RESEARCH COMMUNICATION

Lifetime Occupational Physical Activity and the Risk of Breast Cancer: a Case-control Study

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Abstract

Objective: Epidemiological studies have shown that physical activity is a protective factor for breast cancer, although research findings are inconsistent regarding menopausal status. To determine the impact of occupational physical activity for breast cancer, a hospital-based case-control study was conducted in Poland in 2003-2007. Methods: In total, data on physical activity of 858 invasive breast cancer cases and 1,085 controls were analyzed. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using unconditional logistic regression . Separate calculations were performed for premenopausal and postmenopausal women. Occupational physical activity was measured by sitting time and job titles. The risk estimates were controlled for potential risk factors and lifetime household and recreational activities. Results: A significantly decreased breast cancer risk was found among postmenopausal women declaring physically active jobs (requiring more than 80% of time spent standing, walking) compared with those with low activity jobs (more than 80% of the working time spent in a sitting position, during workhours) (OR=0.66; 95%CI 0.44-0.98, P trend=0.03). A similar inverse association between occupational physical activity and breast cancer risk was also found when activity was evaluated according to job titles provided by subjects. Postmenopausal women with physically demanding jobs, in particular, had a lower risk compared to those in sedentary occupations (OR=0.57; 95%CI 0.36-0.91, P trend=0.02). Conclusion: These findings support observations from previous studies that sufficiently high occupational physical activity may reduce breast cancer risk, particularly among postmenopausal women.

Key Words: Breast cancer - occupational physical activity - case-control study - menopausal status

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Introduction

There is at present tremendous evidence that regular physical activity plays important function in reduction of chronic diseases and cancer. According to the recent systematic reviews of the literature (Monninkhof et al., 2007; Friedenreich and Cust, 2008) and the World Cancer Research Fund/American Institute for Cancer Research lines (WCRF/AICR, 2007) regular moderate-vigorous physical activity may be an important moderator of breast cancer risk. In addition, sedentary behavior has been identified as potentially important risk factor for the development of chronic diseases (Owen et al., 2009). It has been estimated that time spent sitting during adults' waking hours is the longest (9.3 hours/day), and time spent in moderate to vigorous physical activity is the shortest (0.7 hour/day) (Owen et al., 2009). Based on existing evidence, Blair (2009) concludes that "physical inactivity is one of the most important public health problems of the 21st century, and may even be the most important".

Breast cancer is the most common malignancy among women in the world. It has been estimated that 182,460 new breast cancer cases occur among women in the US in 2008 (Jemal et al., 2007). In Poland, the 2005 breast cancer incidence was 13,385 (Krajowa Baza Danych Nowotworowych, 2008) and the standardized mortality about 14.9. The disease is a major public health problem (Ferlay et al., 2004; Bruzewicz, 2008).

I previously reported that Polish women in the Region of Western Pomerania who declared 31 or more hours per week per year of moderate (3-6 METs) physical activity during lifetime occupation had a 48% significantly reduced risk of postmenopausal breast cancer (Kruk, 2009). In the present analysis, the study followed up these findings using another measures of the activity i.e. using a sitting time index during the working hours and a creation of four class index for the physical load of women' occupations basing on the job titles.

Materials and Methods

The present investigation is based on data from a case-control study conducted between January 2003 and May 2007 in the Region of Western Pomerania (Poland), described in detail previously (Kruk, 2007; 2009). Briefly, causes were women aged 28-79 years, with histologically confirmed primary invasive breast cancer identified from the Szczecin Cancer Registry and selected prospectively.

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Letters of invitation and consent forms were sent out by the Regional Oncology Hospital in Szczecin to 2409 randomly selected cases, and 1,187 cases provided written consent. Then structured questionnaires were sent to complete and the overall response rate was 50.6%.

Controls were frequency matched to the cases within 5-year age groups and by place of residence. They were required to be free of any cancer diagnosis and aged <80 years. Control subjects were randomly selected among the out patients of clinics and hospitals located in the Region of Western Pomerania. The overall response rate for controls was 69.4%. Twenty three cases and 36 controls for whom information on physical activity was missing were excluded from analyses. Finally, a total of 858 cases and 1085 controls were included in the analyses. The Ethics Committee of the Pomeranian Medical Academy in accordance with the Polish Department of Health and Human Services approved this study, and a signed informed consent was obtained from each study woman before sending the structured questionnaire.

