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Adiposity and Sex Hormones in Postmenopausal Breast Cancer Survivors

Anne McTiernan, MD, PhD[1,2,3], **Bharat Rajan, MS**[1], **Shelley S. Tworoger**[1,2], **Melinda Irwin, PhD**[4], **Leslie Bernstein, PhD**[5], **Richard Baumgartner, PhD**[6], **Frank Gilliland, MD, MPH**[5], **Frank Z. Stanczyk, PhD**[5], **Yutaka Yasui, PhD**[1], and **Rachel Ballard-Barbash, MD, PhD**[7]

[1] Cancer Prevention Research Program Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109

[2] Department of Epidemiology, School of Public Health, University of Washington, Seattle, Washington 98195

[3] Department of Medicine, School of Medicine, University of Washington, Seattle, Washington 98195

[4] Department of Epidemiology and Public Health, Yale University, New Haven, CT, 06520

[5] University of Southern California, Los Angeles, CA

[6] University of New Mexico, Albuquerque, New Mexico

[7] Applied Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland 20892

Abstract

Purpose—Overweight and obese women with breast cancer have poorer survival compared with thinner women. One possible mechanism is that breast cancer survivors with higher degrees of adiposity have higher concentrations of tumor-promoting hormones. This study examined the association between adiposity and concentrations of estrogens, androgens, and sex hormone binding globulin (SHBG) in a population-based sample of postmenopausal women with breast cancer.

Methods—We studied the associations between body mass index (BMI), body fat mass and percent body fat measured by DXA scan, waist circumference, and waist-to-hip circumference ratio with concentrations of estrone, estradiol, testosterone, SHBG, dehydroepiandrosterone sulfate (DHEAS), free estradiol, and free testosterone in 505 Western Washington and New Mexico postmenopausal women with incident Stage 0-IIIa breast cancer. Blood and adiposity measurements were done between 4–12 months post-diagnosis.

Results—Obese women (BMI ≥ 30) had 35% higher concentrations of estrone and 130% higher concentrations of estradiol, compared with lighter women (BMI < 22.0) (p trend, 0.005 and 0.002, respectively). Similar associations were observed for body fat mass, percent body fat and waist circumference. Testosterone concentrations also increased with increasing levels of adiposity (p trend, 0.0001). Concentrations of free estradiol and free testosterone were doubled to tripled in overweight and obese women compared with lighter-weight women (p trend=0.0001).

Corresponding Author: Anne McTiernan, MD, PhD, Cancer Prevention Research Program, MP-900, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. N, Seattle, WA 98109, Phone: 206-667-7979 Fax: 206-667-7850, amctiern@fhcrc.org.

Conclusions—These data provide information about potential hormonal explanations for the association between adiposity and breast cancer prognosis. These sex hormones may be useful biomarkers for weight loss intervention studies in women with breast cancer.

Keywords

Breast cancer; obesity; estrogen; testosterone; sex steroid hormones

Introduction

Overweight and obese women with breast cancer have poorer survival compared with thinner women, but the reasons for this are unknown. Women with a high body mass index (BMI) have two times greater risk of recurrence over five years and 60% increased risk of death over 10 years compared with normal weight or thinner women.[1] In postmenopausal women without breast cancer, increased BMI is associated with high concentrations of blood estrogens and low concentrations of sex hormone binding globulin (SHBG).[2–4] The high estrogen concentrations likely represent conversion of androgens to estrogens by the enzyme aromatase in adipose tissue.[5,6] Both estrogen and testosterone promote breast cancer cell growth.[7] We assessed the associations of BMI, percent body fat, waist circumference, and waist-to-hip ratio with serum sex hormone concentrations in a population-based cohort of postmenopausal breast cancer survivors - the Health, Eating, Activity, and Lifestyle (HEAL) Study.

