RESEARCH COMMUNICATION

Self-reported Childhood Physical Activity and Breast Cancer in Adulthood

Joanna Kruk

Abstract

The association between physical activity during childhood and breast cancer risk was examined. To study this question data on physical activity in childhood were analyzed. A hospital-based case-control study of 250 Polish incident breast cancer cases (49.2% of eligible) and 301 (41.4% of all selected) frequency matched for age controls was conducted in 2003-2004 in the Region of Western Pomerania. Women were asked to compare their total physical activity at ages 10-12 years and 13-15 years with the activity of their female peers by choose from one of three categories: less active, equally active, more active, the best describing their activity. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using univariate and multivariate logistic regression, fitted by the method of maximum likehood. Women who reported having been physically more active than their peers at ages 10-12 years had an age-adjusted OR=0.88 (95% CI=0.36-2.15, P for trend=0.37) as compared with those reported being less active. Adjustment for potential confounders and total lifetime physical activity decreased the risk estimate to OR=0.25 (95% CI=0.06-1.10, P for trend=0.15). For physical activity at ages 13-15 years, both an age-adjusted and multivariate adjusted ORs were also decreased among women who were at least such active as their peers, but the reductions were not statistically significant. For women who were more physically active than their peers during both age periods the adjusted OR was 0.30 (95% CI=0.11-1.34, P for trend =0.21). These results show no protective role for physical activity in childhood on breast cancer development among women aged 35-75 years. Further investigations employing larger sample sizes with comprehensive assessment of physical activity during the childish years are needed to verify this evidence.

Key words: Case-control study - physical activity - breast cancer - childhood

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Introduction

From a public health perspective identifying primary prevention strategy against breast cancer risk is an important step in reduction of this disease burden. Breast cancer is the leading cause of cancer related deaths in women in most industrialized countries (Parkin et al., 1999; Ferlay et al., 2004). For example, the age standarised morbidity is 65.0 in the United States and 38.7 per 100,000 in Poland (McPherson et al., 2000).

Since it was found by Frisch et al (1985) that the risk of breast cancer was reduced by nearly 50% among women who were college athletes compared to non-athletes, interest in physical activity as a means for the primary prevention of breast cancer has grown rapidly. To date, at least 65 both case-control and cohort studies contributed information on the relation, and about 70% have shown a significant reduction in the risk. The reported reduction ranged from 10% to 80% and was on average 30-40%. An inverse association between physical exercise and breast cancer was found to be stronger among postmenopausal women than for premenopausal women (Friedenreich, 2004). More detailed discussions can be found in several previous excellent reviews (Gammon et al., 1996; Friedenreich, 2001; Thune & Furberg, 2001; Okasha et al., 2003) as well as in recent reviews (e.g., Kruk, 2005; Rieck & Fiander, 2006). For breast cancer the International Agency for Research on Cancer (IARC) evaluated that there is 'convincing evidence' in women for a cancer preventive effect of physical activity (IARC, 2002).

Among those studies that show a protective effect of physical activity there is no consensus on the life period which activity may have its greatest impact (e.g., adolescence, adulthood, recent, lifetime), dose of physical activity (intensity, frequency or duration) that might be required to be protective or types of physical activity (household, occupational or recreational) that might be most beneficial for disease prevention (Gammon et al., 1996;

Institute of Physical Education, Faculty of Natural Sciences, University of Szczecin, Poland Fax: +48-91-4442734 E-mail: Joanna.Kruk@univ.szczecin.pl

Friedenreich, 2001). In addition, only some researchers examined the effect of physical activity on breast cancer risk during childhood. The results show that there is disagreement in the risk estimation caused, probably, by different ways of the physical activity assessment.

Data reported in our previous study (Kruk, 2006) on the physical activity - breast cancer relationship among the Polish women showed that lifetime total physical activity done from age 14 years to age at interview was statistically important associated with a reduced breast cancer risk.

