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Pre-diagnosis physical activity and mammographic density in breast cancer survivors

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Abstract

Purpose—To investigate the association between physical activity (PA) and mammographic density in the year before diagnosis in a population-based sample of 474 women diagnosed with stage 0–IIIA breast cancer and enrolled in the Health, Eating, Activity, and Lifestyle Study.

Methods—We collected information on PA during an interview administered at a baseline visit scheduled within the first year after diagnosis. Participants recalled the type, duration, and frequency of different PAs for the year prior to their diagnosis. Dense area and percent density were estimated, from mammograms imaged approximately one year before diagnosis, as a continuous measure using a computer-assisted software program. Analysis of covariance methods were used to obtain mean density across PA tertiles adjusted for confounders. We stratified analyses by menopausal status and body mass index (BMI) because these factors strongly influence density.

Results—We observed a statistically significant decline in mammographic dense area (p for trend = 0.046) and percent density (p for trend = 0.026) with increasing level of sports/recreational PA in postmenopausal women with a BMI ≥ 30 kg/m^2. Conversely, in premenopausal women with a BMI < 30 kg/m^2, we observed a statistically significant increase in percent density with increasing level of sports/recreational PA (p for trend = 0.037).

Conclusions—Both mammographic dense area and percent density are inversely related to level of sports/recreational PA in obese postmenopausal women. Increasing PA among obese postmenopausal women may be a reasonable intervention approach to reduce mammographic density.

Keywords

breast cancer; body fat; exercise; obesity; weight

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INTRODUCTION

Strong evidence exists that the characteristics of breast tissue as seen on a mammogram, measured as mammographic dense area and percent density, provide information about breast cancer risk. Women with high levels of mammographic density have a four- to six-fold greater risk of developing breast cancer than women with lower levels of mammographic density; thus, mammographic density is a stronger predictor of breast cancer risk than most traditional risk factors such as first degree family history and ages at menarche, menopause, and first term pregnancy (1). Increased mammogram density also lowers sensitivity of screening mammography, which may explain the reduced sensitivity of mammography in premenopausal women who have elevated densities. Mammographic density reflects proliferation of the breast epithelium and stroma, in response to growth factors induced by current and past circulating sex hormone levels (2,3). Mammographic density may vary throughout lifetime, with the pattern reflecting the accumulated breast cancer risk at the time the mammogram was obtained. Factors that change mammographic density may also change breast cancer risk. 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.

Physical activity is associated with a reduced breast cancer risk (4). 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 (4). Only two studies have examined the relationship between physical activity and mammographic density (5,6). Physical activity may influence mammographic density by favorably changing certain hormones associated with mammographic density and breast cancer risk (7). Demonstration of beneficial changes in mammographic density associated with increased physical activity could be used to motivate women to be more physically active.

To investigate the association between physical activity and mammographic density, we examined physical activity levels reported for the year before diagnosis and the mammographic dense area and percent density estimated from mammograms retrieved from the year before diagnosis in a population-based sample of 474 breast cancer patients enrolled in the Health, Eating, Activity, and Lifestyle (HEAL) Study. Because of the known effects of menopausal status and BMI on mammographic density and breast cancer risk (1), we decided to examine the physical activity and mammographic density association separately for pre- and post-menopausal women, as well as women with a BMI < 30 and a BMI ≥ 30 kg/m^2.

METHODS

Study Setting, Subjects, and Recruitment

The 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 (8–10). Women were recruited into the HEAL Study through Surveillance, Epidemiology, End Results (SEER) registries in New Mexico, Los Angeles County (CA), and Western Washington. Details of the aims, study design, and recruitment procedures have been published previously (8–10). Comparable data on pre-diagnosis physical activity levels were available only for New Mexico and Washington. Therefore we limit analyses to participants from these two sites.

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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.

