Moderate Physical Activity in Relation to Mammographic Patterns[1]

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Abstract

High-risk mammographic patterns may be used as a surrogate end point for breast cancer in etiologic research as well as in prevention studies. Physical activity may be one of the few modifiable risk factors for breast cancer. We examined the relationship between physical activity and mammographic patterns among 2720 Norwegian women, ages 40–56 years, who participated in both the Second and Third Tromsø studies. Epidemiologic data were obtained through questionnaires. Two questions from the Second Tromsø study and five questions from the Third elicited information on physical activity. The mammograms were categorized into five groups based on anatomical-mammographic correlations. For analysis, patterns I through III were combined into a low-risk group and patterns IV and V into a high-risk group. Odds ratios that were adjusted for age, education, menopausal status, body mass index, parity, age at menarche, oral contraceptive use, and alcohol intake, with 95% confidence intervals, were estimated using logistic regression. Women who reported moderate physical activity, *i.e.*, more than 2 h/week, were 20% less likely (odds ratio, 0.8; 95% confidence interval, 0.6–1.1) to have high-risk mammographic patterns compared with those who reported being inactive. This relationship remains consistent when stratified by menopausal status, parity, and tertiles of body mass index. However, all of the associations between various measures of physical activity and high-risk patterns found in this study are weak with confidence intervals that include 1.0. Thus, chance is a reasonable explanation for the weak associations found. The relationship between physical activity and high-risk patterns should be examined further as a means to explore the biologic mechanisms relating physical activity to breast cancer risk.

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Introduction

High-risk patterns may be used as a surrogate end point for breast cancer in etiologic research as well as in prevention studies. Women with high-risk or dense mammographic patterns have a risk of breast cancer that is higher than that associated with most other major risk factors for the disease (1–4). The biologic bases for the relationship between mammographic patterns and breast cancer are not understood. Spicer *et al.* (5) hypothesized that mammographic densities reflect mitotic activity in breast tissue that, in turn, is determined by the amount of circulating estradiol and progesterone (6). Previous reports (1, 2, 7) indicate that several hormonally related breast cancer risk factors such as parity, age at menarche, and age at first birth are independently associated with mammographic patterns.

It has been hypothesized that a woman's level of physical activity is inversely associated with her risk of breast cancer (8, 9). A recent review (10) showed that, of the 21 epidemiologic studies published by December 1997, 15 studies supported this notion, whereas 4 studies found no association, and 2 studies found an increased risk of breast cancer associated with physical activity. Use of intermediate end points for breast cancer may be useful when the association between physical activity and breast cancer risk is explored. The relationship between physical activity and high-risk mammographic patterns is largely unknown. The purpose of this study was to investigate whether moderate physical activity may influence the mammographic pattern among women, ages 40–56 years, involved in a population-based screening.

Materials and Methods

Study Population. The Second and Third Tromsø studies, conducted in 1979–1980 and 1986–1987, respectively, included both men and women living in the municipality of Tromsø, northern Norway. The Tromsø studies are collaborative undertakings of the National Health Screening Service and the Faculty of Medicine of the University of Tromsø in close cooperation with the local health authorities. The main objectives were to examine changes in cardiovascular risk factors in the population and determinants of these changes. The participants completed one questionnaire at the screening facility and another at home. The first questionnaire asked about disease history and aspects of living habits including two questions—identical in the two surveys—on the levels of physical activity at work and leisure. Height was measured to the nearest centimeter, and weight was measured to the nearest half kilogram on regularly calibrated scales. A nurse asked the women about menopausal status and pregnancy. In the Third Tromsø study, the second questionnaire elicited information on health-behavior indices including an additional three questions related to physical activity as well as to dietary habits, reproductive variables, and previous diseases. The participants were asked to return this questionnaire by mail. The measurements of height and weight used in this study were obtained in the Third Tromsø study. Mammographic screening was a part only of the

Third Tromsø study. Women ages 40 or older (*n*, 4323) were offered free mammography, with 3653 (85%) accepting. The 10 women diagnosed with breast cancer are excluded from this analysis. Details of the screening and case-finding procedures are given elsewhere (11).

