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Physical Activity and Incidence of Postmenopausal Breast Cancer [Original Articles]

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Outline

- [Abstract](#)
- [Subjects and Methods](#)
 - [The Iowa Women's Health Study Cohort](#)
 - [Questionnaire](#)
 - [Cohort Follow-up](#)
 - [Data Analysis](#)
- [Results](#)
- [Discussion](#)
- [References](#)

Graphics

- [Table 1](#)
- [Table 2](#)
- [Table 3](#)

Abstract

Whether physical activity reduces the risk of postmenopausal breast cancer is uncertain; few studies have addressed this issue. We examined the association of leisure physical activity with breast cancer incidence among 37,105 postmenopausal participants in the Iowa Women's Health Study. Women reporting the highest level of physical activity at baseline compared with women with the lowest level of activity had an age-adjusted relative risk of breast cancer of 0.92 (95% confidence interval = 0.80–1.05). Women reporting any regular leisure-time physical activity

had a relative risk of 0.97 (95% confidence interval = 0.87–1.08) compared with those reporting no such regular physical activity. Adjustment for potential confounders did not appreciably alter the findings. There is little evidence from this study that physical activity later in life is associated to any appreciable extent with breast cancer incidence.

In 1999, an estimated 175,000 new cases and 43,300 deaths from breast cancer in women were expected to occur in the United States. ¹ The vast majority of these events affect postmenopausal women. Several risk factors for breast cancer are known, including early age at menarche, late onset of menopause, and nulliparity. ² Whether physical activity reduces incidence of postmenopausal breast cancer, however, is uncertain. Of 21 studies to address this question, 15 have suggested that higher levels of physical activity (leisure time and/or occupational) performed at varying points during life, are associated with lower incidence of postmenopausal breast cancer. ^{3–17} Five studies documented no apparent association, ^{18–22} whereas one study suggested an increased risk of breast cancer for physically active postmenopausal women. ²³

Among cohort studies that examined the association of physical activity with incidence of breast cancer, only one looked at effects of activity in the postmenopausal years as a possible etiologic factor. ¹⁶ The goal of the present study was to determine the association of incident breast cancer with physical activity reported among postmenopausal women ages 55–69 years in the Iowa Women's Health Study.

Subjects and Methods [†]

The Iowa Women's Health Study Cohort [†]

The initial purpose of the Iowa Women's Health Study was to assess the relation of body fat distribution with cancer incidence and mortality. In January 1986, a 16-page questionnaire was sent to 99,826 randomly selected women ages 55–69 years with Iowa driver's licenses. Questionnaires were returned by 41,837 (42.7%) of the women. Follow-up questionnaires were sent in 1987 (91% response), 1989 (89%), 1992 (83%), and 1997 (79%) to update residence, vital status, and medical history.

Questionnaire [†]

Current physical activity status at baseline was ascertained by three questions. The first question, used in the Gallup Poll, ²⁴ asked: "Aside from any work you do at home or at a job, do you do anything regularly—that is, on a daily basis—that helps you keep physically fit?" The other questions assessed frequency of moderate physical activity (for example, bowling, golf, light sports or physical exercise, gardening, or taking long walks) and vigorous activity (for example, jogging, racket sports, swimming, aerobics, or strenuous sports). Participants could answer "rarely or never," "a few times a year," "a few times a month," "about once a week," "two to four times a week," or "more than four times a week." Three levels of physical activity were derived from the questions about moderate and vigorous activity. Women who participated in vigorous activity two or more times per week and those who reported moderate activity more than four times per week were categorized as having a "high" level of physical activity. Cohort members who reported vigorous activity once per week or moderate activity one to four times per week were classified as having a "medium" activity level. All other women who reported less activity were placed into the "low" activity category.

Family history of breast cancer was classified as "yes" if the mother, a daughter, or a sister had been diagnosed with breast cancer. Women were also asked their height and weight and to have someone measure the circumferences of their waist at one inch above the umbilicus and the hips at maximum. These reliable measurements ²⁵ were used to calculate body mass index (BMI, kg/m²) (both at baseline and 18 years of age) and waist-to-hip circumference ratio. Participants were also asked about estrogen use (never, current, or past) and duration, smoking status (never, current, or past), cigarettes smoked per day, age at menarche, age at first livebirth, age at menopause, reasons for menopause (natural, hysterectomy, medication, or other), medical conditions (including diabetes mellitus and prevalent cancers), whether or not they had had a mastectomy, alcohol intake, and highest level of education obtained. Dietary data were collected by a food frequency questionnaire but were not used for adjustment because dietary variables were not appreciably related to breast cancer incidence in this cohort.

Cohort Follow-up ²⁴

We identified incident cases of breast cancer between 1986 and 1995 from the State Health Registry of Iowa, a member of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER). Cases in the cohort were identified annually using computer linkage by name, maiden name, date of birth, and Social Security number. Deaths were determined through the follow-up questionnaires, the State Health Registry, and the National Death Index.

