Published in final edited form as:

J Clin Oncol. 2007 March 20; 25(9): . doi:10.1200/JCO.2006.07.3965.

Physical Activity, Body Mass Index and Mammographic Density in Postmenopausal Breast Cancer Survivors

Melinda L. Irwin¹, Erin J. Aiello², Anne McTiernan³, Leslie Bernstein, PhD⁴, Frank D. Gilliland, MD, PhD⁴, Richard N. Baumgartner⁵, Kathy B. Baumgartner⁵, and Rachel Ballard-Barbash, MD, MPH⁶

¹Department of Epidemiology and Public Health, Yale School of Medicine, New Haven, CT

²Center for Health Studies, Group Health Cooperative, Seattle, WA

³The Fred Hutchinson Cancer Research Center, Seattle, WA

⁴Department of Preventive Medicine, University of Southern California, Los Angeles, CA

⁵Cancer Research & Treatment Center, Department of Internal Medicine, University of New Mexico, Albuquerque, New Mexico

⁶Applied Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland

Abstract

Purpose—To investigate the association between physical activity, body mass index (BMI) and mammographic density in an ethnically-diverse population-based sample of 522 postmenopausal women diagnosed with stage 0–IIIA breast cancer and enrolled in the Health, Eating, Activity, and Lifestyle Study.

Methods—We collected information on BMI and physical activity during a clinic visit two to three years after diagnosis. Weight and height were measured in a standard manner. Using an interview-administered questionnaire, participants recalled the type, duration, and frequency of physical activities in the past year. We estimated dense area and percent density as a continuous measure using a computer-assisted software program from mammograms imaged approximately one to two years after diagnosis. Analysis of covariance methods were used to obtain mean density across World Health Organization BMI categories and physical activity tertiles adjusted for confounders.

Results—We observed a statistically significant decline in percent density (p for trend = .0001), and mammographic dense area (p for trend = 0.0052), with increasing level of BMI adjusted for potential covariates. We observed a statistically significant decline in mammographic dense area (p for trend = .036) with increasing level of sports/recreational physical activity in women with a BMI ≥ 30 kg/m². Conversely, in women with a BMI < 25 kg/m², we observed a nonstatistically significant increase in mammographic dense area and percent density with increasing level of sports/recreational physical activity.

Conclusions—Increasing physical activity among obese postmenopausal breast cancer survivors may be a reasonable intervention approach to reduce mammographic density.

Keywords

breast cancer; body fat; exercise; obesity; weight; breast tissue; breast density

INTRODUCTION

Mammographic density is a strong risk factor for breast cancer [1]. Dense tissue in more than 50% of the breast could account for approximately one-third of breast cancers [1]. Mammographic density has also been associated with breast cancer tumor characteristics, including tumor size, lymph node status, and lymphatic or vascular invasion in screen-detected cancers [2]. A three-fold increased risk of second breast cancers has also been observed in women diagnosed with ductal carcinoma in situ who have highly dense breasts [3]. Recently, Maskarinec and colleagues observed higher percent densities in women diagnosed with breast cancer than age-matched controls [4].

While, inherited factors explain approximately 60% of the variance in the proportion of the breast occupied by dense tissue [1], mammographic density is also modifiable [5-7]. Increases in mammographic density have been observed in women treated with hormone therapy [5], and decreases in mammographic density have been observed in women treated with tamoxifen [6] or a low-fat diet [7]. Factors that change mammographic density may also change breast cancer risk and prognosis [1-3]. Identification of sources of variation in mammographic density is likely to provide a better understanding of factors that cause breast cancer and new approaches to prevention and treatment.

Physical activity is associated with a reduced breast cancer risk [8]. Changes in sex hormone concentrations, menstrual patterns, and energy balance have been suggested as plausible explanations for the relationship between physical activity and breast cancer, although other mechanisms may account for the consistent data observed in epidemiologic studies [8]. Physical activity may influence mammographic density by favorably changing certain hormones associated with mammographic density and breast cancer risk [9]. We examined the relationship between physical activity and mammographic density in pre- and post-menopausal women, and observed a statistically significant inverse association between sports/recreational physical activity and pre-diagnostic mammographic density in obese postmenopausal breast cancer survivors [10]. To further investigate the association between physical activity and mammographic density, we examined the association between physical activity, BMI, and one to two years post-diagnosis mammographic density in an ethnically diverse sample of postmenopausal breast cancer survivors. To our knowledge, no published studies have examined the associations among BMI, physical activity and mammographic density in breast cancer survivors.

