our primary and secondary outcomes were death from any cause and death from breast cancer. Information on vital status was obtained from Surveillance, Epidemiology, and End Results (SEER) cancer registries. Cause of death codes was acquired from linkages with the relevant SEER database, which obtains data from state and national death certificate files and the Social Security Death Index. Individuals were followed until death or December 31, 2010, the last SEER vital status update, whichever was the most recent. The mean follow-up

time from the 30-month anthropometric assessment through December 31, 2010 was 9.5 years, and during this time, 107 deaths occurred.

Anthropometric measurements

Around 30-month postdiagnosis, anthropometric measurements were conducted by trained staff using a standardized protocol with the participants' wearing light indoor clothing or a hospital gown without shoes [13]. With the woman standing, waist and hip circumferences were measured to the nearest 0.1 cm for New Mexico and California participants and to the nearest 0.5 cm for Washington participants. Height was measured to the nearest 0.02 cm using a wall-mounted stadiometer, and weight was measured to the nearest 0.01 kg with a calibrated-beam balance scale. Measuring equipment was calibrated regularly. All measurements were taken twice, and the averages were used. BMI was calculated as weight (kg)/ height (m²) and was categorized as (<18.5; 18.5–24.9; 25–29.9; 30–34.9; 35 +).

Additional risk factors

At baseline (on average, 6 months postdiagnosis), information on age and race/ethnicity was collected. For participants' breast cancer diagnoses, detailed information on cancer treatment and surgical procedures was obtained from cancer registry, physician, and hospital records. Adjuvant treatment was categorized into four groups: surgery only, surgery and radiation, surgery and chemotherapy, or surgery, radiation, and chemotherapy. At 30-months postdiagnosis, participants reported physician-diagnosed medical conditions and whether any of their current activities of daily living were limited by any of these conditions. A comorbidity summary score was generated based on the number of activity-limiting comorbidities.

Physical activity and diet were both assessed at 30-months postdiagnosis. Participants completed the Modifiable Activity Questionnaire, developed by Kriska et al. [14], which assessed various types and intensities of physical activity reported at the 3-year follow-up interview. For these analyses, metabolic equivalent hours per week (MET-h/wk) of sports/recreational activities were included as a covariate in the analyses (0, 0.1–8.9, 9+ MET-h/wk) given how strongly this domain of postdiagnosis physical activity was related to survival in the HEAL study [15]. Participants also completed a 122-item self-administered food-frequency questionnaire developed and validated for the Women's Health Initiative (WHI) [16], adapted from the Health Habits and Lifestyle Questionnaire [17]. We scored diet quality using the Healthy Eating Index-2005 [18–21] which aligns with US Dietary Guidelines for Americans [22] by establishing a customized link [23] between the nutrient database used to analyze the WHI-FFQ (Nutrition Data Systems for Research, NDS-R, version 2005, University of Minnesota, Minneapolis, MN) [24, 25] and the MyPyramid Equivalents Database [26].

Serum biomarkers

A 30 mL 12-hour fasting blood sample was collected from participants at the 30-month assessment. Blood was processed within 3 h of collection, and serum was stored in 1.8 mL tubes at –70 to –80 °C until analysis.

Insulin was measured using the Beckman Coulter Unicel DxI Access Ultrasensitive Insulin assay (Beckman, Fullerton, CA), and glucose with the Beckman Synchron DxC system, (Beckman, Fullerton, CA). CRP and SAA were measured by latex-enhanced nephelometry using high-sensitivity assays [27] on the Behring Nephelometer II analyzer (Dade Behring Diagnostics, Deerfield, IL) at the University of Washington Medical Center (Seattle, WA). Adiponectin was measured using a highly sensitive radioimmunoassay (RIA) (Linco Research, St. Charles, MI) at the Northwest Research Lipid Laboratories at the University of Washington. C-peptide, IGF-1, and IGFBP-3 were measured using high sensitivity RIAs (C-peptide: Incstar, Stillwater, MN; IGFs: Nichols Institute Diagnostics, San Clemente, CA). C-peptide, IGF-1, and IGFBP-3 were analyzed at the University of Southern California for California participants and at the University of New Mexico for the other two sites.