Mammographic Classification. All screening mammograms except those demonstrating breast cancer were classified into five groups, patterns I–V, according to the Tabar classification by one of the authors (L. T.). This classification is based on anatomical-mammographic correlations made after three-dimensional (thick-slice technique) histopathological-mammographic comparisons rather than the simple pattern reading described by Wolfe (12). The primary difference between the two classification systems concerns Tabar's pattern I. This pattern is regarded as a low-risk pattern but would probably be classified as a high-risk pattern, *i.e.*, either a P2 or a DY depending on the woman's age, in the Wolfe system (12). Patterns II and III would probably be classified as N1 and P1, respectively, while patterns IV and V would probably be classified as a P2 and DY, respectively. Pattern I usually evolves to either pattern II or pattern III. Details of the Tabar classification are given elsewhere (13). The mammographer knew only the age of the screenee at the time of classification. For analysis, patterns I through III were combined into a low-risk group and patterns IV and V into a high-risk group (14).

Physical Activity Indicators. In both surveys, the participants were asked to grade their physical activity during working hours and leisure time during the preceding year. The four categories of physical activity at work were as follows: (*a*) work that was mostly sedentary; (*b*) work involving a lot of walking; (*c*) work requiring a lot of lifting and walking; and (*d*) heavy manual labor. The leisure-time activity was categorized as: (*a*) mostly sedentary; (*b*) walking at least 4 h/week; (*c*) exercising at least 4 h/week; and (*d*) participating in competitive sports several times a week. The three additional questions asked in the 1986–1987 survey were as follows: (*a*) "How frequently are you physically active enough to cause sweating or hard breathing for at least 20 min? (seldom or never, weekly, several times a week, daily)"; (*b*) "If you usually do this at least once a week, how much time do you spend during a week on such activity? (<30 min, 30–60 min, 1–2 h, >2 h)"; and (*c*) "Is your level of physical activity less than, greater than, or about equal to the level that it was 5 years ago?"[3]

Data Analysis. Information from women who participated in both surveys was obtained by linkage of their personal identification numbers with the corresponding identifiers for each survey. Women, ages 40–56 at the time of the mammogram, who participated in both surveys (including returning the questionnaire completed at home) were included in the analysis. The two most extreme categories of work-time activity, of leisure-time activity, and of frequency of being physically active were combined because very few women reported strenuous physical activity. The amount of time per week spent being physically active was categorized as seldom/never, ≤2 h/week, and >2 h/week. A composite variable of work-time physical activity across the two surveys was defined, as was one for leisure-time physical activity. Each composite variable consisted of three levels: sedentary for both individual indices, moderately physically active for both, and the remainder, which consisted of either some physical activity for both or a mixture of indices. Associations among the physical activity indices were assessed using Spearman rank correlation coefficients.

Prevalence ORs[4] with 95% CIs were used to express the degree of association between physical activity indices and mammographic patterns. Univariate and multivariate analyses were conducted. We modeled the data using multiple logistic regression to allow for the effects of several potential confounders (15). Each of the following factors was evaluated as a potential confounder of the physical activity mammographic pattern relation: (*a*) age; (*b*) education; (*c*) menopausal status; (*d*) number of children; (*e*) age at first birth; (*f*) age at menarche; (*g*) body mass index (height in cm divided by weight in kg^2); (*h*) family history of breast cancer; (*i*) oral contraceptive use; (*j*) alcohol intake; and (*k*) dietary intake of fruits, vegetables, meat, and fat at dinner. A factor was considered a confounder if it was associated with mammographic patterns and with at least one of the physical activity indices. χ^2 tests and ANOVA were used to assess potential confounders. Every factor assessed, except family history of breast cancer and the dietary factors, was determined to be a potential confounder and thus included in the logistic regression models. Alcohol intake and education were included in the models as ordinal variables, menopausal status and the use of oral contraceptives as dichotomous variables, and the remainder were entered as continuous variables. Analyses were conducted for the entire study population and were also stratified by menopausal status, parity, body mass index, and change in physical activity. The multiple logistic regression analyses were performed using the logistic procedure in the SAS statistical package (16).