Participants completed in-person interviews at baseline (within their first year after diagnosis, 6 ± 2 months from diagnosis). Among the 817 women enrolled at baseline, 11 women did not complete the physical activity interview, 233 women did not have a pre-diagnosis mammogram, 58 women had mammograms that were of poor quality and could not be read accurately, 18 women had unknown menopausal status, and 23 women did not have a baseline body weight or height measure. Our analyses are based on the remaining 474 women. Baseline demographic and physiologic characteristics of the 474 women included in this analysis and the 817 women enrolled in the study did not differ. Written informed consent was obtained from each subject. 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

Physical Activity Assessment—We collected information on physical activity using an interview-administered questionnaire at a baseline visit scheduled within the first year after diagnosis. Participants were asked to recall the type, duration, and frequency of physical activities for the year prior to their breast cancer diagnosis. 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 (11). 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' (12).

Mammographic Density—Mammographic films, corresponding to approximately one year before diagnosis (15 ± 6 months from diagnosis), were retrieved from individual providers that each woman had specified. Each film was digitized using an Epson 1680 scanner (Epson America Inc., CA). 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 mm^2 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 (13). 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.

Anthropometrics—Trained staff measured weight and height in a standard manner at the baseline visit. 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 m^2. Two BMI categories were created based on the World Health Organization-National Institutes of Health cutoff for obesity: BMI < 30 kg/m^2 and BMI ≥ 30 kg/m^2 (14).

Other Variables—Standardized questionnaire information was collected at the baseline visit on medical history, reproductive history, family history of cancer, physician-diagnosed type 2 diabetes, smoking status, and selected demographic data. We collected information up to the woman's diagnosis separately from information from diagnosis to the time of the baseline interview. Postmenopausal status, assessed at the baseline interview, was defined as ages 55 and over or not menstruating in the past 12 months.

Statistical Analyses

Because of the known effects of menopausal status and higher BMI on mammographic density and breast cancer risk (1), we decided to examine the physical activity and mammographic density association separately for pre- and post-menopausal women, as well as women with a BMI < 30 and a BMI ≥ 30 kg/m^2. We calculated means and standard deviations of demographic and physiological characteristics of the study sample by menopausal status and BMI groups. Differences in means were compared using t-tests. Categorical variables were compared using chi-square analysis. We also examined the mean dense area and percent density by menopausal status and BMI.

We examined the continuous relationship between physical activity and mammographic density using Pearson correlations. 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 *total*, moderate- to vigorous-intensity physical activity and sports/recreational physical activity stratified by menopausal status and BMI. Categories of physical activity were created 1) based on current physical activity recommendations (< 30 min five days/wk or 2.5 hr/wk, 30 to 60 min five days/wk or 2.5 to 5 hr/wk, and ≥ 60 min five days/wk or 5+ hr/wk) (15,16) and 2) based on physical activity tertiles.

We adjusted for covariates associated with mammographic density including age (continuous), BMI (continuous), ethnicity, parity (nulliparous vs. parous), type 2 diabetes, age at menarche (continuous), HRT use, study site, education (continuous), and disease stage. 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 474 women included in this analysis, 151 (32%) were premenopausal and 323 (68%) were postmenopausal. The mean BMI of premenopausal and postmenopausal participants were 25.7 ± 5.2 kg/m^2 and 27.1 ± 5.8 kg/m^2, respectively (Table 1). Women with a BMI ≥ 30 exercise less than women with a BMI < 30.

Among premenopausal women, total breast area and non-dense area were lower, while dense area and percent density were greater among women with a BMI < 30 kg/m^2 compared to women with a BMI ≥ 30 kg/m ($p < .05$) (Table 2). However, among postmenopausal women, while total breast area and non-dense area were also lower, and percent mammographic density greater, among women with a BMI < 30 kg/m^2 compared to women with a BMI ≥ 30 kg/m^2 ($p < .05$), no statistically significant difference was observed in dense area between the two BMI groups.