Methods

Eligibility and Recruitment

HEAL is a population-based, multi-center, multi-ethnic prospective cohort study of 1185 women with breast cancer to determine whether weight, physical activity, diet, sex hormones, and other exposures affect breast cancer prognosis. The current analyses were limited to two of the three centers (Western Washington and New Mexico), since the third center (Southern California) did not collect blood at study enrollment. We identified newly-diagnosed cases of Stage 0-IIIa breast cancer between 1996–1999, who were living in King, Pierce, or Snohomish Counties in Washington, or Bernalillo, Sante Fe, Sandoval, Valencia, or Taos Counties in New Mexico, and able to be interviewed, have clinic measures, and blood drawn within 4–12 months of diagnosis. Of 2073 age, stage, and county of residence-eligible women with breast cancer in Western Washington and New Mexico, 856 (41%) were enrolled. A group of cases (N=278) in Western Washington were interviewed for another study and could not be approached for the HEAL study. Of 202 Western Washington and 654 New Mexico women interviewed, 198 (98%) and 542 (83%) provided a blood sample, respectively.

Written informed consent was obtained from each subject. The study was performed after approval by the Institutional Review Boards of participating centers, in accord with an assurance filed with and approved by the U.S. Department of Health and Human Services.

Data Collection

We used a standardized questionnaire (self-administered in Western Washington, in-person interviews in New Mexico). Anthropometric, body composition, and physical activity data were collected at a clinic visit or at home. The data for the present analyses were limited to those collected at study entry.

Anthropometric Measures

Trained staff measured height and weight in a standard manner at a clinic or home visit. Waist circumference was measured in cm. at the smallest circumference (Western Washington) or just above the superior margin of the iliac crests (New Mexico). Hip circumference was measured in cm. at the largest circumference (Western Washington) or at the maximal posterior projection of the buttocks (New Mexico). Percent body fat was primarily measured from whole body scans using dual-energy x-ray absorptiometry (DXA) scanner (Lunar model DPX in New Mexico; Hologic model 1500 in Western Washington). Two women were missing BMI data and 90 were missing DXA data.

Other Variables

Questionnaire information was collected on dietary intake (120-item food frequency questionnaire); health habits; history of benign breast disease; reproductive and menstrual history (age at menarche, regularity of periods when menstruating, age at menopause, type of menopause, hysterectomy status, pregnancy history including age at first and last full-term pregnancy, lactation history); history of oral contraceptive and hormone replacement therapy use; history of endocrine and other medical problems; history of benign breast disease; family history of breast cancer, other cancers, and diabetes mellitus; history of tobacco, caffeine, and alcohol use; lifetime weight patterns; detailed current and pre-diagnostic leisure, household, and work physical activity habits; mammographic screening; and education, income, race, and ethnicity.

Blood Collection and Sex Hormone Assays

A 30-ml sample of blood was collected at interview either fasting (Western Washington) or non-fasting (New Mexico). Blood was processed within one hour of collection; serum, plasma, and buffy coat were aliquoted into 1.8-ml tubes and stored at −70 to −80 degrees C. Dates of sample collection and processing, time of day of blood collection, current use of tamoxifen, and time since last meal were recorded. There were a small number of cases for which we had insufficient blood to perform all assays (N missing shown in the tables).

Estrone and estradiol assays were performed at Quest Diagnostics, Inc. of San Juan Capistrano, California between February 1999 and June 1999 (for Western Washington) and September 1997 and December 1999 (for New Mexico). Estradiol was not measured in postmenopausal women from New Mexico, hence data are available only for the 118 postmenopausal cases from Western Washington. SHBG and DHEAS assays were conducted at Dr. Richard Baumgartner's laboratory at the University of New Mexico between April 1999 and October 1999 (for Western Washington samples) and September 1997 and December 1999 (for New Mexico samples). Testosterone was conducted at Dr. Richard Baumgartner's laboratory at the University of New Mexico between October 2002 and December 2002 (for Western Washington samples) and September 1997 and December 1999 (for New Mexico samples). Samples were randomly assigned to assay batches and randomly ordered within each batch. Laboratory personnel performing the assays were blinded to subject identity and personal characteristics.

Estrone and estradiol assay methods consisted of organic solvent extraction, followed by celite column partition chromatography prior to quantification by radioimmunoassay (sensitivities of 10 pg/ml and 2 pg/ml, respectively). Testosterone was measured using a Diagnostics Product Corporation radioimmunoassay kit (sensitivity of 40 pg/ml). SHBG was measured with the Radim SHBG Kit, which is a radioimmunoassay quantitation supplied by Wein Laboratories, Inc. (sensitivity of 6 nmol/L). DHEAS concentrations were determined using a DHEAS radioimmunoassay kit supplied by Diagnostic Products Corp. (sensitivity of 1.1 ug/dL).