METHODS

Study Setting, Subjects, and Recruitment

The **Health, Eating, Activity, and Lifestyle** (HEAL) Study is a population-based, multi-center, multi-ethnic prospective cohort study that has enrolled 1,183 breast cancer patients who are being followed to determine whether weight, physical activity, diet, sex hormones, mammographic density and other exposures affect breast cancer prognosis [11-13]. Women were recruited into the HEAL Study through Surveillance, Epidemiology, End Results (SEER) registries in New Mexico, Los Angeles County (CA), and Western Washington. Names and contact information were retrieved from the SEER registries. Participants were contacted to determine interest and eligibility (approximately 41% of women with breast cancer who were eligible by age, stage, and county of residence were enrolled into the

study). Details of the aims, study design, and recruitment procedures have been published previously [11-13].

Briefly, in New Mexico, we recruited 615 women, aged 18 years or older, diagnosed with *in situ* to Stage IIIA breast cancer between July 1996 and March 1999, and living in Bernalillo, Sante Fe, Sandoval, Valencia, or Taos Counties. In Western Washington, we recruited 202 women, between the ages of 40 and 64 years, diagnosed with *in situ* to Stage IIIA breast cancer between September 1997 and September 1998, and living in King, Pierce, or Snohomish Counties. In Los Angeles County, 366 Black women with stage 0 to IIIA breast cancer, who had participated in the Los Angeles portion of the Women's Contraceptive and Reproductive Experiences (CARE) Study, a case-control study of invasive breast cancer, or who had participated in a parallel case-control study of *in situ* breast cancer were recruited for the HEAL Study. Eligible participants from these two studies were the subset of Black women who were diagnosed with breast cancer between May, 1995 and May, 1998. Both studies restricted eligibility to women aged 35 to 64 years at diagnosis who were English speaking and born in the U.S.

Participants completed in-person interviews at baseline (within their first year after diagnosis, 6 + 2 months from diagnosis) and follow-up (approximately 2.5 years after diagnosis). During the follow-up visit, participants also were approached for consent to retrieve their mammograms. Among the 1183 women enrolled at baseline, 944 women returned for the follow-up visit (51 women died before the follow-up visit), and post-diagnosis mammograms were retrieved for 755 participants. We were unable to retrieve mammograms for 189 participants because either (1) the participant refused to consent to mammogram retrieval, (2) the mammogram facility would not release films for their patients, (3) the mammogram films were lost by another facility, or (4) participants were unable/unwilling to provide information regarding the location of the mammograms. Of the 755 post-diagnosis mammograms retrieved, 42 mammograms were of poor quality and could not be read accurately; thus, mammograms were read for 713 participants. Among the 713 participants, 157 were premenopausal, five women did not complete the follow-up physical activity interview and 29 did not have body weight measured at the follow-up visit. Our analyses are based on the remaining 522 women. Demographic and physiologic characteristics, including BMI and physical activity levels, of the 522 women included in this analysis and the 1183 women enrolled in the study did not differ. The study was performed with the approval of 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

Anthropometrics—Trained staff measured weight and height in a standard manner at the follow-up clinic visit (approximately 2.5 years after diagnosis). With the women wearing light indoor clothing and no shoes, weight was measured to the nearest 0.1 kg using a balance-beam laboratory scale. Height was measured, also without shoes, to the nearest 0.1 cm using a stadiometer. All measurements were performed and recorded twice in succession, and averaged for a final value for analyses. Body mass index (BMI) was computed as weight in kg divided by height in m². Three BMI categories were created based on the World Health Organization-National Institutes of Health cutoff for obesity: BMI < 25 kg/m², BMI = 25.0-29.9, and BMI > 30 kg/m² [14].