Results

Of the 2720 women ages 40–56, who participated in both surveys, 19.9% had their mammogram classified as a high-risk pattern. The average age of the women was 46.8 ± 4.9 years. Slightly over one-third (36.0%) of the women were postmenopausal, and the vast majority (91.7%) were parous.

Table 1 shows the distribution of selected physical activity indices: overall and by menopausal status. One-half of the responders reported seldom or never being physically active enough to cause sweating or hard breathing. Relatively few women reported, at both surveys, being physically active either at work (7.1%) or during leisure time (4.1%). More postmenopausal women reported being physically active at work than did premenopausal women ($P < 0.001$).

Hours and frequency of physical activity per week (both assessed only in 1986–1987) were nearly perfectly correlated ($r = 0.95$), and only results for the former are presented. Both indices were weakly correlated with leisure-time activity ($r = 0.38$ and $r = 0.24$ for 1986–1987 and 1979–1980, respectively) but were not correlated with work activity at either survey ($r < 0.10$). Work and leisure activity were not correlated with each other at either survey. Leisure activity was weakly correlated ($r = 0.31$), and work activity was moderately correlated ($r = 0.55$), across the two surveys. None of the correlations differed by menopausal status.

Table 2 displays the crude and adjusted ORs of high-risk *versus* low-risk mammographic patterns associated with selected indices of physical activity, overall and by menopausal status. Overall and among premenopausal women, there is a consistent inverse association between women reporting the highest level of physical activity and high-risk mammographic

[3] The third question is paraphrased.

[4] The abbreviations used are: OR, odds ratio; CI, confidence interval.

Table 1 Distribution of women according to physical activity indicators, Tromsø, Norway

	All %	Premenopausal %	Postmenopausal %
	$n = 2720$	$n = 1741$	$n = 979$
Hours physically active in 1986–1987[a,b]			
Seldom or never	50.5	50.0	51.4
≤2 h/wk	36.9	37.9	35.0
>2 h/wk	12.6	12.1	13.6
Physical activity at work in 1979–1980 and 1986–1987			
Sedentary (at both times)	25.2	25.8	23.8
Some[c]/mixture	67.2	68.0	65.6
Moderate (at both times)	7.7	6.2	10.6***[d]
Missing[e]	326	169	157
Leisure-time physical activity in 1979–1980 and 1986–1987			
Sedentary (at both times)	9.1	9.6	8.1
Some/mixture	86.8	85.6	88.9
Moderate (at both times)	4.1	4.7	3.1*
Physical activity level today[b] compared to earlier[g]			
More than before	10.2	11.4	7.7
Same as before	66.1	67.4	63.6
Less than before	23.8	21.2	28.6***
Missing[e]	337	186	151

[a] Physically active enough to cause sweating or hard breathing.
[b] From Third Tromsø study in 1986–1987.
[c] For work, required a lot of walking; for leisure, walked at least four times a week.
[d] ***$P < 0.001$; *$P < 0.05$.
[e] For work, women who did not work at least part-time.
[f] From Second Tromsø study in 1979–1980.
[g] Self-assessment of how physically active the woman was at the time of the mammogram relative to 5 yrs ago.

patterns. Among postmenopausal women, similar results are displayed for two of the indices, whereas those who reported moderate physical activity during leisure had an OR estimate above unity (OR, 1.3; 95% CI, 0.4–4.2). All of the associations reported in Table 2 are weak, and none are statistically significant. The association with physical activity at work is due primarily to the level of activity reported in the Tromsø II (1979–1980) survey and not the activity reported in Tromsø III (1986–1987), which is when the mammograms were taken. Confounding of the association between physical activity at work and high-risk patterns is almost exclusively explained by parity and body mass index. Analysis was repeated stratified by parity and body mass index because these factors were such strong confounders (Table 3).

Table 3 shows that women who reported being physically active for more than 2 h weekly are less likely to have high-risk patterns compared with those who reported seldom or never being physically active. A stronger association was indicated among nulliparous than parous women; however, neither of the associations achieved statistical significance. Except for the obese women (OR, 1.8; 95% CI, 0.7–4.8), those who reported moderate work physical activity were also less likely to have high-risk patterns compared with those reporting being sedentary. Women who reported moderate leisure physical activity were likewise less likely to have high-risk patterns compared with the reference group for all of the strata of body mass index, whereas the nulliparous women had an OR estimate above unity (OR, 2.5; 95% CI, 0.3–14). All of the associations reported in Table 3 have broad confidence intervals that include 1.0 and may be due to chance.