To estimate intra-assay variability, the Western Washington assays for SHBG and DHEAS included a total of ten blinded replicates in the same assay batch for ten subjects. In addition, samples from two different subjects were included in every assay batch for SHBG and DHEAS to estimate inter-assay variability. For testosterone, 24 pooled quality control samples were included (2 per batch). Replicated samples were not included in the estrogen assays at the baseline analysis; however 20 replicated samples and eight pooled quality control samples (two per batch) were included in an analysis of a follow-up blood assays completed between July 2001 and August 2001 in the same laboratory. The intra- and inter-assay variabilities were derived from these data.

To estimate the intra-assay and total CVs, we used a random effects model to assess the respective variance components. Hormone values were natural log-transformed and ID and batch number were included as random effects in the model. We used the square root of the mean squared error as a measure of the intra-assay CV on the original scale (12). We estimated the total CV by taking the square root of the sum of the mean squared error and the mean squared variability due to the batches. The intra-assay and total CVs were 3.8% and 5.9% for SHBG, respectively, and 4.6% and 9.5% for DHEAS, respectively. For testosterone, the intra-assay CV was 12.0% and the total CV was 14.4%. Results for estradiol and estrone were 28.8% and 13.3%, respectively, for the intra-assay CV and 29.1% and 13.3% for the total CV, respectively. Other than the CVs for estradiol, these CVs are similar to those observed in other studies using similar assay methods to test samples with low concentrations of sex hormones.

Data Analysis

We categorized BMI (kg/m^2) as light (< 22.0), normal weight (22.0 ≤ BMI ≤ 24.9), moderately overweight (25.0 ≤ BMI ≤ 27.5), severely overweight (27.6 ≤ BMI ≤ 29.9), or obese (BMI ≥ 30.0). We also categorized BMI using the World Health Organization public health cutpoints for obese (BMI ≥ 30.0), overweight (BMI ≥ 25.0) and normal or underweight (BMI < 25.0).[8] We categorized percent body fat, waist circumference and waist-to-hip ratio into quartiles. We calculated total fat mass by multiplying DEXA-derived percent body fat by weight, and divided participants into quartiles of this variable.

We calculated free estradiol and free testosterone concentrations (unbound to either SHBG or albumin) using values for estradiol, testosterone, and SHBG with the equations of Sodergard et al..[9] We applied a natural log transformation to all hormone values to reduce the positive skewness of the distributions. We deleted data from two women who had out of range testosterone concentrations (over 4000 pg/ml) and from two women who had out of range estradiol concentrations (319 and 639 pg/mL).

For women who had hormone concentrations below the detectable levels, we assigned a value halfway between zero and the lower limit of detection. Thus, 34 women were assigned an estrone value of 5 pg/ml and 49 women were assigned a testosterone value of 20 pg/ml.

We calculated geometric mean values and 95% confidence intervals for hormone concentrations within categories of four measures of adiposity (BMI, percent body fat, waist circumference, and waist-to-hip ratio). We performed tests for linear trend across increasing categories of adiposity using a generalized linear modeling approach[10,11] to investigate associations between adiposity and hormone values adjusted for the following variables: age, ethnicity, current tamoxifen use (yes/no), breast cancer treatment (surgery alone, surgery plus radiation, surgery plus chemotherapy, surgery plus radiation plus chemotherapy), time between diagnosis and blood draw, oophorectomy and hysterectomy status, physical activity, alcohol use, smoking, and cancer stage at diagnosis. We also performed analyses with and without adjustment for daily caloric intake, and since the

results were similar, we present data unadjusted for this variable. We assessed the associations between adiposity and hormones separately for the Western Washington and New Mexico subjects. The associations between adiposity and hormones did not differ by clinical site, and we therefore combined the data. We adjusted all combined analyses for clinical site. We also analyzed the data separately for Hispanic and non-Hispanic white women, found no differences by ethnicity in the associations between adiposity and hormones, and thus we combined all of the women and adjusted for ethnicity in the analysis.