All samples were randomly assigned to assay batches and randomly ordered within each batch. Personnel performing the assays were blinded to participants' identity and characteristics. Intra-assay coefficients of variation were as follows: 2.8 % (insulin); 7.5 % (glucose); 16.7 % (adiponectin); 5.6–10.5 % (C-peptide); 6.2 % (IGF-1); and 3.5–14 % (IGFBP-3). The inter-assay coefficient of variation for CRP was 5–9 %. We calculated homeostatic model assessment score (HOMA) as $[(\text{insulin}) * (\text{glucose} * 10 / 180)] / 22.5$ and the ratio of IGF-1 to IGFBP3.

Statistical analysis

Means, standard errors, and frequencies of demographic, clinical, and lifestyle characteristics were calculated by quartiles of WC and WHR. Cox proportional hazards models were fit using age as the underlying time metric. We estimated multivariate hazard ratios (HR) and 95 % confidence intervals (CI) for death from any cause associated with increasing quartiles of WC and WHR. We included covariates that improved model fit and changed the magnitude of the HR by 10 % or more: measured BMI; cancer treatment; number of activity-limiting comorbidities; race/ethnicity; Healthy Eating Index 2005 score quartiles; and recreational physical activity. BMI was included in all models to determine the additional mortality risk conferred by central adiposity. Multivariate models are presented with and without physical activity included in the model to investigate the impact of adjustment for physical activity on risk estimates. Additional adjustment for smoking, marital status, menopausal status, HRT, education, alcohol, and current use of tamoxifen had little effect on the magnitude of risk estimates.

We also examined how hazard ratios and statistical significance of models changed, when biomarkers shown to be associated with survival in the HEAL study (C-peptide [28], adiponectin [29], HOMA [29], IGF-1/IGFBP-3 [30], CRP [31]) were entered as quartiles into multivariate models.

All statistical analyses were conducted using SAS (version 9.3., Cary, NC). All tests were two-sided, and a $p < 0.05$ was considered statistically significant.

Results

Women in the highest quartiles of WC and WHR were older, had lower quality diets, less physical activity after diagnosis, higher BMIs, more activity-limiting comorbidities, and were more likely to be African-American (Table 1). As shown in Table 2, after adjustment for measured BMI, treatment, comorbidities, race/ethnicity, diet quality, and physical activity, higher WC was positively associated with all-cause mortality ($HR_{q4:q1}$: 2.99, 95 % CI 1.14, 7.86), but its association with breast cancer-specific mortality was similarly increased but not statistically significant ($HR_{q4:q1}$: 2.69, 95 % CI 0.69, 12.01). Higher WHR was positively associated with all-cause mortality ($HR_{q4:q1}$: 2.10, 95 % CI 1.08, 4.05) and breast cancer mortality ($HR_{q4:q1}$: 4.02, 95 % CI 1.31, 12.31) (Table 3). Inclusion of physical activity in the models attenuated risk estimates by 3–17 %, with the exception of the association of WHR with all-cause mortality.

After adjustment for CRP and HOMA, risk estimates were attenuated for WC by 14–29 % and WHR by 1–11 % and were no longer statistically significant (Table 2; Table 3). Adjustment for adiponectin attenuated hazard ratios by 3–19 % except for the association of WHR with all-cause mortality; this adjustment only affected the statistical significance for the model assessing the association of WC with all-cause mortality. Adjustment for C-peptide or IGF-1/IGFBP-3 did not affect model significance.

Discussion

In this large cohort of early-stage breast cancer survivors, Women with a higher WC had a threefold increased risk of all-cause mortality, and those with a higher WHR had a twofold increased risk of all-cause mortality and a fourfold increased risk of breast cancer mortality. While WC and WHR appear to be linearly related with mortality after breast cancer, it is important to note that the statistically significant risk of any death associated with WC started in Q4 (>99 cm) and with WHR started with Q3 (ratio = 0.83) in our study. For women in the general population, for preventing disease burden, the cut points of WC >88 cm [32] or WHR >0.85 [7] have been suggested in public health recommendations as indicating a hazardous level of abdominal obesity. However, little research has been done to determine levels of WC and WHR that result in adverse mortality risk among survivors, given a certain BMI level. In future larger studies are needed to confirm and expand upon our findings to better define the levels of WC and WHR at which mortality risk increases.