Statistically significant adjusted Pearson correlations were observed between physical activity and mammographic density in obese women (r = −0.16 and r = −0.18 for dense area and percent dense tissue, p < .05). When stratifying by menopausal status, inverse associations were observed in both obese pre- and post-menopausal women, however statistical significance was reached only in obese postmenopausal women (r = −0.15 and r = −.017 for dense area and percent dense tissue, p < .05).

No statistically significant trends were observed between total physical activity or sports/recreational physical activity and dense breast area or percent mammographic density (Table 3); however, when we stratified analyses by menopausal status and BMI, statistical significant associations were observed between physical activity and mammographic density within certain menopausal and BMI subgroups (Table 4). When we categorized physical activity based on current physical activity recommendations, we observed a statistically significant trend of decreasing dense breast area (p for trend = 0.046) and percent mammographic density (p for trend = 0.026) with increasing level of sports/recreational physical activity among postmenopausal women with a BMI ≥ 30 kg/m^2 in the analysis of covariance which adjusted for age, BMI, ethnicity, study site, education, parity, type 2 diabetes, age at menarche, HRT use, and disease stage (Table 4). Conversely, in premenopausal women with a BMI < 30 kg/m^2, we observed a statistically significant trend of increasing percent mammographic density with increasing category of sports/recreational physical activity (p for trend = 0.037). Nonsignficant inverse associations were observed between amount or percent mammographic density and physical activity among premenopausal women with a BMI ≥ 30 kg/m^2 and postmenopausal women with a BMI < 30 kg/m^2. Associations were similar, but not statistically significant, when stratifying physical activity based on tertiles (data not shown). Further, associations were similar, but not statistically significant, when stratifying BMI by the median value (BMI = 25.8) (data not shown).

When we examined associations between physical activity and mammographic density 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 physical activity and mammographic density stratified by ethnicity and HRT use; similar associations were observed for both Non-Hispanic White and Hispanic White women, and HRT users and non-users (data not shown).

DISCUSSION

Both absolute amount of mammographic density and percent mammographic density were inversely related to recommended levels of sports/recreational physical activity among obese postmenopausal women. Specifically, we observed a 3,606 mm^2 or 66% difference in the amount of dense breast area between the least active and most active obese postmenopausal women (p < .05). When we examined associations using tertiles of physical activity rather than recommended levels of physical activity, similar, but not statistically significant, associations were observed. This finding is most likely due to the fact that, when using tertiles, the highest physical activity group was only performing ~2 hr/week of physical activity compared to ~5 hr/week of physical activity when using categories of physical activity based on current physical activity recommendations. Thus, higher amounts of physical activity may be necessary to favorably affect mammographic density in obese postmenopausal women. However, until more physical activity and mammographic density studies are conducted that either confirm or contradict our findings, caution should be used in interpreting our findings. While the overall sample size was relatively large, we did have a small sample of obese postmenopausal women; thus the reduction in mammographic density in the highest activity category may be due to chance.

Inverse associations between physical activity and mammographic density were also observed among obese premenopausal women; however, because of small sample sizes, statistical significance was not reached. Conversely a positive association between physical activity and mammographic density was observed in premenopausal women with a BMI < 30. Non-obese premenopausal women had higher amounts of mammographic density compared to obese premenopausal women and both non-obese and obese postmenopausal women; these latter three groups had similar amounts of dense breast tissue. The higher amounts of mammographic density observed in lean premenopausal women are most likely a reflection of higher circulating sex hormone concentrations (1). The finding that BMI modifies the physical activity and mammographic density association in premenopausal women is not surprising since BMI has been shown to modify the physical activity and breast cancer association (4). Furthermore, BMI is inversely related to breast cancer risk in premenopausal women, but positively related to breast cancer risk in postmenopausal women (17). More research examining the modifying effect of BMI and menopausal status on the physical activity and mammographic density association is necessary.