Data Analysis ²⁴

From the 41,837 participants, we excluded from this analysis women who at baseline were premenopausal (N = 569), had cancer other than skin cancer (N = 2,293), or had had a total or partial mastectomy (N = 1,870). Thus, a total of 37,105 participants were available for follow-up. Cohort members were at risk of developing breast cancer until diagnosis of breast cancer, death, relocation outside of Iowa, or other loss to follow-up. Otherwise, person-years were computed from the date of the 1986 baseline questionnaire through December 31, 1995.

The prevalence of various characteristics of the participants was compared among the three levels of the physical activity index variables. We computed age- and multivariate-adjusted relative risks (RRs) and 95% confidence intervals (CIs) from proportional hazards regression models. The multivariate models included risk factors for breast cancer that were also associated with physical activity: age, age at menopause, age at first livebirth, BMI at 18 years of age, education, family history of breast cancer, and estrogen use. Although a positive association of breast cancer with alcohol intake was previously reported in this cohort, ²⁶ it was not independently associated when analyzed with extended follow-up. The body size variables, waist-to-hip ratio and BMI, were included in a separate model.

Results ²⁴

Women with high or medium levels of physical activity compared with a low level reported, on average, later age at menopause, lower waist-to-hip ratio and BMI, and higher levels of education and alcohol intake (Table 1). Women with high or medium levels of physical activity were less likely to smoke, were less likely to have diabetes mellitus, and had a slightly higher prevalence of estrogen use. Urban and rural women had similar levels of physical activity (data not shown).

TABLE 1. Distribution (%) of Variables by Physical Activity Level among the Iowa Women's Health Study Cohort

Variable*	Physical Activity Level		
	Low N = 17,222	Medium N = 10,030	High N = 9,111
Menarche >12 years	57.4	57.5	56.9
Natural menopause	65.8	67.0	66.9
Menopause age >49 years	46.2	48.8	50.0
Nulliparous	9.0	9.0	9.2
Age at first livebirth ≥30 years	6.6	6.4	5.9
Waist-to-hip ratio >0.82	60.3	52.3	47.0
BMI >26.11 kg/m ²	55.3	48.0	41.8
BMI at age 18 years >21.19 kg/m ²	50.6	50.1	49.5
Education >high school graduate	34.4	41.4	45.4
Alcohol intake ≥5 gm/day	17.8	19.6	19.5
Family history of breast cancer	12.2	11.7	12.4
Current smoker	19.1	12.5	9.9
Both ovaries removed	18.0	18.2	17.3
Uterus removed	33.2	32.9	32.8
Diabetes mellitus	7.2	5.4	5.3
Estrogen use (ever)	37.1	39.7	39.1

BMI = body mass index.

* Number of persons may not equal total for each level because of missing values.

Table 1. Distribution (%) of Variables by Physical Activity Level among the Iowa Women's Health Study Cohort BMI = body mass index. * Number of persons may not equal total for each level because of missing values.

Over the 10 years of follow-up, 1,380 cases of breast cancer occurred among the 37,105 women at risk. There was no apparent association of incident breast cancer with baseline levels of leisure-time physical activity (Table 2). Compared with a low activity level, the multivariate-adjusted RR for the medium level of activity was 1.12 (95% CI = 0.99–1.28) and for the high level, it was 0.95 (95% CI = 0.83–1.10). Women who exercised regularly, vs those who did not, did not have a lower risk of breast cancer (multivariate-adjusted RR of 0.99, 95% CI = 0.89–1.11).

TABLE 2. Relative Risks of Breast Cancer for Physical Activity Variables

	Cases	Person-years	RR*	95% CI	RR†	95% CI	RR‡	95% CI
Physical activity levels								
Low§	638	157,258	1.00		1.00		1.00	
Medium	408	92,417	1.08	0.95-1.22	1.07	0.94-1.22	1.12	0.99-1.28
High	316	84,300	0.92	0.80-1.05	0.89	0.77-1.02	0.95	0.83-1.10
Any regular physical activity								
No§	805	195,697	1.00		1.00		1.00	
Yes	565	140,156	0.97	0.87-1.08	0.95	0.85-1.06	0.99	0.89-1.11
Moderate physical activity								
Rarely or never§	281	68,246	1.00		1.00		1.00	
Few times/month to once/week	394	95,494	1.00	0.86-1.17	1.01	0.86-1.18	1.03	0.88-1.20
2-4 times/week	440	103,135	1.03	0.89-1.20	1.02	0.87-1.19	1.08	0.92-1.26
>4 times/week	256	70,378	0.87	0.73-1.03	0.85	0.71-1.02	0.92	0.77-1.10
Vigorous physical activity								
Rarely or never§	1,103	277,639	1.00		1.00		1.00	
Few times/month to once/week	140	29,065	1.23	1.03-1.47	1.20	1.00-1.44	1.25	1.04-1.50
2-4 times/week	91	20,692	1.13	0.91-1.40	1.10	0.88-1.37	1.14	0.92-1.43
>4 times/week	31	7,748	1.01	0.71-1.45	0.97	0.67-1.41	1.05	0.72-1.52

* Adjusted for age (continuous).