We tested the differences between tamoxifen users and nonusers with respect to adiposity-hormone associations using linear regression. A model was first fitted with an adiposity measure and tamoxifen use, and then with the adiposity measure, tamoxifen use and interaction of these two measures, to determine if there was a significant influence of tamoxifen use for various categories of adiposity. Since the slope of the dose-response curves did not differ between tamoxifen users and nonusers, we present all data for tamoxifen users and nonusers combined.

Results

Table 1 shows select characteristics of the HEAL study participants compared with characteristics of all breast cancer cases from the respective SEER registries from which HEAL participants were recruited, who met eligibility criteria for age, stage at diagnosis, and county of residence. Overall, the HEAL cohort of cases was similar to the SEER cases with respect to age and ethnicity (Table 1). In Western Washington, there was a higher proportion of cases with in situ disease and a lower proportion with stage II disease in the HEAL cohort compared with the SEER registry cases. In New Mexico, the HEAL cohort and SEER cases had similar proportions with in situ breast cancer, but the HEAL cases included a smaller proportion of stage II disease. In both Western Washington and New Mexico, a larger proportion of HEAL cases were lymph node negative compared with SEER cases. In Western Washington, a greater proportion of SEER cases had estrogen receptor positive tumors compared with HEAL cases, while in New Mexico, the opposite trend was observed.

A total of 505 women (mean age 62.2) were postmenopausal at the time of interview and had both BMI and hormone data available. The sample included 80 Hispanic white, 413 non-Hispanic white, 1 African-American, 6 Asian-American, and 5 of unknown race/ethnicity. At diagnosis, 21 percent of the women were stage 0 (*in situ*), 63% were stage I, and 16% were stage II-IIIa. On average, the women were overweight (mean BMI 26.9) and had a high percent of body weight comprised of fat (mean 38.3%). Forty percent of women had a hysterectomy, 20 percent had a history of bilateral oophorectomy, and 43 percent were using tamoxifen at the time of blood collection.

Body Mass Index

Obese women (BMI > 30.0) had a 35% higher concentration of estrone compared with women with BMI < 22.0 (p trend=0.005) (Table 2). Estradiol concentration was increased by 130% in obese women compared with the lightest women (p trend = 0.002). Increasing adiposity was associated with increasing testosterone concentrations; obese women had testosterone concentrations that were almost twice as high as those of the lightest women (p trend, 0.0001). Concentrations of free estradiol and free testosterone were doubled to tripled in overweight and obese women compared with the lightest women (p trend=0.0001). Concentrations of SHBG decreased with increasing BMI; obese women had an average SHBG concentration that was half that of the women with BMI < 22 (p trend, p= 0.0001). Concentrations of DHEAS increased with increasing adiposity, but the test for trend was not statistically significant. When we categorized women by the common cutpoints for “normal”

(BMI < 25.0), “overweight” (BMI 25.0–29.9), and “obese” (BMI ≥ 30.0), a similar gradient of increasing estrogen and decreasing SHBG concentrations was seen, and the results for individual hormones were similarly statistically significant as for the data categorized by the more refined categories (data not shown).

Body Fat

Concentrations of several estrogens and androgens increased, and SHBG decreased, with increasing body fat mass as measured by DEXA scans (Table 3). Women who were in the top quartile for body fat mass had almost twice as high a serum concentration of estradiol compared with women in the lowest quartile, and the result was statistically significant (p trend, 0.048). Free estradiol was significantly increased with increasing quartile of body fat mass (p trend = 0.003). Concentrations of testosterone and free testosterone increased with increasing quartiles of body fat mass (p trend, 0.0001). DHEAS also increased with increasing fat mass, but the result was not statistically significant. The concentration of SHBG decreased significantly with increasing quartile of body fat mass (p trend, 0.0001).

The associations between percent body fat and serum hormone concentrations were very similar to those observed for body fat mass, although the results were only statistically significant for testosterone, free testosterone, and SHBG (data not shown).

Waist Circumference, and Waist-to-Hip Ratio

Clinical site-specific and combined analyses showed that increased waist circumference was positively associated with estrogens and negatively associated with SHBG, similar to the results for BMI and percent body fat (data not shown). There were no associations observed between waist-to-hip circumference and hormone concentrations (data not shown).