Only two previous studies have examined the association between physical activity and mammographic density, both in healthy women. Vachon et al. (5) investigated the association between physical activity and percent mammographic density in 1900 women. Physical activity was not associated with percent mammographic density among either pre- or post-menopausal women. However, their assessment of physical activity was limited to only one question. Gram et al. (6) examined the relationship between physical activity and mammographic density among 2720 Norwegian 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 remained consistent when stratified by menopausal status and tertiles of BMI. One recent study examined sedentary activities and percent mammographic density among 294 healthy Hispanic Women. Lopez et al. (18) observed a higher percent mammographic density for women who reported at least 3.5 hr/day of sedentary activities compared to women reporting less sedentary activities adjusted for age, education, BMI, parity, menopausal status, HRT use, and smoking status (p = 0.056).

One mechanism has been proposed to explain an association between physical activity and mammographic density. Physical activity may influence mammographic density by favorably changing certain hormones *that may be* associated with mammographic density, such as sex steroid hormones. Many published studies have shown an effect of exogenous estrogens on increasing mammographic density (19), however, the only published study 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, and an inverse association between free estradiol and percent dense tissue in postmenopausal women (20). The hypothesized mechanism of physical activity influencing mammographic density via sex hormone changes applies especially to obese postmenopausal women, who have higher levels of sex hormone concentrations than leaner postmenopausal women, due to the formation of estrogens in fatty tissue (10,21,22). 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 (7). In a recently published yearlong randomized controlled trial, exercise had a favorable effect on decreasing circulating sex hormone concentrations among overweight postmenopausal women (7).

The HEAL Study has several limitations and strengths. While the HEAL Study is a prospective cohort study, this analysis is cross-sectional in design. Physical activity was also assessed retrospectively, and is, therefore, subject to recall bias. Other limitations are that we assessed menopausal status and BMI at the baseline visit, which corresponds to approximately six months post-diagnosis or approximately 21 ± 12 months after the time of mammogram. Some women may have experienced changes in menopausal status and BMI from the time of their mammogram to the time of the baseline visit. However, when we defined menopausal status as ages 57 and over, our findings were similar to what we observed when menopausal status was defined as ages 55 and over. Another limitation is that we did not have any information on timing of the mammogram in relation to the menstrual cycle among the premenopausal women. Mammographic density is lower in the follicular phase than in the luteal phase (23). Another limitation is sample size; while our overall sample size was relatively large, we did have a small sample of obese pre- and post-menopausal women; thus associations observed between physical activity and mammographic density among these groups should be interpreted with caution. Lastly, while not necessarily a limitation, physical activity and mammographic mammographic density were measured in women with subclinical disease (i.e., we measured physical activity and mammographic density in women approximately one year before their breast cancer diagnosis). However, we have no reason to believe that associations between physical activity and mammographic mammographic density would be different among a cohort of healthy women since we examined mammographic density in the unaffected breast. We also excluded women diagnosed with bilateral breast cancer.

Major strengths of our study are the quality of the physical activity data that were obtained from a reliable and valid 29-item interview-administered questionnaire; we measured weight and height whereas many previous studies used self report of these measures; we recruited both Non-Hispanic White and Hispanic White women; and we used a computer-assisted method to assess mammographic density.

Measuring mammographic density as a continuous scale may provide more information than the BIRADS or Wolfe categorical measures (1,13), 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 assesses mammographic density with 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 often associated 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 one- and two-dimensional views. Ongoing research focused on developing a more precise volumetric method of assessing mammographic density is currently being conducted by Pawluczyk and colleagues (24).

In conclusion, mammographic density differs from other breast cancer risk factors in the strength of its association with breast cancer, in being present in the tissue from which breast cancer arises, and because it is modifiable (1). Information will soon be available from randomized controlled trials (e.g., the PEPI Trial; 25) designed to determine the effects of interventions on breast cancer risk. Indirectly these trials will provide information on the value of short-term changes in mammographic density in predicting an intervention effect on breast cancer risk. Future exercise trials will then be able to observe if physical activity changes mammographic density a clinically significant amount to affect breast cancer risk.