† Adjusted for age (continuous), age at menopause in years (<45, 45-49, or >49), age at first live birth (<30, ≥30, or nulliparous), body mass index at 18 years of age (continuous), education (<high school, high school, some college, or college+), family history of breast cancer (yes or no), and estrogen use (never, current, or past).

‡ Also adjusted for waist-to-hip ratio (continuous), body mass index (continuous), and body mass index squared (continuous).

§ Referent category.

Table 2. Relative Risks of Breast Cancer for Physical Activity Variables* Adjusted for age (continuous).† Adjusted for age (continuous), age at menopause in years (<45, 45-49, or >49), age at first live birth (<30, ≥30, or nulliparous), body mass index at 18 years of age (continuous), education (<high school, high school, some college, or college+), family history of breast cancer (yes or no), and estrogen use (never, current, or past).‡ Also adjusted for waist-to-hip ratio (continuous), body mass index (continuous), and body mass index squared (continuous).§ Referent category.

We also calculated RRs for the individual questions on moderate and vigorous activity frequency (Table 2). The women with moderate exercise more than four times per week had a multivariate-adjusted RR of 0.92 (95% CI = 0.77-1.10) vs those who rarely or never exercised moderately. Those who exercised vigorously more than four times per week compared with those who exercised vigorously never or a few times per year had a multivariate-adjusted RR of 1.05 (95% CI = 0.72-1.52). Women who participated in vigorous leisure-time physical activity a few times per month up to once per week, however, were 1.25 times more likely than those who rarely or never exercised vigorously to have developed postmenopausal breast cancer (multivariate-adjusted 95% CI = 1.04-1.50). When we adjusted moderate and vigorous activity for each other, the results were similar. For example, in the simultaneous model, the multivariate-adjusted RRs for the four categories of increasing frequency of moderate activity were 1.0, 1.00, 1.03, and 0.90, and for vigorous activity were 1.0, 1.25, 1.14, and 1.16.

The results shown in Table 2 were virtually unchanged when (1) women who reported heart disease at baseline were excluded or when (2) analysis was restricted to women who reported natural menopause (data not shown). There also was no appreciable evidence of heterogeneity of association between physical activity and breast cancer according to strata of BMI, parity, estrogen use, family history of breast cancer, or energy intake (Table 3).

TABLE 3. Age-Adjusted Relative Risk (RR) and 95% Confidence Interval (CI) of Breast Cancer for Physical Activity Levels Stratified by Several Other Characteristics

	RR and 95% CI for Physical Activity Level				
	Low*	Medium		High	
		RR	95% CI	RR	95% CI
BMI quartile					
1	1.00	1.42	1.08-1.86	1.01	0.75-1.35
2	1.00	1.18	0.91-1.54	1.02	0.78-1.35
3	1.00	0.93	0.73-1.18	0.82	0.63-1.07
4	1.00	1.02	0.80-1.30	1.02	0.78-1.33
Parity					
0	1.00	0.74	0.49-1.12	0.80	0.53-1.21
1 or 2	1.00	1.33	1.07-1.65	1.02	0.80-1.30
>2	1.00	1.03	0.88-1.22	0.89	0.74-1.06
Estrogen use					
Never	1.00	1.13	0.97-1.33	0.89	0.74-1.06
Past	1.00	0.97	0.76-1.23	0.97	0.76-1.26
Current	1.00	1.07	0.75-1.52	0.88	0.61-1.28
Family history of breast cancer					
No	1.00	1.05	0.92-1.21	0.92	0.79-1.07
Yes	1.00	1.20	0.88-1.83	0.88	0.63-1.25
Energy intake quartile					
1	1.00	1.18	0.91-1.53	0.98	0.74-1.30
2	1.00	1.03	0.80-1.32	0.85	0.65-1.12
3	1.00	1.12	0.88-1.43	1.02	0.78-1.33
4	1.00	0.99	0.78-1.27	0.81	0.62-1.06

* Referent category.

Table 3. Age-Adjusted Relative Risk (RR) and 95% Confidence Interval (CI) of Breast Cancer for Physical Activity Levels Stratified by Several Other Characteristics* Referent category.

Discussion

Few previous studies have addressed the association of postmenopausal breast cancer with levels of physical activity performed after menopause. All were case-control studies.