Using the structured questionnaire information was collected on demographic and reproductive factors, including age at menarche, menopause, pregnancies, lactation, use of oral contraceptives (OCP), hormone replacement therapy (HRT), family history of breast cancer, body size measures, passive and active smoking, alcohol use, diet, and detailed data on physical activity from all sources beginning at age 14 and ending in the reference year, i.e., the year before cancer diagnosis for cases, the year before selection in the study for controls. Lifetime history of physical activity was assessed using a questionnaire modeled on those of Kriska et al. (1990) and Friedenreich et al. (1998) to allow for self-administration. Assessment of household and outdoor chores and recreational physical activity performed (43 popular activities) was based on recording the number years, months per year, weeks per month, days per week and hours per day, and intensity. The lifetime occupational physical activity (the 33 most common job titles) was estimated by recording job title, number of years, months per year, days per month, number of hours worked/day in a sitting posture, standing and walking, and self-determined level of intensity among defined categories:

1 – jobs requiring only sitting with minimal working,

2 – jobs requiring a minimal amount of standing, slow walking that do not cause sweating,

3 - jobs that required continuous walking and carring loads 2-5 kg (might causing light sweating),

4 – jobs required brisk walking, carring heavy loads (>5 kg) that caused heavy sweating and increased the heart rate.

Occupational physical activity levels were created by the rate physical load of occupation basing on the job titles provided by each participant and an index of a sitting time. Job title was classified into one of four categories of physical demands strength rating, ranging from sedentary to high. None of women declared a job with a strength rating of very heavy. Four classes of job activity were employed: class 1 (sedentary) consisted of jobs involving sitting. Professions in this class included for example office workers, secretaries, cashier, telephonists, telegraphists, lawyers and judges. Class 2 involved jobs remaining sitting and handling heavier items (light). Professions in this class included dressmakers, engineers, information scientists, technicians in health departments, tram drivers, management related occupations. Class 3 was for jobs with light physical activity and included mainly teachers, scientists, librarians, waitresses, pharmacists, hairdressers and shopkeepers. Class 4 involved women holding occupations with medium physical demands (high), including farmers, craftswomen, physicians, nurses, cleaners, cooks. These classes were chosen in line with a previous study of occupational physical activity and breast cancer (Rintala et al., 2002).

For variables representing a sitting time index three levels of occupational physical activity were considered: (1) low activity (for long sitting time jobs >80%); (2) moderate activity as 20-80% of working hours sitting; (3) high activity that required less than 20% of the time sitting. The method based on the amount of time in a sitting posture in a job has been successfully used in earlier occupational physical activity studies (Zheng et al., 1993; Peters et al., 1989).

Unconditional logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) as estimates of relative risks (Kleinbaum, 1994). A two-sided P-test was used, with statistical significance set up $P<0.05$. All analyses were conducted using statistical package STATISTICA 98 (stat Soft Polsca, Kraków, Poland). For each analysis, OR was assessed in two models; one adjusted only for age and the other adjusted for age and other potential confounding variables that were selected a priori. Variables considered as confounders included: age at enrollment, place of residence, family income, education, marital status, body mass index at reference year (BMI), age at menarche, parity, menstrual cycles, age at menopause, age at first birth, duration of breast feeding, OCP use, HRT use, family history of breast cancer, stress experience, active smoking, passive smoking, alcohol consumption, intake of animal fat, red meat, vegetables, and fruits, and additional physical activities. Separate analyses for premenopausal and postmenopausal women were performed. Women were considered postmenopausal if their periods had stopped more than 1 year before their reference date or they had reached age 55 years and reported a lack of menstruation. The remaining women and also those who reported a hysterectomy or taking HRT and their reference date were under 42 years were considered as premenopausal. The final models included confounding variables that were found to influence the quality of the model fit, and those variables that were statistically linked with breast cancer.