Physical Activity Assessment—We collected information on physical activity using an interview-administered questionnaire at the follow-up visit scheduled within women's third year after diagnosis. Participants were asked to recall the type, duration, and frequency of

physical activities for the past year. The questionnaire was based on the Modifiable Activity Questionnaire developed by Kriska and colleagues, which was designed to be easily modified for use with different populations, and which has been shown to be reliable and valid [15]. The sports/recreation and household activities listed on the questionnaire addressed 29 popular activities.

We then estimated hours per week for each activity by multiplying frequency and duration together. Two mutually exclusive groups were created based on type of activity, sports/recreation including walking or household/gardening. Each activity was also categorized as light (< 3 METs)-, moderate (3-6 METs)-, or vigorous (> 6 METs)-intensity based on Ainsworth et al's 'Compendium of Physical Activities' [16].

Mammographic Density—Mammographic films, corresponding to approximately 1.5 years after diagnosis, were retrieved from individual providers that each woman had specified. Each film was digitized using either an Epson 1680 scanner (Epson America Inc., CA) (Washington) or Cobrascan CX-812 M large format 12-bit X-ray scanner (New Mexico and Los Angeles). We measured the cranio-caudal (CC) view contralateral to the breast diagnosed with breast cancer for mammographic percent density and dense area (measured in thousands of pixels and converted to mm² by multiplying by 0.0676). The density readings were conducted by one of the authors (EJA) using Cumulus 108, a computer-assisted mammogram-reading program developed at the University of Toronto. This method has been described in detail elsewhere [17]. Briefly, the reader uses a sliding scale to outline the breast edge and then the dense breast area based on pixel brightness. Percent density is the proportion of dense breast area relative to the total area of the breast.

Other Variables—Standardized questionnaire information was collected at the baseline and follow-up visit on medical history and selected demographic data. Postmenopausal status, assessed at the follow-up interview, was defined as ages 55 and over or not menstruating in the past 12 months, surgery to remove ovaries or a hysterectomy. Information on disease stage, adjuvant therapy, and hormonal therapy was collected from the participant's physician.

Statistical Analyses

Because of the known effects of BMI on mammographic density and breast cancer risk [1], we decided to examine the physical activity and mammographic density association separately for women with a BMI < 25, BMI = 25.0-29.9, and a BMI > 30 kg/m². We calculated means and standard deviations of demographic and physiological characteristics of the study sample by BMI groups. Differences in means were compared using analysis of covariance methods. Categorical variables were compared using chi-square analysis.

We used analysis of covariance methods to estimate least squares means and test for differences in the dense area and percent density across categories of BMI, and total, moderate-to vigorous-intensity physical activity and sports/recreational physical activity. The physical activity analyses were further stratified by BMI. Categories of physical activity were created based on physical activity tertiles using the whole sample.

We adjusted for covariates associated with mammographic density including age (continuous), ethnicity, study site, education, parity (nulliparous vs. parous), disease stage, tamoxifen use, adjuvant therapy (no adjuvant therapy, radiation only, chemotherapy only, or radiation and chemotherapy), breast cancer recurrence, smoking, ever use of hormone therapy, and months from diagnosis to mammogram. We used Tukey's Honestly Significant Difference test to identify statistically significant differences between groups with the

overall level of statistical significance constrained to 5%. All analyses were conducted using SAS Version 8.2.

RESULTS

Among the 439 women included in this analysis, 171 (39%) had a BMI < 25 kg/m², 137 (31%) had a BMI between 25.0 and 29.9 kg/m², and 131 (30%) had a BMI > 30 kg/m² (Table I). Women who had a BMI > 30 kg/m² participated in significantly less physical activity than women with a BMI < 30 kg/m² ($p < .05$).

We observed a statistically significant lower percent density (p for trend = 0.0001), but not mammographic dense area (p for trend = 0.11), with higher levels of BMI after adjusting for age, ethnicity, study site, education, parity, disease stage, adjuvant therapy, tamoxifen use, breast cancer recurrence, smoking, time from diagnosis to mammogram, and ever use of hormone therapy (Table II).

We observed a statistically significant lower mammographic dense area (p for trend = .027) with higher levels of sports/recreational physical activity in women with a BMI > 30 kg/m² after adjusting for covariates (Table III). Conversely, in women with a BMI < 25 kg/m², we observed a nonstatistically significant higher mammographic dense area with higher levels of sports/recreational physical activity ($p = .19$).