Our study is the first, to our knowledge, to report evidence on potential pathways connecting central adiposity to survival after breast cancer. Our results suggest that some of the association between postdiagnosis WC and overall mortality, and possibly breast cancer mortality, is due to mediation by insulin resistance and inflammation. These pathways are biologically plausible to explain some of the association between abdominal obesity and mortality. Increased visceral adipose tissue is associated with a range of metabolic abnormalities, including decreased glucose tolerance, reduced insulin sensitivity, increased chronic inflammation, and increased adipose-derived cytokines and hormones, all of which have been implicated as potential pathways by which obesity may affect survival after cancer [4]. Potential mediation by the biomarkers examined was less evident for WHR. We

did not find evidence of mediation by IGF-1/IGFBP3 or by C-peptide, although these pathways could still have an independent, possibly additive association. Future studies with the ability to examine the effects of changes in WC and WHR on these biomarkers among breast cancer survivors could shed light on the strength of these potential mechanisms.

This study builds on our previous work in HEAL demonstrating a positive association between sarcopenia and all-cause mortality [33] and suggests that in addition to skeletal muscle mass, the location of body fat mass may be important for determining risk of mortality. Our study is consistent with WHR-all-cause mortality results in the California Breast Cancer Consortium. Although HEAL is not as large, the results from the consortium are more challenging to interpret because the central adiposity measurement timing (pre or post diagnosis) and method (by patient or trained staff) varied by study included [34]. Our study measured WC and WHR after treatment, all measurements were by trained staff, and we were also able to control for postdiagnosis BMI and physical activity. Our study is in contrast with the null findings in the Shanghai Breast Cancer Study; however, that study did not adjust for BMI or activity-related comorbidities, only examined central adiposity at diagnosis (not after treatment), and had a narrower range of central adiposity [35]. Our study is also consistent with findings among adults without cancer in the BMI and mortality pooling project which found a linear association of WC with all-cause mortality among 650,000 adults, controlling for BMI, physical activity, and other factors [8] and with findings in the EPIC study of 359,387 adults [36].

Our study had several strengths. We had extensive high-quality data on clinical characteristics and treatment abstracted from reliable sources (physician, hospital, and SEER records). Further, waist circumference, hip circumference, weight, and height were measured by trained staff, and we were able to assess potential independent effects of WC and WHR, when adjusting for BMI, thereby comprehensively examining how the location of body fat is related to mortality. Additionally, we had serum samples for 90 % of our sample enabling the first investigation among breast cancer survivors, to our knowledge, of pathways connecting central adiposity and mortality. Finally, our sample was a multiethnic cohort of women recruited from SEER-based registries.

Our study also had limitations. Although we had detailed data allowing us to carefully control for the major confounders, given the observational nature of this study, it remains possible that those with higher WC or WHR had poorer prognoses for reasons that we did not examine. Our results are only generalizable to women who have survived at least 30-months after diagnoses of breast cancer. However, as our interest was in predictors of long-term survival, measuring exposures 30-months postdiagnosis allowed us to separate out treatment effects. Last, although our analysis was well-powered to detect hazard ratios close to 3 for breast cancer mortality, given the lower number of breast cancer deaths and resulting wide confidence intervals around estimates, future large cohorts are needed to understand if measured postdiagnosis WC and WHR perform similarly in predicting breast cancer mortality.

In this racially and ethnically diverse cohort study with comprehensive data pertinent to the evaluation of energy balance and cancer outcomes, WC and WHR were positively associated

with all-cause mortality. Replication of results is warranted, but the study suggests the collection of these measures may be important for identifying survivors at increased risk of obesity-related morbidity and mortality due to the accumulation of abdominal fat. Future interventions designed to reduce postdiagnosis central adiposity can provide needed evidence on how changes in central adiposity are causally related to these biomarkers and mortality among women with breast cancer.

