RESEARCH ARTICLE

Lifetime Physical Activity and Breast Cancer: a Case-Control Study in Kelantan, Malaysia

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Abstract

Background: Physical inactivity has been identified as the fourth leading risk factor for global mortality and is associated with increased breast cancer diagnosis and recurrence. Purpose: To examine the association between adult lifetime physical activity and breast cancer risk in a case-control analysis. Materials and Methods: This study involved 122 cases of breast cancer and 121 controls in the state of Kelantan in Malaysia. A comprehensive measure of lifetime physical activity was used to assess occupational, household, and recreational/sports activity. For every type of activity, a metabolic equivalent (MET) score was assigned using the compendium of physical activities. MET-hours/week per year for all types of activities at different levels of intensities for different age groups were calculated. Logistic regression analysis was used to estimate odds ratios between various measures of physical activity and breast cancer risk. Conclusions: The mean MET-hours/week per year for all activities were 120.0 and 132.9 of MET-hours/week per year for cases and controls respectively. Household activities accounted for about 70% of the total lifetime physical activities. Only about 2.5% of the total lifetime physical activities were in the form of recreational/sports. This study found no association between lifetime occupational and recreational/sports physical activities with breast cancer risk among Kelantanese women. However, higher intensity lifetime household activities seemed to significantly reduce risk of breast cancer.

Keywords: Lifetime physical activity - breast cancer - metabolic equivalent score - Malaysia

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Introduction

Breast cancer is the most common cancer among women worldwide and the incidence has been increasing over the years with industrialization and urbanization. In Malaysia, the mean age of breast cancer diagnosis was 50.6 years old. A study by Abdullah et al.(2013), based on a complete data set of 10,230 breast cancer cases between 2000 to 2005, indicated that the overall 5-year survival rate was 49% with median survival time of 68.1 months. Indian women had a higher survival rate of 54% compared to Chinese women (49%) and Malays (45%). The same study concluded that the overall 5-year survival rate of breast cancer patient among Malaysian women was still low as compared to survival rates in developed nations.

In the United States, the National Cancer Institute (NCI) considers breast cancer as the most frequently diagnosed cancer in the United States. It is the second leading cause of cancer-related death in women, after lung cancer. It was estimated that in 2015 there will be 231,840 new cases of invasive breast cancer expected to be diagnosed and 40,290 breast cancer deaths among women (American Cancer Society, 2015). The same report also showed that an estimation of 1 in 8 women in the United States will be diagnosed with breast cancer at some time in their lives.

Established risk factors for breast cancer include genetic factors such as family history of breast cancer (Jatoi et al., 2008), and being a carrier of BRCA-1, or BRCA-2 mutations (Key et al., 2001). Reproductive factors such as early age at menarche, late age at first birth, nulliparity, and late age at menopause were also associated with higher breast cancer risk (Colditz and Rosner, 2000; Chu and Anderson, 2002). Hormonal factors including the usage of combined estrogen plus progestin postmenopausal hormone therapy (Monninkhof et al., 2007) and recent use of oral contraceptives (Rosenberg et al., 2009) were among the risk factors as well.

Roughly 24% of breast cancers were diagnosed before the age of 50 (Brinton et al., 2008). Therefore, reducing breast cancer incidence in young women requires that prevention efforts begin much earlier in life. Lahmann et al. (2007) estimated that 30-40% of breast cancer cases can be prevented by a healthy lifestyle. A healthy lifestyle, include healthy diet and proper physical activity level, prevents obesity which is also another risk factor for

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breast cancer. Most studies reported that high physical activity was associated with decreased risk for breast cancer. Monninkhof et al. (2007) reviewed 48 studies on physical activity and breast cancer and about 50% of them indicated that increasing levels of physical activity could lower breast cancer risk. Physical inactivity and leanness in early life and obesity in later life were found to be some of the established breast cancer risk factors (Dorn et al., 2003; Slattery et al. 2007) . Studies in non-western nations also show similar outcomes where physical activity was associated with lower breast cancer risk (Pronk et al., 2011; Nasui and Ciuciuc, 2013).

Several studies have assessed lifetime physical activity on breast cancer risk with inconsistent results. According to Dalal et al. (2007), an average lifetime of more than 5 hours per week of vigorous recreational activities was significantly associated with reduced risk of breast cancer in a cohort of premenopausal and post menopausal women. However, Dorn et al. (2003) and Slattery et al. (2007) indicated no significant relationship between breast cancer risk with an average of more than 3 hours per week lifetime vigorous physical activity. Most consistent associations have been found for strenuous recreational physical activity in lowering breast cancer risk (McTiernan et al., 2003). Pronk et al. (2011) also found that both higher recreational and occupational physical activity were associated with lower breast cancer risk.