When we examined associations between physical activity and mammographic density stratified by BMI and using participation reported in total physical activity and moderate- to vigorous-intensity physical activity rather than sports/recreational activity, similar, but not statistically significant, trends in the same direction were observed (data not shown). We also examined associations between BMI and mammographic density and physical activity and mammographic density stratified by age groups, ethnicity, disease stage, adjuvant therapy, tamoxifen use, and hormone therapy use; however, none of these variables modified the associations between BMI and mammographic density or physical activity and mammographic density (data not shown).

DISCUSSION

Mammographic density was inversely related to sports/recreational physical activity among obese breast cancer survivors. Approximately 32% of breast cancer survivors do not participate in the recommended amounts of physical activity [12]. Physical inactivity and obesity have been associated with a recurrence of breast cancer and poor survival [18,19]. Mammographic density is a strong risk factor for breast cancer, and has been associated with breast cancer tumor characteristics [1,2]. Increasing physical activity among obese breast cancer survivors may be a reasonable intervention approach to reduce mammographic density, and in turn, improve breast cancer prognosis. However, until more physical activity and mammographic density studies are conducted that confirm or contradict our findings, caution should be used in interpreting our findings.

Only four previous studies have examined the association between physical activity and mammographic density, all in healthy women. Vachon et al. [20] investigated the association between physical activity and percent mammographic density in 1900 pre- and post-menopausal women. Physical activity was not associated with percent mammographic density. However, their assessment of physical activity was limited to only one question. Gram et al. [21] examined the relationship between physical activity and mammographic density among 2720 Norwegian pre- and post-menopausal women. Women who reported moderate physical activity, i.e., more than two hours per week, were 20% less likely (OR = 0.80, 95% CI: 0.60 -1.10) to have high-risk mammographic patterns compared with those

who reported being inactive. This relationship was consistent across strata of BMI and menopausal status. Recently, Suijkerbuijk and colleagues examined physical activity in relation to mammographic density in the Dutch Prospect-European Prospective Investigation into Cancer and Nutrition (EPIC) Cohort [22]. They observed, in 620 pre- and post-menopausal women, a slight trend of higher levels of physical activity and lower absolute density. Subgroup analysis for postmenopausal women showed similar results. Lastly, we recently reported a statistically significant inverse relationship between physical activity and pre-diagnostic mammographic density in obese postmenopausal breast cancer survivors [10].

Physical activity may influence mammographic density by favorably changing certain hormones that may be associated with mammographic density, such as sex steroid hormones. A recent publication of US women enrolled in the Postmenopausal Estrogen/ Progestin Interventions (PEPI) Trial observed strong associations between higher levels of endogenous estrone, estradiol, bioavailable estradiol and greater mammographic density ($p < .01$) [23]; however, two published studies that examined the association between mammographic density and endogenous estrogens observed no association between total estradiol and percent density in both pre- and post-menopausal women [24,25]. The hypothesis that endogenous hormones may mediate the relationship between physical activity and mammographic density applies particularly to obese postmenopausal women whose major source of estrogen is the aromatization of androstenedione in body fat [13,26,27]. Thus, higher levels of physical activity may be associated with decreased mammographic density levels among obese postmenopausal women by decreasing sex hormone concentrations directly or indirectly by reducing body fat [9]. In a recently published yearlong randomized controlled trial, exercise had a favorable effect on decreasing circulating estrogen concentrations among overweight postmenopausal women; however the effect was limited to women who lost body fat [9].

Breast cancer incidence rates in the United States are lower, yet mortality rates from breast cancer are higher, among African American women than among non-Hispanic or Hispanic White women [28]. Mammographic density may reflect these ethnic differences in incidence or mortality. In our study, African American women had lower unadjusted and adjusted amounts of dense breast tissue than non-Hispanic and Hispanic White women. Percent breast density was similar among all three ethnic groups; however, after adjusting for potential covariates, percent breast density was higher in African American women than among non-Hispanic and Hispanic White women. African American women also had a higher BMI and reported less participation in physical activity than non-Hispanic and Hispanic White women. Yet, the associations among BMI, physical activity and mammographic density did not differ by ethnic group. However, our sample of African American and Hispanic White women was small; thus, we had insufficient statistical power to determine whether race/ethnicity modified the associations.