Discussion

A statistically significant association between obesity and recurrence or survival was reported in 23 studies (total N=27,077 women) while no association was reported in 7 studies (total N=4,155 women).[7] The negative effect of body weight and BMI on breast cancer recurrence and survival has been observed in both premenopausal and postmenopausal women.[7,12–16] However, potential interactions among adjuvant therapy, obesity, and clinical outcome have not been systematically addressed.

In a meta-analysis, the hazard ratio for recurrence at five years by body weight (highest vs. lowest category) was 1.91 (1.52–2.40) and for death at ten years was 1.6 (1.38–1.76), suggesting women with excess weight at diagnosis were significantly more likely to develop recurrence and less likely to survive.[1] Goodwin et al. found that after three to nine years of follow-up, women with newly diagnosed breast cancer (N=535, median age 50 years) with BMI ≥ 27.8 had a 70% increased risk of recurrence (90% confidence interval 1.3–2.3) and an 80% increased risk of death (95% confidence interval 1.3–2.5) compared with lighter-weight women.[15]

In several studies, overweight and obese postmenopausal women without breast cancer have been observed to have higher estrogen and androgen concentrations, and lower SHBG concentrations, compared with lighter-weight women.[2–4, 17–22] High concentrations of estrogens and androgens have been associated with increased risk for incident breast cancer in several cohort studies,[23] suggesting that these hormones may be breast tumor promoters.[7]

One study examined the association between BMI and sex hormone concentrations in 36 women with breast cancer and 36 controls, and found that testosterone increased with increasing BMI (p=.08).[24] Furthermore, SHBG level was positively associated with

increased upper body fat distribution as measured by skin folds. No association between BMI and estrone was observed. However, the sample included both premenopausal and postmenopausal women, and data for cases and controls were combined in the analysis. Therefore, ours is the first study to report on the association between adiposity and sex hormones in a relatively large cohort of breast cancer survivors limited to postmenopausal women.

We found statistically significant trends toward increasing estrone, estradiol, testosterone, free estradiol, and free testosterone with increasing BMI, body fat mass, percent body fat, and waist circumference. SHBG significantly decreased with increasing levels of all measures of adiposity.

Our consistent findings among several measures of adiposity (BMI, body fat mass, percent body fat, and waist circumference) and the finding that waist-to-hip was not associated with hormone concentrations at either clinical site suggest that overall amount of body fat may be more important than distribution of body fat in determining sex hormone concentrations in postmenopausal women with breast cancer. On the other hand, numerous studies have reported that hyperandrogenism is more strongly associated with centralized or visceral obesity than generalized obesity in post-menopausal women, and is associated with increased cortisol and insulin levels in this obesity phenotype.[25] Some investigators have suggested that waist-to-hip circumference ratio may be an inadequate index of body fat distribution, particularly in post-menopausal women, for a variety of reasons including the influence of age-related variation in muscle mass and tone.[26]

There are several limitations to these data. While the study was population-based, only 41% of age- and stage- eligible incident cases were enrolled into the cohort. Although our analyses were limited to within-cohort comparisons, we cannot be sure that these associations pertain to all breast cancer survivors. Certain race/ethnic groups were under-represented in theses analyses, namely African-American and Asian-American women. Since an additional HEAL site in Los Angeles County has enrolled 273 African-American women with breast cancer (blood not available at baseline), we will be able to assess body mass-hormone associations in blood collected during the follow-up stage of the study for that racial group.

The methods of data collection were not identical between the sites for several measures, namely the type of DXA scanner, method of waist circumference measurement, and fasting status at blood draw. We assessed all associations first within each clinical site, and only combined data when associations were the same between the two sites, and we adjusted for clinical site in all analyses to compensate for these differences.

The CVs for some hormones, particularly estradiol, were large although consistent with published CVs for these hormones and reflect the difficulty with measuring estrogens at the low levels present in postmenopausal women. We did not collect information on whether women were currently undergoing chemotherapy or radiation treatment at the time of their blood draw, and thus the results could be confounded by current treatment status. However, we did not see a difference in association between serum hormones and adiposity by stage, which suggests that current treatment is unlikely to have been a major confounder since few women with in situ disease underwent radiation or chemotherapy.