The purpose of this study was to explore further previous observations by evaluating the role of physical activity at ages 10-12 years and 13-15 years on breast cancer development in adulthood and to analyse changes in activity.

Methods

The present investigation is based on data from a case-control study conducted between January 2003 and May 2004 in the Region of Western Pomerania. This study received Ethics Committee Approval from the Pomerania Medical Academy (no. BN-001/254/02, 2002.12.09) in accordance with assurances approved by the Polish Department of Health and Human Services. Cases (545 women) were identified from the Szczecin Regional Cancer Registry. Of those 545 cases, 327 (60%) agreed for interview but 268 (82%) of them completed a questionnaire. Briefly, 250 women aged 35-75 years (mean age, 56.9±8.6 years) diagnosed with histologically confirmed, invasive or in-situ breast cancer operated in the Szczecin hospitals during January 1999-December 2003 provided the basic physical activity questions answered and were included in the statistical analyses. Control participants (778) were women free of any cancer diagnosis and without earlier physical limitation. They were chosen among patients admitted to clinic ambulatories and hospitals for health controlling, acute traumas, disc disorders, or eye, skin, laryngological diseases. Of those 778 women contacted, 403 (51.8%) agreed to participate in a study, but completed questionnaire were received from 322 (79.9%), only. After excluding controls who were missing data on physical activity, 301 women (mean age, 56.4±8.8 years) were included in the analysis. A written informed consent form for participation in the study was signed by each case and control participant. Participants were interviewed using a 8-page self-administered questionnaire received from the doctors or the nurses of clinic or by mail. The questionnaire included information on socio-demographic characteristics (marital status, education, place of residence, occupation), family history of breast cancer, height, weight, menstrual and reproductive history, tobacco smoking, alcohol drinking, and validated section of diet (18 main Polish-style food groups), and experience of psychological stress. Women were first asked to compare their total physical activity at ages 10-12 years and 13-15 years with the activity of their female peers by choose from one of three categories: less active, equally active, more active, the best describing their activity. In addition, details about lifetime physical activity, in separate sections was ascertained for household, occupational and leisure-time activities (during four periods at ages: 14-20, 21-34, 35-50 and above 50 years) up to a woman's reference year (date of diagnosis for cases and a comparable date assigned for controls). A modified version of the Friedenreich et al. (1998a) and Kriska at al. (1990) questionnaires was used to obtain information on household tasks, walking, cycling and 43 different sports and exercise activities. Details of the questionnaire and procedures of data collection have been described previously (Kruk, 2006).

The duration, frequency, and intensity of the activity were measured. Additionally, a specific metabolic equivalent MET score, defined as the ratio of working metabolic rate to resting metabolic rate (Ainsworth et al., 1993; Ainsworth et al., 2000) was assigned to each reported activity basing on the description of the activity. Total lifetime physical activity was calculated as the sum of household, occupational and recreational activity. The variables estimated for analyses in previous paper (Kruk, 2006) were expressed as the average hours per week per year or average MET-hours per weak per year spent in total lifetime physical activity over a woman's lifetime. Total physical activity was categorized into three levels: <40, 40-50, >55 hours/week/year or <110, 110-150, >150 MET-hours/week/year, respectively. For example, a women reporting an average rate of energy 110 MET-hours/week/year could accumulate this level of activity by doing 40 hours of job remaining long sitting time (1.5 METs, e.g., sitting-light office work), 10 hours of light home activities (2.5 METs, e.g., cooking, cleaning-light) and 8 hours of recreational activity (3.5 METs, e.g., walking for pleasure or 6 hours of working in garden, 4-6 METs) per week. Using the total lifetime physical activity estimated in previous paper (Kruk, 2006) individuals were further categorized in order to determine changes in the activity over time. For this purpose, the levels of total physical activity were dichotomized into women who participated in no or low activity (inactive: below 40 hours/week/year or below 110 MET-hours/week/year), and those who participated in moderate or high physical activity (active:>40 hours/week/year or >110 MET-hours/week/year). Using these data the effect of changes in physical activity throughout life was evaluated.