The HEAL Study has several limitations and strengths. While the HEAL Study is a prospective cohort study, this analysis is cross-sectional in design. Mammographic density was obtained using mammograms that were obtained about 20 months post-diagnosis, whereas physical activity and BMI were measured on average 30 months post-diagnosis. Participants were asked to recall physical activity for the past year, which would correspond to the time when the mammograms were taken. Thus, while mammographic density and physical activity were assessed at approximately the same time point, BMI was measured on average 10 months later. However, it is unlikely that women would move into different BMI categories in the ten month period (the correlation between BMI measured at approximately 6 months post-diagnosis and 30 months post-diagnosis was $r = .96$, $p = .0001$).

Major strengths of our study are the quality of the physical activity data that were obtained using a reliable and valid 29-item interview-administered questionnaire; we measured weight and height whereas many previous studies used self reported measures; all measures were collected after the women completed adjuvant therapy (i.e., chemotherapy and/or radiation therapy); we recruited a multi-ethnic cohort of breast cancer survivors; and we used a computer-assisted method to assess mammographic density with assessments done by a single reader. Measuring mammographic density on a continuous scale may provide more information than the BIRADS or Wolfe categorical measures [1,29], which most previous mammogram density studies have used. However, even though the computer-assisted continuous scale is considered the gold standard of assessing mammographic density, the currently available method used only a 2-dimensional view. A more accurate method would involve a 3-dimensional view, or volumetric approach, that captures overall volume. The need for volumetric measures is clearly reflected in the uncertainty of results observed in this study and others related to mammographic density and BMI. With two-dimensional views, one does not get a complete picture of the overall volume of the breast. Uncertainty regarding the overall volume is a problem for women with large breasts, which is common in women with a higher BMI. While percent mammographic density may be low for heavier women (due to fatty breasts), if they have a large breast volume, they may actually have more dense breast tissue than observed with two-dimensional views. Research is ongoing to develop a more precise volumetric method of assessing mammographic density [30]. Lastly, another future research need is being able to differentiate between ductal and stromal breast tissue and their contribution to mammographic density. Each tissue may explain different patterns of mammographic density and may be differentially related to physical activity and BMI.

CONCLUSION

Although it remains to be determined whether the effect of increasing physical activity decreases mammographic density, it is known that physical inactivity, obesity and mammographic density are all independently associated with breast cancer risk and prognosis [1,18,19]. Increasing physical activity among obese breast cancer survivors may be a reasonable intervention approach to reduce mammographic density, and **potentially** influence breast cancer prognosis.

Acknowledgments

This study was supported through NCI contracts N01-CN-75036-20, N01-CN-05228, N01-PC-67010, and training grant T32 CA09661. A portion of this work was conducted through the Clinical Research Center at the University of Washington and supported by the National Institutes of Health, Grant M01-RR-00037, and the University of New Mexico, NCRN M01-RR-0997. We would like to thank Kristin LaCroix, Shelley Tworoger, and Lynda McVarish for their contributions to the HEAL study, as well as the HEAL participants for their ongoing dedication to this study. Written consent was obtained from the participants for publication of study.

REFERENCES

1. Boyd NF, Rommens JM, Vogt K, et al. Mammographic breast density as an intermediate phenotype for breast cancer. *Lancet Oncol.* 2005; 6(10):798–808. [PubMed: 16198986]
2. Aiello EJ, Buist DS, White E, Porter PL. Association between mammographic breast density and breast cancer tumor characteristics. *Cancer Epidemiol Biomarkers Prev.* 2005; 14(3):662–8. [PubMed: 15767347]
3. Habel LA, Dignam JJ, Land SR. Mammographic density and breast cancer after ductal carcinoma in situ. *J Natl Cancer Inst.* 2004; 96(19):1467–72. [PubMed: 15467036]