Demonstration of beneficial changes in mammographic density associated with increased physical activity levels could be used to motivate women to be more physically active. Although it remains to be determined whether the effect of increasing physical activity decreases mammographic density, it is known that both physical inactivity and mammographic density are associated with breast cancer risk (1,4). Furthermore, many studies have identified obesity as an important negative factor for postmenopausal breast cancer risk and prognosis, and physical activity is associated with weight loss and maintenance (26). Increasing physical activity among obese pre- and post-menopausal women may be a reasonable intervention approach to reduce mammographic density, thereby influencing breast cancer risk and recurrence.

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References

1. Boyd NF, Lockwood GA, Byng JW, et al. Mammographic densities and breast cancer risk. CEBP 1998;7:1133–44.
2. Oza AM, Boyd NF. Mammographic parenchymal patterns: a marker of breast cancer risk. Epidemiol Rev 1993;15:196–208. [PubMed: 8405204]
3. Byrne C, Colditz GA, Willett WC, et al. Plasma insulin-like growth factor, IGF-binding protein 3, and mammographic density. Cancer Research 2000;60:3744–48. [PubMed: 10919644]
4. Berglund G. Anthropometry, physical activity and cancer of the breast and colon. IARC Sci Publ 2002;156:237–41. [PubMed: 12484177]
5. 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]
6. Gram IT, Funkhouser E, Tabar L. Moderate physical activity in relation to mammographic patterns. CEBP 1999;8:117–122.
7. McTiernan A, Tworoger SS, Ulrich CM, et al. Effect of Exercise on Serum Estrogens in Postmenopausal Women A 12-Month Randomized. Clinical Trial Cancer Research 2004;64:2923–28.
8. 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]
9. 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.
10. 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]
11. Kriska A. Modifiable activity questionnaire. Med Sci Sports Exer 1997;29:S73–78.
12. 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.
13. 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. JNCI 1995;87:670–5. [PubMed: 7752271]
14. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults – the evidence report. Obesity Res 1998;6(Suppl 2):51S–209S.

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15. Pate RR, Pratt M, Blair S, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995;273(5):402–7. [PubMed: 7823386]
16. Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrates, Fiber, Fat, Protein and Amino Acids (Macronutrients): A Report of the Panel on Macronutrients, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Washington, DC: National Academies Press; 2002. p. 12-23.
17. Cleary MP, Maihle NJ. The role of body mass index in the relative risk of developing premenopausal versus postmenopausal breast cancer. Proc Soc Exp Biol Med 1997;216(1):28–43. [PubMed: 9316608]
18. Lopez P, Van Horn L, Colangelo LA, et al. Physical inactivity and percent breast density among Hispanic women. Int J cancer 2003;107(6):1012–6. [PubMed: 14601063]
19. Marchesoni D, Driul L, Ianni A, et al. Postmenopausal hormone therapy and mammographic breast density. Maturitas. 2005 June 3;
20. 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]
21. White J. Breast density and cancer risk: what is the relationship? JNCI 2000;92:443. [PubMed: 10716955]
22. Potischman N, Swanson CA, Siiteri P, Hoover RN. Reversal of relation between body mass and endogenous estrogen concentrations with menopausal status. JNCI 1996;88:756–58. [PubMed: 8637031]
23. White E, Velentgas P, Mandelson MT, Lehman CD, Elmore JG, Porter P, Yasui Y, Taplin SH. Variation in mammographic breast density by time in menstrual cycle among women aged 40–49 years. J Natl Cancer Inst 1998;90(12):906–10. [PubMed: 9637139]
24. 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]
25. Ursin G, Palla SL, Reboussin BA, Slone S, Wasilauskas C, Pike MC, Greendale GA. Post-treatment change in serum estrone predicts mammographic percent density changes in women who received combination estrogen and progestin in the Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. JCO 2004;22(4):2842–8.
26. Irwin ML, Yasui Y, Ulrich C, et al. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. JAMA Jan 15;2003 289(3):323–30. [PubMed: 12525233]

Table 1

Physiological and demographic characteristics of HEAL participants stratified by pre-diagnostic menopausal status (N = 474).