Table 4 displays the association between the same three physical-activity indices and high-risk patterns stratified by the level of physical activity during the 5 years before the mammography screening. Women who reported being physically active for more than 2 h/week at the time of the mammogram but having been more active 5 years earlier (*i.e.*, they are less active today) had an OR of 0.2 (95% CI, 0.0–1.2) for having high-risk mammographic patterns compared with those who reported being sedentary. Likewise among women who reported that they used to be more active, those who reported being in the highest category of physical activity at work were 50% less likely (OR, 0.5; 95% CI, 0.1–4.7), and those in the highest category of leisure time activity were 40% less likely (OR, 0.6; 95% CI, 0.1–6.0) to have high-risk patterns compared with those who reported being sedentary.

Discussion

Our study finds that moderate physical activity, *i.e.*, more than 2 h/week, is weakly inversely associated with high-risk mammographic patterns. This relationship is also seen when stratified by menopausal status, parity, and tertiles of body mass index. The strongest association between physical activity and high-risk mammographic patterns is found among the women who were in the highest category of physical activity at the time of the mammography screening and who reported that they used to be even more active. The study also suggests that sustained moderate physical activity at work or leisure is weakly inversely associated with high-risk mammographic patterns. This relationship was shown among premenopausal and parous women as well as among those who were not obese. However, all of the associations between various measures of physical activity and high-risk patterns found in this study are weak, with CIs that include 1.0. Thus, chance is a reasonable explanation for the weak associations displayed.

No previous study has, to our knowledge, examined the relationship between physical activity and mammographic patterns or mammographic densities. Several studies based on self-reported physical activity suggest an overall inverse association between physical activity and breast cancer risk (17–24), but not all of them have found an inverse association (25–30). The recent report from the Nurses' Health Study II, which comprised more than 100,000 women, did not reveal any association between breast cancer risk in young women and self-reported physical activity in late adolescence or in the recent past (30). The inconsistent results in the above-mentioned breast cancer studies, as well as those in our own study, may indicate that the findings are due to chance. The inconsistency may also be due to an inability to measure physical activity adequately. The two questions about leisure-time and work-related physical activity in our study were identical with those in the study by Thune *et al.* (22), in which an inverse association between physical activity and breast cancer risk was found in a cohort of 25,000 Norwegian women. Neither of the questions used in that study was designed to explore the relationship between physical activity and breast cancer. However, these questions have been validated and found useful in previous screening studies that focused on coronary heart disease (31–33). In our study, the highest level of physical activity was moderate activity and included less than 10% of the population in any physical activity index. One-half of the women in our study were sedentary, and few were involved in strenuous physical activity. Thus, the crude measures of physical activity and the narrow range of the various physical activity levels in our population are two major limitations.

Another limitation is that we do not have information on the temporal relationship between the physical activity and the mammographic patterns. The mammograms were obtained in

Table 2 Odds ratio (and 95% confidence intervals) estimates of high-risk mammographic patterns[a] associated with indices of physical activity, overall and by menopausal status, surveyed at a population screening, Tromsø, Norway, 1979–1980 and 1986–1987.