4. Maskarinec G, Pagano I, Lurie G, Kolonel L. A longitudinal investigation of mammographic density: The Multiethnic cohort. *Cancer Epidemiol Biomarkers Prev.* 2006; 15(4):732–9. [PubMed: 16614116]
5. Marchesoni D, Driul L, Ianni A, et al. Postmenopausal hormone therapy and mammographic breast density. *Maturitas.* Jun 3.2005
6. Cuzick J, Warwick J, Pinney E, et al. Tamoxifen and breast density in women at increased risk of breast cancer. *J Natl Cancer Inst.* 2004; 96(8):621–8. [PubMed: 15100340]
7. Boyd NF, Greenberg C, Lockwood G, et al. Effects at two years of a low-fat, high-carbohydrate diet on radiologic features of the breast: results from a randomized trial. *Canadian Diet and Breast Cancer Prevention Study Group. J Natl Cancer Inst.* 1997; 89(7):488–96. [PubMed: 9086005]
8. Berglund G. Anthropometry, physical activity and cancer of the breast and colon. *IARC Sci Publ.* 2002; 156:237–41. [PubMed: 12484177]
9. McTiernan A, Tworoger SS, Ulrich CM, et al. Effect of Exercise on Serum Estrogens in Postmenopausal Women A 12-Month Randomized Clinical Trial. *Cancer Res.* 2004; 64:2923–28. [PubMed: 15087413]
10. Irwin ML, Aiello E, McTiernan A, et al. Pre-diagnosis physical activity and mammographic density in breast cancer survivors. *Breast Cancer Res Treat.* Nov 30.2005 :1–8.
11. Irwin ML, Crumley D, McTiernan A, et al. Physical activity levels before and after a diagnosis of breast carcinoma: The Health, Eating, Activity, and Lifestyle (HEAL) Study. *Cancer.* 2003; 97:1746–57. [PubMed: 12655532]
12. Irwin ML, McTiernan A, Bernstein L, Gilliland G, Baumgartner R, Baumgartner K, Ballard-Barbash R. Physical activity levels among breast cancer survivors. *Med Sci Sports Exer.* 2004; 36(9):1484–1491.
13. McTiernan A, Rajan B, Tworoger S, et al. Adiposity and sex hormones in postmenopausal breast cancer survivors. *J Clin Oncol.* May 15; 2003 21(10):1961–6. [PubMed: 12743149]
14. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults – the evidence report. *Obes Res.* 1998; 6(Suppl 2):51S–209S. [PubMed: 9813653]
15. Kriska A. Modifiable activity questionnaire. *Med Sci Sports Exer.* 1997; 29:S73–78.
16. Ainsworth B, Haskell W, Whitt M, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exer.* 2000; 32:S498–516.
17. Boyd NF, Byng JW, Jong RA, et al. Quantitative classification of mammographic densities and breast cancer risk: results from the Canadian National Breast Screening Study. *J Natl Cancer Inst.* 1995; 87:670–5. [PubMed: 7752271]
18. Holmes MD, Chen WY, Feskanich D, et al. Physical activity and survival after breast cancer diagnosis. *JAMA.* 2005; 293(20):2479–86. [PubMed: 15914748]
19. Chlebowski RT, Aiello E, McTiernan A. Weight loss in breast cancer patient management. *J Clin Oncol.* 2002; 20(4):1128–43. [PubMed: 11844838]
20. Vachon CM, Kuni CC, Anderson K, et al. Association of mammographically defined percent breast density with epidemiologic risk factors for breast cancer. *Cancer Causes Control.* 2000; 11:653–662. [PubMed: 10977110]
21. Gram IT, Funkhouser E, Tabar L. Moderate physical activity in relation to mammographic patterns. *Cancer Epidemiol Biomarkers Prev.* 1999; 8:117–122. [PubMed: 10067808]
22. Suijkerbuijk K, Van Duijnhoven F, Van Gils C, et al. Physical activity in relation to mammographic density in the Dutch Prospect-European Prospective Investigation into Cancer and Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev.* 2006; 15(3):456–60. [PubMed: 16537701]
23. Greendale GA, Palla SL, Ursin G, et al. The association of endogenous sex steroids and sex steroid binding proteins with mammographic density: results from the Postmenopausal Estrogen/Progestin Interventions Mammographic Density Study. *Am J Epidemiol.* 2005; 162(9):826–34. [PubMed: 16177147]
24. Boyd NF, Stone J, Martin LJ, et al. The association of breast mitogens with mammographic densities. *Br J Cancer.* 2002; 87(8):876–82. [PubMed: 12373602]