	Premenopausal		**Postmenopausal**	
	BMI < 30	**BMI ≥ 30**	**BMI < 30**	**BMI ≥ 30**
	Mean ± SD (n = 127)	**Mean ± SD (n =24)**	**Mean ± SD (n = 240)**	**Mean ± SD (n= 83)**
Age (years)	46.0 ± 4.7	47.5 ± 4.7	62.7 ± 9.3	60.0 ± 8.2
Weight (kg)	64.5 ± 9.8	92.1 ± 13.6 [a]	64.4 ± 9.1	89.9 ± 14.2 [b]
Height (cm)	164.6 ± 6.8	161.8 ± 7.5	162.4 ± 6.6	160.8 ± 6.8
BMI (wt in kg/ht in m^2)	23.8 ± 3.1	35.2 ± 4.3 [a]	24.4 ± 3.2	34.7 ± 4.3 [b]
Education (% H.S. graduate)	99%	100%	95%	95%
Site				
New Mexico	70%	63%	75%	63%
Seattle	30%	37%	25%	37%
Ethnicity				
Non-Hispanic White	82%	79%	84%	87%
Hispanic	18%	21%	16%	13%
Type 2 diabetes (%)	2.4%	0%	4.2%	18.1% [b]
Nulliparous (%)	24%	37%	15%	16%
Current HRT use[1] (%)	9%	17% [a]	80%	69% [b]
Age at menarche (yrs)	12.7 ± 1.6	12.6 ± 1.6	12.7 ± 1.6	12.1 ± 1.7
Total PA (hr/week) [2]	*18.3 ± 11.1*	*18.0 ± 15.5*	*19.7 ± 14.4*	*19.5 ± 15.3*
Total PA (METhr/week)	*58.1 ± 33.9*	*53.0 ± 40.4*	*58.2 ± 42.8*	*54.8 ± 44.2*
Sports PA (hr/week) [2]	3.9 ± 4.6	2.1 ± 3.7 [a]	3.1 ± 3.8	1.9 ± 3.1 [b]
Sport PA (METhr/week)	19.4 ± 21.8	10.2 ± 19.0 [a]	13.6 ± 17.1	7.8 ± 12.6 [b]

[1] HRT = Hormone replacement therapy

[2] Year-before diagnosis physical activity assessed from interview-administered physical activity questionnaire conducted at baseline (i.e., within 1st year after diagnosis).

[a] Significant difference between premenopausal women with a BMI < 30 vs. premenopausal women with a BMI ≥ 30, p < .05.

[b] Significant difference between postmenopausal women with a BMI < 30 vs. postmenopausal women with a BMI ≥30, p < .05.

Table 2

Unadjusted mammographic density measures by menopausal status and body mass index (BMI) (N = 474).

	Premenopausal		Postmenopausal	
	BMI < 30	**BMI ≥ 30**	**BMI < 30**	**BMI ≥ 30**
	Mean ± SD (n = 127)	**Mean ± SD (n =24)**	**Mean ± SD (n = 240)**	**Mean ± SD (n= 83)**
Total Breast Area (mm^2)	22,342 ± 9,087	32,911 ± 12,702[a]	25,278 ± 8,635	35,158 ± 15,259[b]
Non-dense (fatty) area (mm^2)	14,794 ± 8,145	27,318 ± 9,981[a]	19,915 ± 8,373	30,166 ± 13,800[b]
Dense Area (mm^2)	7,549 ± 3,969	5,592 ± 6,534[a]	5,363 ± 4,150	4,992 ± 5,338
% Dense Tissue	36.2% ± 16.9	15.6% ± 13.4%[a]	22.1% ± 15.0%	14.2% ± 12.6[b]

[a] Significant difference between premenopausal women with a BMI < 30 vs. premenopausal women with a BMI ≥ 30, p < .05.