The odds ratios, ORs, estimates of relative risk associated with breast cancer for physical activity and their 95% confidence intervals (CIs) were estimated by using logistic regression models. The main outcome were incident cases of cancer, the main independent variable was physical activity which was entered as dummy variable. Relative units of physical activity for the 10-12, 13-15 age periods were evaluated as tertiles using indicator variables. The same model was applied for linear trend test in ordinal variables using the logistic analog to the controlled for age. Multivariable-adjusted models with a full evaluation of confounding by other established and putative breast cancer risk factors were also constructed.

Variables considered as confounders were examined by

Table 1. Demographic, Health-related and Lifestyle Characteristics among 250 Cases and 301 Controls by Disease Status

Characteristic	Cases	Controls	P-value
Age (years) in reference year, mean (SD*)	56.9 (8.6)	56.4 (8.8)	0.48
Height (cm), mean (SD*)	161.6 (5.5)	162.3 (5.7)	0.18
Body mass index (kg/m^2), mean (SD*)	26.9 (4.9)	25.6 (4.1)	0.001
Low family income (number, %)	11.0 (4.4)	24.0 (8.0)	0.49
Age at menarche (years), mean (SD*)	13.8 (1.5)	13.8 (1.7)	0.64
Age at first birth (years), mean (SD*)	21.0 (8.2)	21.6 (8.1)	0.40
Age at menopause (years), mean (SD*)	48.6 (5.2)	49.9 (5.0)	0.008
Breast-feeding (months), mean (SD*)	6.4 (7.5)	8.2 (9.4)	0.02
Red meat consumption (servings/week, mean (SD*)	1.8 (1.5)	1.8 (1.6)	0.55
Alcohol drinking (drinks‡/week), mean (SD*)	0.7 (0.8)	0.7 (0.9)	0.74
Vegetable consumption (servings/week), mean (SD*)	3.3 (1.8)	3.6 (1.6)	0.045
Ever users of oral contraceptives (number, %)	41.0 (16.4)	44.0 (14.6)	0.71
Ever users of HRT (number, %)	78.0 (31.6)	118.0 (39.2)	0.18
Stress experience (yes, number, %)	149.0 (59.6)	146.0 (48.5)	0.15
Active smoker (number, %)	100.0 (40.0)	88.0 (29.2)	0.002
Passive smoker (number, %)	73.0 (25.2)	54.0 (17.9)	0.006
Family history of breast cancer in mother/sister (number, %)	31.0 (12.4)	44.0 (14.7)	0.50
Total lifetime physical activity, mean (SD*)			
Hours/week/year	47.0 (17.6)	52.7 (16.7)	<0.001
MET-hours/week/year	138.1 (58.1)	151.8 (61.1)	0.003

*SD, standard deviation; MET, metabolic equivalent; †, Kruk, 2006; HRT, hormonal replacement therapy; ‡ one alcoholic drink, tin of beer or a small bottle, 125ml of wine or 30g of high-grade alcohols.

using the difference between deviances of the models with and without the variable. Variables that contributed significantly to the models ($p<0.05$, by Wald test) were retained and likehood ratio tests were conducted to examine differences between models (Schlesselman, 1982). The variables tested included: place of residence, education, family income average over the past 10 years, marital status, body mass index (BMI) at reference year (weight (kg)/ height^2 (m^2)), age at menarche, age at first birth, number of pregnancies, duration of breast feeding, use of oral contraceptives, postmenopausal hormone replacement therapy use, family history of breast cancer, menopausal status, control of breast, stress experience, smoking status, alcohol consumption, red meat consumption, consumption of fruits, vegetables.

The final models were adjusted for those variables found to influence of quality of the model fit. Those variables associated statistically significantly with breast cancer and physical activity are given in legends of tables. Differences between group means were tested by the Student's t test and Pearson's test, respectively. All tests were two-sided and a P-value<0.05 was used as the cut-off for statistically significance. Statistical analyses were performed using statistical package STATISTICA 98 (stat Soft Polsca, Krakow, Poland).