Results

A comparison of case patients and control subjects by established breast cancer risk factors has been previously reported (Kruk, 2007). Established by epidemiologic studies breast cancer risk factors on the whole prevailed in this study population. In both premenopausal and postmenopausal women increased

Table 1. Selected Characteristics of Breast Cancer Cases and Controls

Characteristics	Cases (858)	Controls (1,085)
Educational level*		
Elementary school	262 (30.5)	253 (23.3)
Middle school	339 (39.5)	379 (34.9)
High school (university)	257 (30.0)	453 (41.8)
Current BMI (kg/m^2)*		
≤22.5	181 (21.1)	305 (28.1)
22.6<25.0	211 (24.6)	267 (24.6)
25.0-<30.0	311 (36.2)	372 (34.3)
≥30	155 (18.1)	141 (13.0)
Age at menarche		
≤12	158 (18.4)	51 (4.7)
=13	201 (23.4)	409 (37.7)
≥14	499 (58.2)	625 (57.6)
Age at first childbirth (parous only)		
<20	85 (11.0)	83 (8.3)
20-27	590 (76.4)	767 (76.8)
≥28	96 (12.4)	149 (14.9)
Number of pregnancies		
0	86 (10.0)	87 (8.0)
1	188 (21.9)	247 (22.8)
2	394 (45.9)	512 (47.2)
≥3	190 (22.1)	239 (22.0)
Months of breast feeding*		
0	86 (10.0)	87 (8.0)
<6	526 (61.5)	457 (42.2)
6-12	145 (16.9)	206 (19.0)
>12	99 (11.6)	334 (30.8)
First-degree family history of breast cancer*		
No	720 (83.9)	1,003 (92.4)
Yes	138 (16.1)	82 (7.6)
Smoking status- Active smokers*		
Non-smokers	444 (51.8)	729 (67.3)
<10 stuck/day	161 (18.8)	146 (13.5)
≥10 stuck/day	252 (29.4)	209 (19.2)
Passive smoking-Smoking husband*		
Non-smoker husband	363 (44.2)	718 (67.4)
<20 sticks/day	210 (25.6)	198 (18.6)
≥20 sticks/day	248 (30.2)	149 (14.0)
Alcohol consumption*		
Never	365 (42.8)	491 (45.3)
≤1 drink/week	334 (39.2)	467 (43.1)
2-4 drinks/week	148 (17.3)	117 (10.8)
≥5 drinks/week	6 (0.7)	8 (0.8)
Stress experience*		
No	366 (42.7)	588 (54.2)
Yes	492 (57.3)	497 (45.8)
Ever OCP use*		
No	705 (82.2)	927 (85.4)
Yes	153 (17.8)	158 (14.6)
Ever HRT use	301 (35.1)	371 (34.2)
Age	53.3 ± 9.7#	54.8 ± 9.5#
Age at menopause*	48.4 ± 5.3#	49.4 ± 4.5#
Duration of work (years)	27.9 ±10.6#	28.4 ± 9.8#
Lifetime physical activity (hours/week)		
Household	16.6 ±11.8#	19.4 ±11.3#
Recreational	4.2 ± 6.3#	5.3 ± 4.6#

Due to missing values, some categories do not sum to 100%; BMI, body mass index; OCP, oral contraceptive; HRT, hormone replacement therapy; #Mean and SD, standard deviation; *P value < 0.05.

risk was associated with a family history of breast cancer, active and/or passive smoking, psychological stress experience. Higher BMI, alcohol consumption increased risk among postmenopausal women, only. In turn, animal fat and red meat consumption, OCP use, low family income increased risk in premenopausal women. Decreased risks were associated with late age at menarche, ≥6 months of breast-feeding, higher frequency of vegetables and fruits consumption, higher levels of: education, household and recreational physical activities. The average age at diagnosis for cases was 55.3 years (SD, 9.6 years). For controls, the average age at the reference was 54.8 (SD, 9.5 years).