Friedenreich et al. (2001) found no associations between lifetime physical activity and breast cancer for premenopausal women but for postmenopasual women, risk reduction was indicated for those with high MET-hours/week per year.

Measuring physical activity itself can be very challenging. Inconsistencies in the methodology used may occur with regards how physical activity is measured, the type of activity that is included for assessment, the intensities of each activity and the time period in life assessed. Some studies have collected data by mode of activity (recreational, occupational, and household), assigned intensities and then converted to activity-related energy expenditure (e.g., MET-hours/week) and used the MET-hours/week to compare activity by mode and duration. Some take into consideration lifetime physical activity and some only a certain time period. Inconsistencies in associations between physical activity and breast cancer risk may also exist due to population characteristics. Menopausal status, race/ethnicity are some possible effect modifiers (Dalal et al., 2007; Slattery et al., 2007). There may be a modifying effect on the physical activity and breast cancer association by other characteristics of the women such as reproductive factors including nulliparity or age at first pregnancy.

In this study the main objective was to examine whether there is a critical time period when physical activity influences breast cancer risk and to better understand the types and the intensities of physical activity and breast cancer association. As most consistent associations with lower breast cancer risk have been found for strenuous recreational physical activity, uncertainties remain regarding the impact of household, outdoor, or occupational activities, especially if only light or moderate ranges of activities are involved.

Materials and Methods

This study involves 122 cases of breast cancer and 121 controls in Kelantan Malaysia. Eligible cases were women age 35 years or above and diagnosed with breast cancer. Potentially eligible controls (n = 121) who were free of any cancer diagnosis, were matched to the cases by geographical area, ethnicity and by age within 5-year age-groups. Respondents were approached for personal interviews by trained interviewers. Data collection was conducted between year 2013 and 2014 after obtaining of ethical approval from the Human Research Ethics Committee, Universiti Sains Malaysia in January 2013.

The structured questionnaire covered demographic information, occupational history, medical and reproductive history, hormone use, smoking, alcohol use, diet, cancer history in female relatives, and lifetime physical activity. Data on physical activity were classified into household/outdoor chores, occupational and exercise/sports activities. Each was recorded separately throughout a woman's lifetime using a table format modified version of the Friedenreich (2011). The three types of physical activity were examined for the four age periods (onset of menstruation-21, 22-34, 35-50, and 51-65 years).

The measure of physical activity is metabolic equivalent tasks (MET) (defined as a ratio of the working and the resting metabolic rate) and MET per hour score which is a measure of the intensity of physical activity. A comprehensive measure of lifetime physical activity had been used to assess occupational, household, and recreational/sports activity (Friedenriech et al., 1998), we adopted the instruments and manuals provided in our data collection and enumerator training. Recall and memory-probing aids gave us some ideas on how to probe and we adapted some of the suggested aids; instead of a recall calendar, we spent some time talking with respondents to gain their confidence and slowly asked them to recall their lifetime physical activities. Enumerators will probe and record the different types of physical activity performed in each setting, and rated the intensity of each activity (light,moderate, heavy). The frequency and duration of these activities were assessed by recording the number of years, months per year, weeks per month, days per week, and hours per day that each activity was performed. For every type of activity, a metabolic equivalent (MET) score was assigned using the Compendium of Physical Activities developed by Ainsworth et al. (2000).

Household activities included light, moderate/heavy chores, and moderate/heavy chores related to caring for children, aged and other individuals. In addition, household activities included some moderate/heavy chores that were performed outdoors (not including those done as part of a paid job) relating to gardening, sweeping, mopping, chopping wood, carrying water from river or well, or caring for larger animals. Women were asked about the total number of hours spent on the particular category of activity per day, week, month, or year over specific age ranges, namely from onset of menstruation to 21, 22 to 34, 35 to 50 and 51 to 65.

The occupational history covered physical activity at each reported job held longer than 6 months, questions on estimated number of hours per day and how many days in a week, how many months and years. Activities at work were given the intensity levels based on whether the job include more of sitting, standing, walking with no lifting, walking with some lifting and doing heavy physical work. The data were then converted to the number of hours per week/months/year for each type of activity. For every type of activity, a metabolic equivalent (MET) hours/week per year score was assigned using the Compendium of Physical Activities developed by Ainsworth et al. (2000). Similar technique was use to calculate the MET hours/week per year score for lifetime household and recreational/sports activity.

We performed logistic regression analyses to estimate odds ratios (ORs) and 95% confidence intervals (CIs) as the measure of association between various measures of physical activity and breast cancer risk. Household, occupational and recreational lifetime physical activities were categorized according to the tertile distribution in both cases and controls, with the least active tertile used as the referent. Based on existing knowledge, a priori list of potential confounders was formulated, which included age, age at menarche, menopausal status, age at menopause, breast-feeding, weight change , breast cancer in first degree female relatives, oral contraceptive use, marital status, education, tobacco smoke exposure as well as tobacco and alcohol use. The final models included only variables that remained statistically significant ($P < 0.05$) in the multivariate analyses.