Results

The descriptive characteristics for cases and controls are given in Table 1. The mean age of cases was 56.9 years and that of controls 56.4 years. Briefly, compared with controls cases had higher BMI levels, earlier age at menopause, shorter durations of breastfeeding, lower weekly average vegetables consumption, and were more likely to be active smokers. Data on height, low family income, age at menarche, age at first birth, frequency of red meat consumption, weekly average alcohol intake, hormone use history, family history of breast cancer, and experience of stress were similarly distributed between cases and controls. The average level of total physical activity (occupational, household and recreational combined) reported by cases over their lifetimes was lower than that of controls (P for trend=0.003) (Kruk, 2006).

Results from analysis of self-reported comparative physical activity at ages 10-12 years, 13-15 years and 10-15 years are reported in Table 2. Women who were physically active such as their peers or more active at ages 10-12 years had only slightly reduced age-adjusted risks compared with the lowest tertile, however, none of these reductions was statistically significant. Inclusion of the other variables listed in the 'Material and Methods' and total lifetime physical activity decreased the risk estimates, e.g., from OR=0.88 to a multivariate OR=0.25 for 'more active', still their confidence intervals a little exceeded 1.00 (95% CI=0.06-1.09, 95% CI=0.06-1.10, respectively); the dose-response trend was also not significant (P for trend=0.15).

For physical activity at ages 13-15 years, both the simple and multivariate adjusted odds ratios for breast cancer were also decreased among women who were at least such active as their peers, but the reductions were not statistically significant. The relations found between physical activity and breast cancer risk did not vary much in women who were more physically active than their peers at ages 10-15 years.

Table 2. Physical Activity at Ages 10-12 Years, 13-15 Years and 10-15 Years and Risk of Breast Cancer

Activity comparison	Number of cases	Number of controls	OR* (95% CI*) Age adjusted	OR* (95% CI*) Multivariable adjusted
Activity at age 10-12 years				
Less active	11	11	1.00	1.00[a]
Equally active	137	178	0.81 (0.34-1.92)	0.26 (0.06-1.09)
More active	102	112	0.88 (0.36-2.15)	0.25 (0.06-1.10)
P for trend			0.37	0.15
Activity at age 13-15 years				
Less active	11	11	1.00	1.00[b]
Equally active	142	184	0.78 (0.33-1.84)	0.27 (0.06-1.30)
More active	97	106	0.91 (0.37-2.00)	0.32 (0.07-1.55)
P for trend			0.38	0.28
Activity at age 10-15 years				
Less active	16	10	1.00	1.00[c]
Equally active	125	158	0.49 (0.17-1.40)	0.35 (0.12-1.55)
More active	86	90	0.55 (0.19-1.61)	0.30 (0.11-1.34)
P for trend			0.78	0.20

OR, odds ratio; CI, confidence interval. [a]Adjusted for age, BMI, age at menopause, passive cigarette smoking, vegetable and fruits consumption. [b]Adjusted for age, BMI, family income, age at menopause, passive cigarette smoking, vegetable and fruits consumption. [c]Adjusted for age, BMI, passive cigarette smoking.

Table 3. Odds Ratios for Breast Cancer According to Physical Activity at Ages 10-12 Years and Lifetime Total Physical Activity Measured from Age 14 Years till Age in Reference Year

	Number of cases	Number of controls	OR* (95% CI*) Age adjusted	OR* (95% CI*) Multivariable adjusted
Lifetime total physical activity, hours/week/year				
Inactive	97	67	1.00	1.00[a]
Active	142	223	0.44 (0.30-0.64)	0.45 (0.28-0.64)
Lifetime total physical activity,MET-hours/week per year				
Inactive	88	77	1.00	1.00[b]
Active	151	213	0.62 (0.43-0.90)	0.64 (0.43-0.92)

OR, odds ratio; CI, confidence interval. [a]Adjusted for age, BMI, and vegetables and fruits consumption. [b]Adjusted for age and BMI.