These data were cross-sectional only, and do not imply cause and effect. Specifically, we did not measure the effect of gain or loss of body mass or body fat on sex hormones. Similarly, although we adjusted our analyses for variables that might be associated with both body mass and hormone levels, there could be other confounding factors that we did not take into account.

Differential variation in sex hormones by body mass and body fat may be one explanation for the poorer survival experienced by overweight women with breast cancer and the poorer response to tamoxifen therapy in overweight or obese women.[7] In the HEAL population-based cohort of breast cancer survivors, 30 percent were overweight (body mass index 25.0–29.9) and 23% were obese (body mass index ≥ 30.0). Thus, if reduction of body fat can improve prognosis and survival, a large number of breast cancer survivors might be expected to benefit from weight-loss interventions.

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Abbreviations

BMI	body mass index
CI	confidence interval
CV	coefficient of variation
DHEAS	dehydroepiandrosterone sulfate
HEAL	Health, Eating, Activity, and Lifestyle study
kg	kilogram
m^2	meters squared
SEER	Surveillance, Epidemiology and End Results Programs
SHBG	sex hormone binding globulin

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Table 1

Characteristics of the HEAL Cases Compared with All Eligible SEER Cases[a] (Western Washington and New Mexico only)

	Western Washington			New Mexico		
	SEER Cases	**All HEAL Cases (202)**	**Postmenopausal HEAL Cases (120)**	**SEER Cases**	**All HEAL Cases (654)**	**Postmenopausal HEAL Cases (485)**
Age[b] (mean, s.d.)	52.4 (6.7)	52.5 (6.4)	56.2 (4.8)	60.4 (13.9)	59.5 (12.7)	64.1 (10.0)
Race/ethnicity[c]						
White, non-Hispanic	1259 (89.0)	174 (86.1)	109 (90.9)	1227 (74.1)	497 (76.0)	304 (79.0)
African-American	51 (3.6)	1 (0.5)	1 (0.8)			
Hispanic	0	6 (3.0)	2 (1.7)	429 (25.9)	153 (23.4)	78 (20.2)
Asian-American	75 (5.4)	14 (7.0)	6 (5.0)			
Am. Indian	2 (0.1)	2 (1.0)	1 (0.8)		4 (0.6)	3 (0.8)
Unknown	27 (1.9)	5 (2.5)	1 (0.8)			
Stage of disease						
0 (in situ)	327 (23.1)	66 (32.4)	34 (28.3)	285 (17.2)	121 (18.5)	69 (17.9)
I	605 (42.8)	100 (49.5)	63 (52.5)	674 (40.7)	409 (62.5)	256 (66.5)
II	424 (30.0)	33 (16.3)	20 (16.7)	482 (29.1)	122 (18.7)	60 (15.6)
III	58 (4.1)	3 (1.4)	3 (2.5)	13 (2.0)		
Unable to determine				182 (11.0)	2 (0.3)	
Lymph nodes						
none	1036 (73.2)	160 (79.2)	95 (79.2)	1176 (71.0)	494 (75.5)	307 (79.7)
regional	336 (23.8)	34 (16.8)	23 (19.2)	398 (24.0)	137 (20.1)	68 (17.7)
distant	0	0	0	1 (0.1)	0	0
unknown	42 (3.0)	8 (4.0)	2 (1.6)	81 (4.9)	23 (3.5)	10 (2.6)
Estrogen Receptor						
positive	872 (61.7)	115 (56.9)	75 (62.5)	721 (43.5)	374 (57.1)	237 (61.6)
negative	168 (11.9)	21 (10.4)	11 (9.2)	351 (21.2)	91 (13.9)	40 (10.4)
borderline	0	0	0	11 (0.7)	2 (0.3)	0
unknown/not done	379 (26.4)	64 (31.7)	34 (28.3)	575 (34.6)	187 (28.6)	108 (28.0)

[a] SEER data for female breast cancer, Stage 0–IIIa, residence of King, Pierce, or Snohomish Counties of W. Washington or of Bernalillo, Santa Fe, Sandoval, Valencia, or Taos Counties of New Mexico