[b] Significant difference between postmenopausal women with a BMI < 30 vs. postmenopausal women with a BMI ≥30, p < .05.

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Table 3

Adjusted[1] mean amount and percent of mammographic breast density by tertiles of total and sports/recreational physical activity (N = 474).

Total Physical Activity	**n**	**Dense Area (mm^2)**	**Breast Density (%)**
0.36–34.99	158	6125 ± 356	25.2 ± 1.2
35.00–63.49	158	5646 ± 355	22.8 ± 1.2
63.50+	158	5941 ± 355	24.5 ± 1.1
P for trend		0.72	0.66
Sports/Recreational Physical Activity	**n**	**Dense Area (mm^2)**	**Breast Density (%)**
0.00–2.25	158	5890 ± 362	22.9 ± 1.2
2.26–13.49	158	6025 ± 356	25.1 ± 1.2
13.50+	158	5798 ± 365	24.6 ± 1.2
P for trend		0.86	0.30

[1] Adjusted for age, BMI, ethnicity, study site, education, parity, age at menarche, type 2 diabetes and current HRT use.

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Table 4

Adjusted[1] mean amount and percent of mammographic breast density by recommended levels of sports/recreational physical activity[2] stratified by menopausal status and body mass index in kg/m^2 (BMI) (N = 474).

	Premenopausal				Postmenopausal			
	BMI < 30		BMI ≥30		BMI < 30		BMI ≥ 30	
	Mean ± SE (n = 127)		Mean ± SE (n = 24)		Mean ± SE (n = 240)		Mean ± SE (n= 83)	
Physical Activity[2]	**n**	**Dense Area (mm^2)**	**n**	**Dense Area (mm^2)**	**n**	**Dense Area (mm^2)**	**n**	**Dense Area (mm^2)**
0.0–7.49	46	6867 ± 604	17	6848 ± 1662	126	5557 ± 371	59	5504 ± 638
7.5–14.99	24	7200 ± 804	3	2412 ± 4105	39	5249 ± 678	15	5334 ± 1322
15.0+	57	8247 ± 530	4	2643 ± 3616	75	5144 ± 486	9	1898 ± 1696[a]
P for trend		0.10		0.34		0.50		0.046
Physical Activity[2]	**n**	**Breast Density (%)**	**n**	**Breast Density (%)**	**n**	**Breast Density (%)**	**n**	**Breast Density (%)**
0.0–7.49	46	32.8 ± 2.4	17	18.6 ± 2.9	126	22.7 ± 1.3	59	16.1 ± 1.5
7.5–14.99	24	34.4 ± 3.2	3	6.7 ± 7.1	39	21.5 ± 2.4	15	15.0 ± 3.1
15+	57	39.7 ± 2.1[b]	4	9.2 ± 6.2	75	21.5 ± 1.7	9	5.4 ± 3.9 [a]
P for trend		0.037		0.22		0.60		0.026

[1] Adjusted for age, BMI, ethnicity, study site, education, parity, age at menarche, type 2 diabetes and current HRT use.

[2] Categories of sports/recreational MET-hr/wk: 0.0 to 7.49 is equivalent to less than ~ 2.5 hr/wk at a 3 MET level; 7.5 to 14.99 is equivalent to ~2.5 to 5 hr/wk at a 3 MET level; 15.0+ is equivalent to ~ 5+ hr/wk at a 3 MET level.

[a] $p < 0.05$ compared to 0.0–7.49 and 7.5–14.99 MET-hr/wk

[b] $p < 0.05$ compared to 0.0–7.49 MET-hr/wk