Friedenreich and Rohan⁷ asked Australian cases and controls to report hours per week spent on recreational activity for both the summer and winter seasons. Among 258 pairs of postmenopausal women, those who exerted greater than 4,000 kcal/week (the highest quartile) had an adjusted breast cancer odds ratio (OR) of 0.73 (95% CI = 0.44-1.20) compared with those who did not exercise. There was no evidence of a dose response. In Japan, Ueji *et al*¹⁵ compared reported recreational physical activity during adulthood between 59 postmenopausal breast cancer cases and 127 controls. Moderate levels of activity were associated with a slight reduction (OR = 0.71; 95% CI = 0.21-2.18) and high levels with a large reduction in the OR (0.49; 95% CI = 0.22-1.94). Similar results were observed when level of occupational physical activity was analyzed. In another case-control study,⁹ Japanese postmenopausal women who "exercised for health" two times per week or more had an OR of 0.72 (95% CI = 0.53-0.97), and those who exercised occasionally had an OR of 0.93 (95% CI = 0.75-1.16) compared with those who did not exercise for health. Among 938 postmenopausal women more than 55 years of age in Washington State,¹¹ the OR of breast cancer was 0.6 (95% CI = 0.5-0.9), comparing those who reported any, vs no, regular physical activity. There was also an inverse association with other indices of physical activity: energy expenditure, hours per week, and intensity level. In a prospective study of college alumnae in the United States, Sesso *et al*¹⁶ measured baseline physical activity among women age 55 years and older. Compared with women who reported the lowest level of physical activity, the risk of breast cancer (N = 81 events) was slightly reduced in those who reported moderate activity (RR = 0.95; 95% CI = 0.58-1.57) and substantially reduced in those who reported high levels of activity (RR = 0.49; 95% CI = 0.28-0.86).

In the large cohort study presented here, there was no evidence to support the hypothesis that regular physical activity is associated with reduced breast cancer risk in postmenopausal women.

In fact, vigorous activity from a few times per month up to once per week was associated with slightly increased breast cancer incidence. The differing conclusions between this and previous studies may relate to differences in size and design. Unlike the case-control studies, our cohort study would not be subject to recall bias, as measurements for this study were taken before the onset of breast cancer. Furthermore, difficulties of appropriate selection of a control group were avoided by using a prospective design.

A possible explanation for our null finding, however, could be error in the measurement of physical activity. This study had a single assessment, which would be less valid than multiple measures. We assessed current, leisure-time activity; we did not measure past or nonleisure physical activity. We also did not measure duration or intensity of physical activities. The questionnaire was mailed in winter, which could have resulted in misclassification for some women who were seasonally active only. It is also unknown what type of physical activity might be most important to breast cancer. Nevertheless, these same physical activity measures were inversely associated with overall and cardiovascular disease mortality in this cohort, indicating that the questionnaire is sensitive enough to detect major disease trends. [27,28](#)

The relevant period in life during which physical activity might impact on breast cancer risk is incompletely known. Significant premenopausal physical activity can delay age at menarche and cause alterations in the menstrual cycle, reducing the risk of breast cancer. Exercise after menopause may or may not impact on biological mechanisms thought to mediate carcinogenesis in the breast. It is plausible that postmenopausal exercise decreases risk of breast cancer, for example, by altering body weight and decreasing serum levels of estradiol, estrone, and androgens or improving insulin sensitivity. [29](#)

Other prospective cohort studies have investigated the association of leisure-time physical activity and postmenopausal breast cancer incidence, but none measured exercise among exclusively postmenopausal women at baseline. In the first National Health and Nutrition Examination Survey (NHANES I), both recreational and nonrecreational activity were measured at baseline among both pre- and postmenopausal women. Women who were in the lowest exercise level were 1.7 times (95% CI = 0.8–2.9) more likely to develop postmenopausal breast cancer compared with those who were very active. [5](#) Thune *et al*[12](#) followed a cohort of Norwegian women. Women who indicated that they exercise regularly in the baseline survey had a 33% reduction in risk (95% CI = 0.41–1.10) for postmenopausal breast cancer incidence compared with those who indicated minimal leisure-time activity. [12](#) In a study of college alumnae, the combined RR for pre- and postmenopausal breast cancer of those subjects who participated in sports during college was 0.96. [18](#) In the Framingham Heart Study, exercise was measured at baseline in both pre- and postmenopausal women who were then followed for up to 28 years. The majority of cases (106 of 111) were postmenopausal at time of diagnosis. Women in the highest activity quartile had an RR of breast cancer of 1.6 (95% CI = 0.9–3.0) compared with those in the lowest activity quartile. [23](#)

In conclusion, these data from the Iowa Women's Health Study do not support the hypothesis that postmenopausal leisure-time physical activity reduces incidence of postmenopausal breast cancer. It remains possible, however, that a weak effect was missed by our brief assessment of physical activity.

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