To test whether physical activity in specific periods of adult life was more important than in other periods, we additionally analyzed the association between breast cancer and physical activity separately for activities reported for the age period starting from onset of menstruation to 21, 22 to 34, 35 to 50 and 51 to 65.

Results

Table 1 shows the socio demographic and lifetime physical activity measures of the cases and controls. As expected the cases and controls were of a similar age and the majority were of Malay ethnic origin and practising the

Table 1. Socio-Demographic Characteristics, Risk factors and Lifetime Physical Activity Measures of Cases and Controls (n= 243)

Characteristic		Cases (n=122)	Controls (n=121)	P value (t-test)
Age (years) (mean (SD*))		51.5 (8.38)	50.8 (8.77)	0.551
Ethnicity				
Malay (%)		111 (91.0)	116 (95.9)	
Chinese (%)		9 (7.4)	5 (4.1)	
Indian (%)		1 (0.4)	0	
Siamese (%)		1 (0.4)	0	
Educational level				
None (%)		9 (7.4)	2 (1.7)	0.011a##
Primary (%)		15 (12.3)	18 (14.9)	
Secondary (%)		64 (52.5)	82 (67.8)	
Post-secondary (%)		34 (27.9)	19 (15.7)	
Ever married	Yes (%)	122 (100)	115 (95)	0.014b##
Ever smoke	Yes (%)	5 (4.1)	1 (0.8)	0.11b
Secondary tobacco smoke exposure	Yes (%)	74 (60.7)	61 (50.4)	0.11a
Age (years) at first menstrual period (mean (SD))		13.4 (1.60)	13.07 (1.48)	0.091#
Menopause attained	Yes (%)	84 (68.8)	52(43.0)	<0.001a###
Breastfeed >6 months	Yes (%)	72 (59.0)	89 (73.6)	0.017a##
Oral contraceptive use	Yes (%)	49 (40.2)	38 (31.4)	0.15a
Lifetime household physical activity (MET*-hours/week per year) (mean (SD))		79.3 (43.19)	94.5 (43.95)	0.007##
Lifetime occupational physical activity (MET-hours/week per year) (mean (SD))		37.6 (33.77)	36.23 (29.16)	0.731
Lifetime recreational/sports physical activity (MET-hours/week per year) (mean (SD))		3.3 (4.94)	2.13 (4.03)	0.053#
Lifetime total physical activity (MET-hours/week per year) (mean (SD))		120.2 (45.85)	132.9 (43.06)	0.027##
Total physical activity puberty-21 yrs of age (MET-hours/week per year) (mean (SD))		93.2 (60.10)	101.7 (57.8)	0.262
Total physical activity 22-34 yrs of age (MET-hours/week per year) (mean (SD))		150.9 (71.08)	161.9 (59.17)	0.192
Total physical activity 35-50 yrs of age (MET-hours/week per year) (mean (SD))		116.5 (64.86)	135.1 (62.61)	0.024##
Total physical activity 51-65 yrs of age (MET-hours/week per year) (mean (SD)) Cases n=63; Controls n=58		56.6 (45.66)	82.6 (69.26)	0.017##
Total physical activity in the past 12 months (MET-hours/week per year) (mean (SD))		71.9 (65.08)	112.7 (68.67)	<0.001###

*SD, standard deviation; IQR, interquartile range; MET, metabolic equivalent, [a]Pearson's Chi Square or b Fisher's exact test, [#]P<0.10; [##]P<0.05; ###P<0.001

Table 2. Odds Ratios for Lifetime Total Physical Activity and Total Physical Activity for Specific Periods of Cases and Controls (n=243), Kelantan , Malaysia, 2013-2014