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Demographic, clinical, and lifestyle characteristics of 621 women in the Health, Eating, Activity, and Lifestyle study by quartiles of waist circumference and waist-to-hip ratio scores

Table 1

	Waist circumference				Waist-to-hip ratio			
	Q1 (59.4–79.5 cm)		Q4 (99.1–150 cm)		Q1 (0.64–0.77)		Q4 (0.88–1.04)	
	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)	N (%)	Mean (SE)
Number of participants	156		154		155		155	
Age		56.5 (0.8)		57.5 (0.8)		55.7 (0.8)		60.7 (0.8)
Race/ethnicity								
White, non-Hispanic	109 (70)		67 (44)		105 (68)		73 (47)	
Hispanic	17 (11)		12 (8)		13 (8)		19 (12)	
African-American, non-Hispanic	23 (15)		72 (47)		33 (21)		60 (39)	
Asian/American/Indian/other	7 (5)		3 (2)		4 (3)		3 (2)	
Treatment								
Surgery only	37 (24)		38 (25)		36 (23)		46 (30)	
+Radiation	67 (43)		45 (29)		63 (41)		54 (35)	
+Chemotherapy	15 (10)		25 (16)		16 (10)		20 (13)	
+Radiation and chemotherapy	37 (24)		46 (30)		40 (26)		35 (23)	
Activity-limiting comorbidities		0.1 (0.03)		0.9 (0.1)		0.2 (0.04)		0.7 (0.08)
HEI-2010 score (100 points possible)		68.3 (0.9)		63.7 (1.0)		69.5 (0.9)		63.5 (0.5)
MET-hours/week of postdiagnosis recreational physical activity		17.9 (2.0)		8.6 (1.3)		17.3 (0.2)		7.4 (1)
BMI		22.0 (0.2)		35.7 (0.5)		24.6 (0.4)		30.3 (0.5)

^a *p* value for Chi square test for categorical variables or trend test for continuous variables

Associations of postdiagnosis waist circumference and mortality among 621 breast cancer survivors in the Health, Eating, Activity, and Lifestyle study

Table 2

Waist circumference	Multivariate hazard ratios (95 % CI) death from any cause					Multivariate hazard ratios (95 % CI) breast cancer death				
	Q1 (59.4–79.5 cm)	Q2 (79.8–88.7 cm)	Q3 (88.8–99.0 cm)	Q4 (99.1–150.0 cm)	p trend	Q1 (59.4–79.5 cm)	Q2 (79.8–88.7 cm)	Q3 (88.8–99.0 cm)	Q4 (99.1–150.0 cm)	p trend
N	156	153	158	154		156	153	158	154	
Deaths	23	23	25	36		10	10	10	18	
Base model ^a	1.00	1.41 (0.75, 2.67)	2.01 (0.92, 4.36)	3.06 (1.16, 8.03)	0.023	1.00	1.38 (0.54, 3.53)	1.92 (0.60, 6.17)	3.22 (0.76, 13.6)	0.11
Full model ^b	1.00	1.48 (0.78, 2.81)	1.87 (0.86, 4.06)	2.99 (1.14, 7.86)	0.033	1.00	1.39 (0.54, 3.58)	1.66 (0.52, 5.35)	2.69 (0.69, 12.01)	0.145
Full model + C-peptide ^c	1.00	1.39 (0.71, 2.71)	1.78 (0.77, 4.13)	2.74 (1.00, 7.52)	0.05	1.00	1.35 (0.51, 3.59)	1.96 (0.59, 6.55)	2.89 (0.64, 13.06)	0.167
Full model + HOMA ^d	1.00	1.28 (0.66, 2.48)	1.62 (0.69, 3.80)	2.19 (0.79, 6.10)	0.133	1.00	1.31 (0.49, 3.48)	1.78 (0.51, 6.14)	2.20 (0.46, 10.49)	0.32
Full model + IGF1-BP3 ratio ^e	1.00	1.39 (0.72, 2.68)	1.77 (0.77, 4.06)	3.07 (1.13, 8.35)	0.028	1.00	1.49 (0.56, 3.93)	2.11 (0.64, 6.93)	3.39 (0.76, 15.20)	0.111
Full model + C-reactive protein ^f	1.00	1.13 (0.58, 2.22)	1.41 (0.61, 3.29)	2.13 (0.78, 5.80)	0.129	1.00	1.22 (0.45, 3.28)	1.52 (0.43, 5.38)	2.33 (0.50, 10.9)	0.276
Full model + adiponectin ^g	1.00	1.28 (0.66, 2.48)	1.58 (0.67, 3.71)	2.45 (0.90, 6.67)	0.077	1.00	1.27 (0.48, 3.39)	1.74 (0.50, 6.00)	2.56 (0.55, 11.92)	0.23