[b] W. Washington: ages 40–64 only; New Mexico: ages 18+

[c]W. Washington: all races eligible except African-American who could not be approached due to being interviewed for another FHCRC study; New Mexico: Hispanic and non-Hispanic whites only eligible

Table 2

Association between BMI and Serum Hormones: Geometric Means (95% Confidence Intervals) Among a Sample of 503 Postmenopausal Women with Breast Cancer

		Body Mass Index					
		<22	22–25	25–27.5	27.5–30	>30	
	N	107	112	99	60	125	p[a]
Estrone (pg/ml)	491	19.7 (17.1, 22.7)	22.3 (19.1, 26.1)	21.2 (18.8, 24.0)	22.7 (19.6, 26.3)	26.5 (23.9, 29.3)	0.005
Estradiol[b] (pg/ml)	118	4.7 (3.4, 6.4)	8.3 (6.2, 11.0)	8.0 (5.6, 11.3)	10.6 (6.6, 17.0)	10.7 (8.6, 13.4)	0.002
DHEAS (ug/dL)	502	50.5 (43.3, 58.8)	53.2 (46.4, 61.1)	55.6 (48.5, 63.7)	60.0 (51.6, 69.8)	59.3 (52.2, 67.4)	0.21
SHBG (nmol/L)	495	73.9 (67.2, 81.3)	66.2 (60.8, 72.0)	52.1 (47.7, 56.9)	43.4 (37.9, 49.6)	38.1 (34.2, 42.4)	0.0001
Testosterone (pg/ml)	498	94.5 (77.1, 115.7)	118.1 (100.7, 138.5)	127.4 (105.7, 153.6)	126.0 (96.7, 164.1)	176.5 (151.4, 205.7)	0.0001
Free Estradiol[b] (pg/ml)	118	.10 (.09, .14)	.18 (.14, .24)	.20 (.14, .27)	.28 (.17, .46)	.28 (.23, .36)	0.0001
Free Testosterone (pg/ml)	495	2.1 (1.6, 2.6)	2.9 (2.4, 3.5)	4.0 (3.2, 5.0)	4.6 (3.3, 6.6)	7.6 (6.2, 9.3)	0.0001

[a] Test for linear trend.

[b] Number of subjects for estradiol and free estradiol for the five categories of BMI: 23, 26, 27, 14, and 40, respectively.

Table 3

Association between Body Fat Mass and Serum Hormones: Geometric Means (95% Confidence Intervals) Among a Sample of 60 Postmenopausal Women with Breast Cancer (Western Washington)

		Quartiles of Body Fat Mass (kg)				
		<20	20–27	27–34	>34	
	N	106	121	94	93	p[a]
Estrone (pg/ml)	404	19.9 (17.3, 22.9)	21.2 (18.4, 24.3)	20.7 (18.5, 23.2)	26.1 (23.1, 29.5)	0.009
Estradiol (pg/ml)	59	6.6 (4.2, 10.5)	6.4 (4.8, 8.4)	5.8 (3.6, 9.4)	12.2 (8.4, 17.7)	0.048
DHEAS (ug/dL)	413	48.4 (41.8, 56.0)	55.1 (48.1, 63.2)	55.0 (47.6, 63.6)	57.3 (50.0, 65.6)	0.121
SHBG (nmol/L)	407	73.6 (67.0, 81.0)	62.5 (56.8, 68.7)	49.7 (44.1, 56.1)	38.4 (33.4, 44.1)	0.0001
Testosterone (pg/ml)	409	99.9 (82.8, 120.6)	112.5 (95.5, 132.6)	132.1 (109.1, 160.0)	168.6 (139.8, 203.4)	0.0001
Free Estradiol[b] (pg/ml)	59	0.14 (0.09, 0.22)	0.13 (0.10, 0.18)	0.14 (0.09, 0.22)	0.35 (0.24, 0.50)	0.003
Free Testosterone(pg/ml)	407	2.2 (1.7, 2.7)	2.8 (2.2, 3.4)	4.1 (3.2, 5.3)	7.2 (5.5, 9.4)	0.0001

[a]Test for linear trend.