	All		Premenopausal		Postmenopausal	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Hours physically active[b] in 1986–1987						
Seldom/never	1.0	1.0	1.0	1.0	1.0	1.0
≤2 h/wk	0.9	0.9 (0.8–1.2)	1.1	1.1 (0.9–1.5)	0.7	0.6 (0.4–0.9)
>2 h/wk	0.9	0.8 (0.6–1.1)	0.8	0.7 (0.5–1.1)	1.0	0.8 (0.4–1.3)
Work-time physical activity[c] in 1979–1980 and 1986–1987						
Sedentary (both times)	1.0	1.0	1.0	1.0	1.0	1.0
Some/mixture	0.7	1.0 (0.8–1.3)	0.8	1.0 (0.8–1.4)	0.6	0.9 (0.6–1.5)
Moderate (both times)	0.5	0.8 (0.5–1.5)	0.5	0.8 (0.4–1.6)	0.5	0.8 (0.4–1.7)
Leisure-time physical activity in 1979–1980 and 1986–1987						
Sedentary (both times)	1.0	1.0	1.0	1.0	1.0	1.0
Some/mixture	1.0	1.1 (0.8–1.6)	0.9	1.0 (0.7–1.5)	1.4	1.4 (0.7–2.8)
Moderate (both times)	1.0	0.9 (0.5–1.7)	0.8	0.8 (0.4–1.5)	1.9	1.3 (0.4–4.0)

[a] Low-risk patterns are I–III (reference group) and high-risk patterns, IV and v. ORs were adjusted for age, education, number of children, body mass index, age at menarche, alcohol intake, oral contraceptive use, and menopausal status for the entire study population. Sedentary group is referent.
[b] Physically active enough to cause sweating or hard breathing.
[c] Total number for analysis was 2394 (excluding women who did not work at least part-time); for premenopausal women, 1572; for postmenopausal women, 822.

Table 3 Odds ratio estimates of high-risk mammographic patterns[a] associated with indices of physical activity, according to parity and body mass index, surveyed at a population screening, Tromsø, Norway, 1979–1980 and 1986–1987

	Parous		Body mass index		
	Yes n = 2430 OR (95% CI)	No n = 220 OR (95% CI)	<22.4 kg/m^2 n = 919 OR (95% CI)	22.4–25.0 kg/m^2 n = 915 OR (95% CI)	>25.0 kg/m^2 n = 844 OR (95% CI)
Hours physically active[b] in 1986–1987					
Seldom/never	1.0	1.0	1.0	1.0	1.0
≤2 hr/week	0.9 (0.7–1.2)	0.9 (0.4–1.7)	0.8 (0.6–1.1)	1.1 (0.8–1.6)	1.1 (0.7–1.8)
>2 hr/week	0.8 (0.6–1.2)	0.3 (0.1–1.0)	0.7 (0.4–1.1)	0.9 (0.5–1.6)	0.7 (0.3–1.6)
Work time physical activity[c] in 1979–1980 and 1986–1987					
Sedentary (both times)	1.0	1.0	1.0	1.0	1.0
Some/mixture	0.9 (0.7–1.2)	0.7 (0.4–1.4)	0.8 (0.6–1.2)	1.0 (0.6–1.4)	1.8 (0.9–3.7)
Moderate (both times)	0.8 (0.4–1.3)	0.6 (0.1–2.9)	0.7 (0.3–1.5)	0.5 (0.2–1.3)	1.8 (0.7–4.8)
Leisure time activity in 1979–1980 and 1986–1987					
Sedentary (both times)	1.0	1.0	1.0	1.0	1.0
Some/mixture	1.0 (0.7–1.4)	1.5 (0.5–4.5)	0.9 (0.5–1.4)	1.1 (0.6–2.2)	2.0 (0.8–5.3)
Moderate (both times)	0.8 (0.4–1.5)	2.5 (0.3–14.0)	0.9 (0.4–2.0)	0.7 (0.2–2.0)	0.8 (0.1–7.6)

[a] Low-risk patterns are I–III (reference group), and high-risk patterns are IV and V. All ORs are adjusted for age, education, menopausal status, age at menarche, alcohol intake, and oral contraceptive use. Those stratified by parity are also adjusted for body mass index, and those stratified by body mass index are also adjusted for number of children. Sedentary group is referent.
[b] Physically active enough to cause sweating or hard breathing.
[c] Numbers for analysis: parous, 2190; nulliparous, 204; for the three levels of body mass index: 836, 819, and 836.