^a Adjusted for measured BMI (<18.5, 18.5–24.9, 25–29.9, 30–34.9, 35+); treatment(surgery, +radiation, +chemo, +radiation and chemo); number of activity-limiting comorbidities; race/ethnicity (non-Hispanic white, Hispanic, African-American, other); Healthy Eating Index 2005 score quartiles

^b Base model + adjustment for postdiagnosis recreational physical activity (0, 0.1–8.9, 9 + MET-h/wk)

^c Among 562 women

^d Among 546 women

^e Among 561 women

^f Among 556 women

^g Among 560 women

Associations of postdiagnosis waist-to-hip ratio and mortality among 621 breast cancer survivors in the Health, Eating, Activity, and Lifestyle study

Waist-to-hip ratio	Multivariate hazard ratios (95 % CI) death from any cause					Multivariate hazard ratios (95 % CI) breast cancer death				
	Q1 (0.64–0.77)	Q2 (0.78–0.83)	Q3 (0.83–0.88)	Q4 (0.88–1.04)	<i>p</i> trend	Q1 (0.64–0.77)	Q2 (0.78–0.83)	Q3 (0.83–0.88)	Q4 (0.88–1.04)	<i>p</i> trend
<i>N</i>	155	155	156	155		155	155	156	155	
Deaths	17	23	29	38		5	13	14	16	
Base model ^a	1.00	1.38 (0.71, 2.66)	1.93 (1.00, 3.7)	2.04 (1.06, 3.94)	0.026	1.00	3.16 (1.09, 9.17)	3.37 (1.14, 10.02)	4.31 (1.41, 13.17)	0.018
Full model ^b	1.00	1.53 (0.79, 2.95)	2.08 (1.07, 4.01)	2.10 (1.08, 4.05)	0.028	1.00	3.32 (1.14, 9.62)	3.38 (1.14, 10.02)	4.02 (1.31, 12.31)	0.029
Full model + C-peptide quartiles ^c	1.00	1.76 (0.87, 3.57)	2.67 (1.30, 5.48)	2.47 (1.20, 5.09)	0.017	1.00	3.27 (1.09, 9.82)	3.59 (1.14, 11.23)	4.19 (1.27, 13.90)	0.032
Full model + HOMA quartiles ^d	1.00	1.66 (0.82, 3.35)	2.33 (1.13, 4.82)	2.09 (1.02, 4.29)	0.062	1.00	3.32 (1.10, 10.04)	3.19 (1.00, 10.16)	3.78 (1.12, 12.68)	0.061
Full model + IGF1-BP3 ratio quartiles ^e	1.00	1.65 (0.83, 3.31)	2.44 (1.21, 4.92)	2.40 (1.19, 4.84)	0.014	1.00	3.35 (1.12, 10.00)	3.61 (1.18, 11.04)	4.28 (1.33, 13.84)	0.024
Full model + C-reactive protein quartiles ^f	1.00	1.60 (0.80, 3.20)	2.17 (1.07, 4.40)	1.98 (0.97, 4.04)	0.075	1.00	3.10 (1.04, 9.27)	3.19 (1.02, 9.93)	3.60 (1.11, 11.68)	0.06
Full model + adiponectin quartiles ^g	1.00	1.66 (0.83, 3.34)	2.42 (1.20, 4.90)	2.17 (1.06, 4.44)	0.041	1.00	3.16 (1.07, 9.35)	3.26 (1.06, 10.07)	3.72 (1.15, 12.05)	0.049

^a Adjusted for measured BMI (<18.5, 18.5–24.9, 25–29.9, 30–34.9, 35+); treatment(surgery, +radiation, +chemo, +radiation and chemo); number of activity-limiting comorbidities; race/ethnicity (non-Hispanic white, Hispanic, African-American, other); Healthy Eating Index 2005 score quartiles

^b Base model + adjustment for postdiagnosis recreational physical activity (0, 0.1–8.9, 9+ MET-h/wk)

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