The data on physical activity at ages 10-12 years and from age 14 years to the reference year enabled to evaluate the effect of changes in the activity throughout a woman's life. Due to the small numbers of cases and controls who reported that they had been less active than their peers, analyses were restricted only to women who reported equel or higher physical activity than their peers. Fifty nine percent of cases and 77% of controls (physical activity measured in hours/week per year) and similarly 63% cases and 73% controls (physical activity in MET-hours/week/year) who were active as peers or more active than their peers were active at older ages (Table 3). Women who continued their physical activity after age 10-12 years had statistically significant strong risk reductions for both measurements of the activity (55% reduction and a 36% reduction, respectively). The risk estimates were not substantially changed after adjustment for possible confounding variables.

Discussion

This study is the first to assess the association between physical activity in childhood and breast cancer risk among the Polish women. The relationship was examined for self-determination of physical activity at ages 10-12 years, 13-15 years and 10-15 years compared with the activity of women's peers. No evidence of a dose response relationship was seen, although much greater reduction in the risk was found among those women reporting the same or higher physical activity than their peers. A potential threshold effect was of borderline statistical significance for ages 10-12 years in multivariable-adjusted models with a full examination of confounding by other established and putative risk factors (OR=0.25, 95% CI=0.06-1.10 for the highest versus the lowest tertile, P for trend 0.15).

Although based on different methods for physical activity ascertainment these findings agree with some but not all previous studies on the association between physical activity in early period of a woman's life and breast cancer risk (Lagerros et al., 2004). Lagerros and co-workers (2004) have reported in their meta-analysis of 19 case-control and four cohort studies on adolescent and/or young adulthood (12-24 years) physical activity and breast cancer that relative risk ranged from 0.2 to 1.4 among women of high versus low physical activity and that the summary relative risk was found to be 0.81 (0.73-0.89). In this quantitative review two reports out of 23 studies showed increased risk.

The reported study is similar to four studies with regard to analysis of the physical activity at age 10-12 years - breast cancer relation (Gammon et al., 1998; Marcus et al., 1999; Trentham-Dietz et al., 2000; Verloop et al., 2000). Gammon et al. (1998) in a case-control study in US (1,668 cases, 1,505 controls) did not found any association for highest versus lowest quartile of physical activity measured in MET-score (OR=0.99, 95% CI=0.79-1.24, P for trend=0.33). In a population-based case-control study performed in US by Marcus et al. (1999), (864 cases, 789 controls), which is the most similar with comparative physical activity measure used in the present study, a relative risk of 0.9 (95% CI=0.7-1.2) was reported for women who were more active than peers compared with women who were less active than their pears (P for trend=0.78). Also, nonsignificant reduction in the risk was observed when the activity had been evaluated in METs/week (OR=0.6, 95% CI=0.1-1.1) for women in the highest category of activity. In turn, Trentham-Dietz et al. (2000), in a population-based case-control study carried out in US (5,659 women), reported borderline statistically significant small reduction in breast cancer risk (RR=0.92, 95% CI=0.3-1.1) among women whose activity was >35 MET-score per week versus no. The next, a population-based case-control study by Verloop et al. (2000), (918 cases, 918 controls), similar to the present study with regard two time windows, i.e., at ages 10-12 years and ages 13-15 years and comparative measure of physical activity, demonstrated an inverse association between breast cancer and physical activity among more active women than their pears at age 10-12 years (OR=0.68, 95% CI=0.49-0.94) and borderline statistically significant reduction in the risk at age 13-15 years (OR=0.77, 95% CI=0.57-1.05).