Table 2. Odd Ratios and 95% Confidence Intervals by Level of Occupational Physical Activity

Activity level	Cases	Controls	OR (95% CI) Age-adjusted	OR (95% CI) Multivariate*
All women				
Sedentary	280	301	1.00	1.00
Light	119	152	0.84 (0.63-1.12)	0.89 (0.63-1.26)
Medium	241	368	0.71 (0.56-0.89)	0.80 (0.58-1.09)
High	159	185	0.94 (0.72-1.22)	0.77 (0.54-1.11)
P for trend			0.11	0.88
Housewives	15	28	0.58 (0.30-1.12)	0.59 (0.27-1.27)
Not known	43	51	0.92 (0.59-1.43)	0.81 (0.47-1.37)
Premenopausal women				
Sedentary	106	126	1.00	1.00
Light	38	67	0.67 (0.42-1.09)	0.66 (0.38-1.17)
Medium	91	191	0.54 (0.38-0.78)	0.68 (0.49-1.11)
High	54	51	1.26 (0.79-2.00)	1.25 (0.68-2.31)
P for trend			0.44	0.89
Housewives	4	7	0.62 (0.17-2.23)	0.81 (0.19-3.38)
Not known	16	33	0.57 (0.30-1.10)	0.47 (0.21-1.04)
Postmenopausal women				
Sedentary	174	175	1.00	1.00
Light	81	85	0.97 (0.67-1.40)	1.00 (0.71-1.77)
Medium	150	177	0.85 (0.63-1.15)	0.95 (0.66-1.39)
High	105	135	0.79 (0.57-1.10)	0.57 (0.36-0.91)
P for trend			0.06	0.02
Housewives	11	21	0.54 (0.25-1.17)	0.42 (0.16-1.12)
Not known	27	18	1.50 (0.79-2.82)	1.54 (0.71-3.36)

OR, odds ratio; CI, confidence interval. P for trend by Wald test - two-sided. * Adjusted for age, BMI, lifetime recreational physical activity, age at menarche, age at first full-term pregnancy, parity, months of breastfeeding, intake of vitamins, active smoking, passive smoking, family history of breast cancer.

Table 1 shows briefly the distributions of risk factors among cases and controls. Controls were more educated, had later menarche, later menopause, lower frequencies of histories of breast cancer risk in first degree female relatives, were less frequent active and passive smokers, 2-4 drinks/week alcohol consumers, OCP users and rarely experienced psychological stress. Controls declared more frequently longer duration of breast feeding. Likewise, obesity was less common in controls than cases. There were statistically important differences between cases and controls on the lifetime average number of hours per week per year spent in household and recreational physical activity; controls spent significantly more time with the activities than cases.

The analyses of association between the physical load of women' occupations basing on the job titles and breast cancer risk are presented in Table 2. Among postmenopausal women high level of occupational physical activity was significantly inversely associated with breast cancer risk (OR=0.57, 95%CI:0.36-0.91 in

Table 3. Odd Ratios and 95% Confidence Intervals According to Occupational Physical Activity Index of Sitting Time

Sitting time	Cases	Controls	OR (95% CI) Age-adjusted	Multivariate*
All women				
Long	243	311	1.00	1.00
Moderate	383	439	1.14 (0.91-1.41)	1.14 (0.88-1.47)
Short	231	335	0.88 (0.70-1.20)	0.86 (0.64-1.16)
P for trend			0.31	0.16
Premenopausal women				
Long	74	137	1.00	1.00
Moderate	147	211	1.30 (0.91-1.86)	1.47 (0.96-2.24)
Short	88	127	1.25 (0.84-1.86)	1.16 (0.72-1.87)
P for trend			0.24	0.37
Postmenopausal women				
Long	169	174	1.00	1.00
Moderate	236	228	1.07 (0.81-1.41)	1.05 (0.74-1.48)
Short	143	208	0.70 (0.52-0.95)	0.66 (0.44-0.98)
P for trend			0.022	0.03

OR, odds ratio; CI, confidence interval. P for trend were derived from the Wald test, and are two-sided. *Adjusted for age, BMI, lifetime household physical activity, lifetime recreational physical activity, age at menarche, age at first full-term pregnancy, parity, months of breastfeeding, active and passive smoking

the multivariable-adjusted model, P trend=0.02). Although risk estimates at higher level of activity comparing with sedentary were generally below 1.00 for most associations for all classes of jobs involving bodily motion, they did not reach statistical significance except as mentioned above. Women who had been housewives during their lifetime had nonsignificantly decreased breast cancer risk.