the last survey, and we do not know whether the mammographic patterns had changed between the two surveys. We consider the classification of mammograms used in this study a strength. We have previously shown the overall agreement in the intrarater reliability assessment to be high (83.3%) when classifying the mammograms into high- and low-risk groups (13). Furthermore, the mammographer had no knowledge of the risk factors surveyed. We have previously shown (7, 34) that several breast cancer risk factors (*e.g.*, parity and age at first birth) are strongly associated with the Tabar classification of high-risk patterns in the expected direction. This suggests that both the risk factors and the mammograms had an internal valid classification in the present study. The study was part of a large population-based screening with a high attendance rate. We assume that selection bias was small because the attendees had previously been shown not to differ from the nonattendees with respect to several breast cancer risk factors (35). We also found that the women who attended both the Tromsø II and Tromsø III studies did not differ from those who attended only the latter on hours physically active, activity at work and leisure, overall, and by menopausal status. Thus, restricting our study population to include only those with physical activity measures from both studies should not bias our findings.

Numerous biologic mechanisms such as changes in hormonal concentrations, immune function, energy balance, body size, and menstrual patterns have been suggested as plausible explanations for the relationship between physical activity and breast cancer (36). Bernstein *et al.* (37) have reported that moderate physical activity may be associated with luteal phase insufficiency as well as anovulation. Changing the hormonal

Table 4 Odds ratio estimates of high-risk mammographic patterns[a] associated with sustained levels of physical activity for women surveyed at a population screening, Tromsø, Norway, 1979–1980 and 1986–1987

Selected indices of physical activity	Physical activity level today[b] compared with 5 yr ago	
	Similarly active $n = 1531$ OR (95% CI)	Less active $n = 566$ OR (95% CI)
Hours physically active[c] in 1986–1987		
Seldom/never	1.0	1.0
≤2 h/wk	0.8 (0.6–1.1)	0.9 (0.6–1.5)
>2 h/wk	0.7 (0.5–1.1)	0.2 (0.0–1.2)
Work time physical activity[d] in 1979–1980 and 1986–1987		
Sedentary (both times)	1.0	1.0
Some/mixture	1.0 (0.6–1.5)	1.0 (0.5–2.3)
Moderate (both times)	0.8 (0.4–1.7)	0.5 (0.1–4.7)
Leisure time physical activity in 1979–1980 and 1986–1987		
Sedentary (both times)	1.0	1.0
Some/mixture	1.0 (0.6–1.5)	1.2 (0.6–2.7)
Moderate (both times)	0.9 (0.4–1.9)	0.6 (0.1–6.0)

[a] Low-risk patterns are I–III (reference group), and high-risk patterns are IV and V. ORs were adjusted for age, education, number of children, body mass index, age at menarche, alcohol intake, oral contraceptive use, and menopausal status for the entire study population. Sedentary group is referent.
[b] Self-assessment of how physically active the woman was at the time of the mammography, relative to 5 yr ago.
[c] Physically active enough to cause sweating or hard breathing.
[d] Numbers for analysis: same, 1396; less, 487.

environment has been proposed as the most effective method of preventing breast cancer (38). It has been hypothesized that physical activity reduces lifetime exposure of cyclic estrogen and progesterone thus lowering breast cancer risk (39).

Several studies have shown that nulliparous women are more likely to have high-risk patterns than those with many children (1–2, 7). This supports the role of hormonal influences on mammographic patterns. One explanation for the stronger association seen among nulliparous, compared with parous, women may be that nulliparous women are more prone to hormonal changes induced by exercise because they have not been exposed to the hormonal changes induced by giving birth. However, few women in our study were nulliparous, and very few of them were in the highest category of physical activity; these results may be due to chance. The weak, although consistent, associations seen among the more than 2000 parous women in our study also have wide CIs, which also makes chance a likely explanation for the findings.

The use of subjective measures of physical activity is another limitation of this study as well as of several other studies (40). The category of obese women claiming to be at the highest level of physical activity at work reported at the same time that they were physically active enough to cause sweating or hard breathing for less than 1 h/week. Thus, misclassification may be one explanation for the increased likelihood of having high-risk mammographic patterns among the women in this category.

Physical activity may be one of the few modifiable breast cancer risk factors. Our study is only suggestive of an inverse association between moderate physical activity and high-risk patterns. Our findings are also consistent with the null hypothesis. The relationship between physical activity and high-risk mammographic patterns should be examined further as a means to explore the biological mechanisms relating physical activity to breast cancer risk.

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