25. Aiello EJ, Tworoger SS, Yasui Y, et al. Associations among circulation sex hormones, insulin-like growth factor, lipids, and mammographic density in postmenopausal women. *Cancer Epidemiol Biomarkers Prev.* 2005; 14(6):1411–7. [PubMed: 15941949]
26. White J. Breast density and cancer risk: what is the relationship? *J Natl Cancer Inst.* 2000; 92:443. [PubMed: 10716955]
27. Potischman N, Swanson CA, Siiteri P, Hoover RN. Reversal of relation between body mass and endogenous estrogen concentrations with menopausal status. *J Natl Cancer Inst.* 1996; 88:756–58. [PubMed: 8637031]
28. del Carmen MG, Hughes KS, Halpern E, et al. Racial differences in mammographic breast density. *Cancer.* 2003; 98(3):590–6. [PubMed: 12879477]
29. Boyd NF, Byng JW, Jong RA, et al. Quantitative classification of mammographic densities and breast cancer risk: results from the Canadian National Breast Screening Study. *J Natl Cancer Inst.* 1995; 87:670–5. [PubMed: 7752271]
30. Pawluczyk O, Augustine B, Yaffe M, Rico D, Yang J, Mawdsley G, Boyd N. A volumetric method for estimation of breast density on digitized screen-film mammograms. *Med Phys.* 2003; 30(3): 352–64. [PubMed: 12674236]

Table 1

Characteristics of HEAL breast cancer survivors stratified by BMI (N = 439).

	BMI < 25 Mean ± SD (n = 171)	BMI: 25 - 29.9 Mean ± SD (n = 137)	BMI 30 Mean ± SD (n = 131)	All Mean ± SD (n = 439)
Age (years)	63.6 ± 10.1	61.0 ± 9.4 ^a	59.1 ± 8.9 ^b	61.5 ± 9.7
Weight (kg)	60.3 ± 7.5	73.3 ± 6.7 ^a	93.7 ± 16.4 ^{bc}	74.3 ± 17.5
Height (cm)	165.7 ± 6.4	163.4 ± 6.4	162.7 ± 7.7	164.1 ± 6.9
BMI (wt in kg/ht in m ²)	21.9 ± 2.2	27.4 ± 1.3	35.3 ± 4.9	27.6 ± 6.3
Diagnosis to interview (months)	29 ± 3	30 ± 4	30 ± 3	30 ± 4
Diagnosis to mammogram (months)	21 ± 6	19 ± 6	20 ± 6	20 ± 6
Mammogram to Interview (months)	-9 ± 6	-11 ± 7 ^a	-10 ± 7	-10 ± 7
Education (% H.S. graduate)	96%	93%	95%	95%
Site				
New Mexico	46%	32% ^a	22% ^{bc}	59%
Seattle	33%	31%	36%	24%
Los Angeles	22%	30% ^a	48% ^{bc}	17%
Ethnicity				
Non-Hispanic White	44%	32% ^a	24% ^{bc}	69%
Non-Hispanic Black	22%	30% ^a	48% ^{bc}	17%
Hispanic	40%	34%	26% ^b	14%
Disease Stage				
In Situ	35%	38%	27%	21%
Stage I	42%	30%	28%	58%
Stage II-III A	34%	28%	38%	21%
Tamoxifen Use	55%	51%	49%	52%
Nulliparous	13%	12%	13%	13%
Total PA (hr/week) ²	22.3 ± 14.6	21.5 ± 16.0	20.4 ± 14.4 ^b	21.5 ± 15.0
Total PA (METhr/week)	66.1 ± 44.8	61.2 ± 44.8	56.5 ± 39.3	61.7 ± 43.4
Sports PA (hr/week) ²	3.4 ± 4.6	2.7 ± 3.9	1.7 ± 2.6 ^{bc}	2.7 ± 3.9

	BMI < 25 Mean ± SD (n = 171)	BMI: 25 - 29.9 Mean ± SD (n = 137)	BMI ≥ 30 Mean ± SD (n = 131)	All Mean ± SD (n = 439)
Sport PA (METhr/week)	15.9 ± 24.0	11.3 ± 16.3 ^a	7.3 ± 12.3 ^b	11.9 ± 19.0

^f Past year physical activity assessed from interview-administered physical activity questionnaire conducted at the follow-up interview (i.e., ~30 months post-diagnosis).