Table 3 shows age and multivariable-adjusted risk estimates for associations of three indices of physical activity percent of time spent on activities at work with breast cancer incidence in all women and menopausal groups. Risk estimates were similar after multivariable adjustment for several risk factors, including BMI and also after mutually adjusting for lifetime household and recreational activities. In all women occupational activity was not statistically significantly associated with breast cancer risk (P trend=0.16); however, the risk was suggestively decreased among women in the highest tertile (OR=0.86; 95%CI:0.64-1.16). In premenopausal women, occupational activity did not appear to be associated with breast cancer risk. Postmenopausal women who reported that their job required >80% time spent walking experienced a 34% decreased risk compared with women in the lowest tertile of occupational activity (>80% time spent sitting), OR=0.66, 95%CI:0.44-0.98 in the multivariable-adjusted model, P trend=0.03.

Discussion

Occupational physical activity is an important component of total physical activity. The present investigation found that jobs required more than 80% walking was associated with a small 16% statistically nonsignificant decrease in breast cancer risk in the study participants as a whole. However, when the relation of occupational activity to breast cancer was evaluated among postmenopausal women, the association became markedly stronger with statistically significant risk decreasing by about 34% among the most physically active women. In contrast no association between the job physical activity and breast cancer risk was found among premenopausal women. Similar associations were found when the physical load of participants' was rating considering job titles.

The risk estimate for postmenopausal women is higher than average 13% risk reduction reported in a previous review for this type of activity and breast cancer risk linkage (Friedenreich and Cust, 2008). A direct comparison risk estimates with the literature data is difficult due mainly to differences in the study population, study design, variation in measurement of physical activity. It is assumed in the subject literature that decreases in the risk are observed among women declaring heavy or very tiring jobs (Gammon et al., 1998; Friedenreich and Cust, 2008; Peplonska et al., 2008). In the current study most jobs required low energy expenditure; and none of women declared jobs above 6 METs. Heavier physical work was reported by relatively small numbers the study participants. Although based on different methods for physical activity measurement, findings of this paper showed that jobs remaining mainly walking were inversely associated with breast cancer risk. These findings are consistent with conclusion of two systematic reviews (Gammon et al. 1998; Friedenreich and Cust, 2008) and two epidemiological studies who found significant risk reduction among postmenopausal women for walking, lifting or heavy manual labor (Friedenreich et al., 2001; John et al., 2003). Friedenreich et al. (2001) created average MET-hours/week per year spent in occupational activity over the subject's lifetime finding a 33% reduction in breast cancer associated with activity at least 47.5 MET-hours/week per year (P trend=0.003). John et al. (2003) found that lifetime mostly moderate or strenuous jobs lasting at least 10.3 hours/week per year was associated with a 30% reduction of breast cancer risk. These findings are also consistent with those of our previous report from a case-control study conducted in Stettin province (Poland) during 1997-1998 (Kruk and Aboul-Enein, 2003) as well as with those reported recently for the Compendium of Physical Activities - based assigned levels of activity (Kruk, 2009). In contrast, Thune et al. (1997) found that heavy occupational physical activity significantly reduced the risk in all women and premenopausal group. Similarly, the reduction in risk in a study women as a whole for medium/heavy occupational physical activities was reported by Coogan and Aschengrau (1999), Levi et al (1999), Rintala et al. (2002), and Peplonska et al (2008). In turn, Moradi et al. (2000) observed that women in sedentary occupations during 25-44 year of age had a 50% higher breast cancer risk for postmenopausal women than that of women in moderately or highly physically demanding jobs. Also, Zheng et al. (1993) based on measurement of sitting time and energy expenditure found significantly elevated standardized incidence of breast cancer among women with low physical activity occupations and reduced risk for the high levels. Finally some studies, e.g., Dorn et al. (2003),

Lahmann et al (2007), and Sprague et als (2007) reported no such association.