The results of this analyses of association between exercise performed at ages 10-15 years, i.e., around the age of menarche, and the risk of developing breast cancer can be compared with two studies that reported effects for similar time periods (Chen et al., 1997; Verloop et al., 2000). Likewise as the present study, in a study by Verloop et al. (2000) it was found that women who were more active than their peers in both mentioned time windows had no further breast cancer risk reduction (OR=0.72, 95% CI=0.50-1.03) compared with particular time periods. In turn, in a study by Chen et al. (1997) among the three-country Seattle metropolitan area residents no evidence of a trend with increasing recreational activity at ages 12-16 years measured by averages weekly frequency, total hours spent in physical activity or energy expenditure was observed. The ORs for the highest compared with the lowest level of physical activity were 0.92 (95% CI=0.55-1.53), 1.19 (95% CI=0.75-1.87), and 1.24 (95% CI=0.75-1.87), respectively.

The reported study showed a large effect of confounding in analysis such as age at menarche, BMI, passive smoking, and consumption of vegetables and fruits. These findings are consistent with those from majority other studies (as reviewed by Okasha et al., 2003). Another noteworthy finding was a continuation of increased physical activity at older ages by women active during childhood. This result is consistent with the finding reported by Alfano et al. (2002) who found that women who are physically active during childhood and adolescence are more likely to be active as adults.

The association between physical activity and breast cancer risk is complex. Various hypothesized biological mechanisms for role of physical activity in breast cancer etiology have been proposed. They include changes in endogenous sexual hormone (estrogens), growth factors, changes in the immune function, alterations in free radical production, and decreased obesity in postmenopausal women, although, hormonal level, energy balance and body composition are most often cited (Friedenreich et al., 1998b; Hoffman-Goetz et al., 1998; Lagerros et al., 2004). The effect of exercise in early life particularly at the time of puberty or in early adulthood, with a subsequent reduction of breast cancer risk is due to delaying the age at menarche and the regularity of menstrual cycles or shortening luteral phase; all they decrease the overall exposure to estrogens (Bernstein et al., 1987). Exercise can also modify central body fat distribution and decrease weight gain thereby alter estrogen metabolism. This is particularly important for women after menopause because postmenopausal obesity is considered as a risk for several types of cancer (Westerlind, 2003).

Before drawing conclusions from the present report certain potential limitations and strengths should be considered. One methodological issue is possibility of recall bias because women were asked to report on their activity in several previous years decades. However, a major methodological issue of this study is self-reported comparative measure of physical activity, instead of examining frequency, duration, and intensity of physical activity, that may be subjective. It is also possible that all participants may have overreported their activity at childhood, hence the small number of cases and controls reported that they were less active than their pears. Although the assessment method of physical activity applied in the study is similar to that in a US study (Verloop et al., 2000), which reported significant reduction in breast cancer risk. Misclassification of exposure may be non-differential because of the same method was applied to collect information from cases and controls. Another limitation of the study, as well as studies of other researches, is a lack of information on caloric intake. In addition, due to the small sample size (11cases, 11 controls) reporting that they were less active than their pears did not allow to evaluate the association stratified by effect modifiers such as age at menarche, body mass index, passive smoking and diet.

The present study has a number of strengths. The study included only cases who have had histologically confirmed incident, invasive or in-situ breast cancer. In addition, a wide range of possible confounders of the physical activity-breast cancer relationship was measured and assessed in logistic models. Also, the study included a relative large sample of cases and controls whom the responses rate was high (>70%), and the physical activity-breast cancer relation was examined for two age periods and their combining.

In conclusion, this study presents only limited support for protective effect of physical activity at ages 10-12 years for breast cancer occurring in adulthood. This is consistent with findings from other studies that did not show a relation and considered short-term physical activity (see, for example Gammon et al., 1998 and references cited therein). The finding is in contrast to results from studies that found decreased risk factors with increased recreational or lifetime total activity (see Friedenreich, 2004) as well as to our previous study (Kruk, 2006) which employed this cohort of women and comprehensive assessment of long-term total physical activity (between 14 years and the reference year). Further research employing larger sample sizes with comprehensive assessment of physical activity in childhood is warranted to clarify the relation of physical activity to breast cancer risk.

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