^a Significant difference between BMI < 25 vs. BMI: 25-29.9, *p* < .05.

^b Significant difference between BMI < 25 vs. BMI ≥ 30, *p* < .05.

^c Significant difference between BMI: 25-29.9 vs. BMI ≥ 30, *p* < .05.

Table II

Adjusted[/] mammographic density measures by BMI in kg/m² (N = 439).

	BMI < 25 Mean ± SE (n = 171)	BMI: 25 - 29.9 Mean ± SE (n = 137)	BMI 30 Mean ± SE (n = 131)	P for trend
Total Breast Area (mm ²)	21,140 ± 778	27,752 ± 864 ^a	31,923 ± 925 ^{bc}	0.0001
Non-dense (fatty) area (mm ²)	17,030 ± 739	23,989 ± 820 ^a	28,521 ± 879 ^{bc}	0.0001
Dense Area (mm ²)	4,110 ± 277	3,763 ± 308	3,401 ± 330	0.11
% Dense Tissue	30.0% ± 1.1	20.4% ± 1.2% ^a	14.5% ± 1.3% ^{bc}	0.0001

[/] Adjusted for age, race/ethnicity, education, parity, disease stage, adjuvant therapy, tamoxifen use, breast cancer recurrence, smoking, physical activity, ever use of hormone replacement therapy, and time from diagnosis to mammogram.

^a Significant difference between BMI < 25 vs. BMI: 25-29.9, p < .05.

^b Significant difference between BMI < 25 vs. BMI 30, p < .05.

^c Significant difference between BMI: 25-29.9 vs. BMI 30, p < .05.

Adjusted¹ mean $\pm$ SE amount and percent of mammographic density by tertiles of sports/recreational physical activity stratified by BMI (N = 439).

Table III

<i>Dense Area</i>		BMI < 25 Mean $\pm$ SE (n = 171)		BMI: 25 - 29.9 Mean $\pm$ SE (n = 137)		BMI 30 Mean $\pm$ SE (n = 131)	
Physical Activity ²	n	Dense Area (mm ²)	n	Dense Area (mm ²)	n	Dense Area (mm ²)	
0.00 - 1.79	43	3666 $\pm$ 475	42	3530 $\pm$ 562	61	4058 $\pm$ 614	
1.80 - 10.99	51	4034 $\pm$ 428	51	3439 $\pm$ 474	45	3468 $\pm$ 675	
11.00 $\pm$	77	4445 $\pm$ 335	44	4541 $\pm$ 534	25	1474 $\pm$ 922 ^a	
<i>P for trend</i>		0.19		0.22		0.027	
<i>Percent Breast Density</i>							
Physical Activity ²	n	Breast Density (%)	n	Breast Density (%)	n	Breast Density (%)	
0.00 - 1.79	43	24.9 $\pm$ 2.6	42	18.2 $\pm$ 2.4	61	16.7 $\pm$ 1.7	
1.80-10.99	51	25.7 $\pm$ 2.3	51	21.5 $\pm$ 2.0	45	14.6 $\pm$ 1.5	
11.00 $\pm$	77	27.5 $\pm$ 1.8	44	22.1 $\pm$ 2.3	25	13.5 $\pm$ 2.3	
<i>P for trend</i>		0.43		0.27		0.17	

¹ Adjusted for age, race/ethnicity, education, parity, disease stage, adjuvant therapy, tamoxifen use, breast cancer recurrence, smoking, physical activity, ever use of hormone replacement therapy, and time from diagnosis to mammogram.

² The past 12 months of physical activity, in MET-hr/wk, was recalled during an in-person interview conducted at the follow-up clinic visit (~30 months after diagnosis)

^a Significant difference between 0.00 - 1.79 and 11.00+, p < .05.