Several biological mechanisms by which physical activity can act on breast cancer development have been proposed (Shephard and Shek, 1998; Lewis, 2006; McTiernan, 2008). They include lowering of the endogenous sex hormones levels (McTiernan et al., 2006; Coyle, 2008), leptin concentrations (Tworoger et al., 2007), enhancing immunity and reducing chronic inflammation (Wetmore and Ulrich, 2006; McTiernan, 2008). A reduced breast cancer risk among postmenopausal women with higher physical activity occupations as measured by either sitting time or job titles is biologically plausible because there is some evidence that a high intensity or long-lasting practice moderate physical activity is associated with a reduction of estradiol (Jasienska et al., 2006), androgen levels (Coyle, 2008) and enhanced sensitivity to insulin (Chlebowski et al., 2004). Exercise may also increase serum levels of sex hormone-binding globulin, which may reduce concentrations of estradiol, and by reducing estrogen bioavilability (Neilson et al., 2009). In addition, physical activity can decrease body fat, thereby lowering production of estrogen, a major source of the hormone in postmenopausal women (Neilson et al., 2009).

The lack of modification of the physical activity - breast cancer relation by BMI in the current study supports independent effect of physical activity on the risk reported by several studies, reviewed recently by Friedenreich and Cust (2008). Up till now it is not clear whether or not physical activity lowers estrogen and its metabolites concentrations independently of weight loss (Neilson et al., 2009). The serum levels of sex hormones were found to be decreased with participation in recreational physical activity of moderate intensity (Ellison and Lager, 1986; Bernstein et al, 1987; McTiernan et al, 2004; Jasienska et al., 2006; Chan et al., 2007). In turn, Campbell et al (2007) observed none change the estrogen metabolism in premenopausal women under of aerobic exercise. A question that remains is if this mechanism can operate for occupational physical activity, although Florack et al. (1994) reported a significant effect of moderate occupational physical activity on the menstrual cycle.

There are some limitations of the present study. Similarly as most case-control study the results may have been influenced by selection bias and recall bias. The possibility of selection bias cannot be ruled out because of a relative low response rate in cases and selection of controls from outpatients as the reference group. Although, the overall response rates were comparable to other studies (Bernstein et al., 1994; Marcus et al., 1999), they were lower than, for example, in a study of Pep_o_ska et al. (2008), but higher than reported by Steindorf et al. (2003). Moreover, expected associations between the risk of breast cancer and established risk factors in the subject literature were found in examined women recently (Kruk, 2007).

To evaluate the possible discrepancy between the study controls and the general population of Polish women, the controls were compared with the women surveyed by the Chief Central Statistical Office in the Polish Population Health Survey on several medical, lifestyle and social characteristics (GUS, 2004). Also, cases and controls were compared with those in the large population-based study evaluating risk factors by breast cancer tumor characteristics (Garcia-Closas et al., 2006). The comparisons showed that both groups of women were very similar in several characteristics.

A further methodologic limitation, misclassification of exposure, was addressed by recording lifetime physical activity from all sources. The intensity of activity was assessed by the study participants for each title of a job, which helped to distinguish sufficiently between low, moderate and vigorous. In addition, comprehensive assessment of physical activity was based on the questionnaire of which the validity has been previously examined by its authors (Friedenreich et al., 1998). Nevertheless, the nondifferential misclassification error cannot be excluded. Other potential limitation that should be taken into account is multiple jobs held by participants and a lack of adjustment for energy intake.

Among the strengths of this study are a large sample size, histological confirmation of invasive breast cancer, and extensive data about established and potentially confounding variables. Moreover, the study is one of the few that have completed data for three important sources of physical activity (household, occupational and recreational) allowing adjustment for interactions. Associations were estimated in two ways: based on the job titles and a sitting time index, and similar effects of physical activity on risk of breast cancer were observed with both.

In conclusion, these findings support observations from previous studies that occupational physical activity, if high enough, may reduce breast cancer risk, particularly among postmenopausal women.

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