Physical activity (MET*-hours/week per year)	Cases (n=122)	Controls (n=121)	Crude OR*	95% CI*	Age adjusted OR	95% CI	Multivariable+ adjusted OR	95% CI
Total Lifetime								
<102.0 (tertile 1)	49	32	1		1		1	
102.0-140.2 (tertile 2)	36	45	0.52##	0.280, 0.976	0.49##	0.261, 0.931	0.42##	0.211, 0.846
>140.2 (tertile 3)	37	44	0.55#	0.294, 1.025	0.52##	0.274, 0.977	0.53#	0.266, 1.066
P-value for trend			0.08#		0.054#		0.043##	
Total physical activity between menarche to 21 years old								
<63.3 (tertile 1)	44	35	1		1		1	
63.3-110.1 (tertile 2)	44	38	0.92	0.495, 1.714	0.91	0.490, 1.699	1.22	0.622, 2.402
>110.1 (tertile 3)	34	48	0.56#	0.302, 1.052	0.55#	0.294, 1.034	0.7	0.354, 1.367
P-value for trend			0.148		0.133		0.244	
Total physical activity between 22 to 34 years old								
<127.3 (tertile 1)	46	32	1		1		1	
127.3-<179.7 (tertile 2)	34	49	0.48##	0.257, 0.905	0.48##	0.256, 0.901	0.44##	0.225, 0.878
>179.7 (tertile 3)	42	40	0.73	0.391, 1.355	0.71	0.378, 1.337	0.63	0.315, 1.245
P-value for trend			0.074#		0.073#		0.065#	
Total physical activity between 35 to 50 years								
<90.6 (tertile 1)	51	30	1		1		1	
90.6-146.0 (tertile 2)	38	43	0.52##	0.278, 0.974	0.52##	0.275, 0.968	0.40###	0.199, 0.798
>146.0 (tertile 3)	33	48	0.40###	0.215, 0.761	0.40###	0.209, 0.746	0.40###	0.203, 0.799
P-value for trend			0.015##		0.013##		0.011##	

*MET, metabolic equivalent; OR, odds ratio; CI, confidence interval, +Multivariable adjusted for current age, menopausal status, secondary smoke exposure and 6-month history of breastfeeding, #P<0.10; ##P<0.05; ###P<0.01

Table 3. Odds Ratios for Lifetime Total Physical Activity by Activities: Household, Occupational and Recreational/ Sports of Cases and Controls (n=243), Kelantan Malaysia, 2013-2014

Physical activity (MET*-hours/week per year)	Cases (no.)	Controls (no.)	Crude OR*	95% CI*	Age adjusted OR	95% CI	Multivariable+ adjusted OR	95% CI
Lifetime household physical activity								
0-<61.1 (tertile 1)	50	31	1		1		1	
61.1-<101.9 (tertile 2)	38	43	0.54##	0.284, 1.020	0.53##	0.278, 1.005	0.52#	0.261, 1.046
>101.9 (tertile 3)	34	48	0.44##	0.221, 0.861	0.42##	0.212, 0.835	0.41##	0.190, 0.867
P-value for trend			0.042##		0.034##		0.051#	
Lifetime occupational physical activity								
0- <20.0 (tertile 1)	39	41	1		1		1	
20.0- <42.9 (tertile 2)	41	40	0.92	0.482, 1.771	0.95	0.496, 1.837	0.91	0.415, 1.829
>42.9 (tertile 3)	42	40	0.87	0.454, 1.685	0.88	0.456, 1.697	0.9	0.448, 1.829
P-value for trend			0.922		0.927		0.952	
Lifetime recreational/sports physical activity								
0-<0.22 (tertile 1)	37	43	1		1		1	
0.22-<1.8 (tertile 2)	37	46	0.78	0.407, 1.478	0.87	0.443, 1.713	0.93	0.449, 1.919
>1.8 (tertile 3)	48	32	1.47	0.765, 2.841	1.65	0.830, 3.280	1.58	0.759, 3.279
P-value for trend			0.139		0.126		0.272	

*MET, metabolic equivalent; OR, odds ratio; CI, confidence interval, +Multivariable adjusted for current age, menopausal status, secondary smoke exposure and 6-month history of breastfeeding, #P<0.10; ##P<0.05

Muslim faith. Although efforts were made to match both the ethnicity and age of the respondents, it was not possible to source Indian and Siamese controls during the data collection period. Compared to controls, there were more uneducated as well as higher (post-secondary) educated cases. All the cases and 95% of the controls were either married or had been married. There were more smokers and ex-smokers among the cases but it was not significant (Fisher's exact test, one sided: P=0.11). Over half of both cases and controls reported exposure to second hand smoke either at home or in the workplace with more cases reporting exposure (60.7%) but this was not significantly different (Pearson's Chi Square 2.581, P=0.11).

For hormonal and reproductive risk factors for breast cancer which are also shown in Table 1, there was no significant difference in the reported age of menarche as well as reported oral contraceptive use between the two groups. Use of hormone replacement therapy was not asked for in this study. There was, however, a significant difference between the history of breastfeeding at least 6 months between cases and controls with cases reporting less breastfeeding.

A big proportion of lifetime physical activities among women in Kelantan were from household activities where the mean value for MET-hours/week per year for cases and controls were 79.3 and 94.5 respectively. There was a significant difference between the two groups pertaining to household activities. Higher intensity household activities were mainly recorded in the younger days of the respondents when many households did not own washing machine for laundry and gas stoves for cooking. Clothes were hand-washed, household chores include scrubbing the floors, some respondents collected firewood for cooking, carried water from the river or well and rear chicken and plant vegetables for their own consumption. Other common household activity was childcare. Almost

all the respondents were married or had been married, and the majority of them did their own childcare.

About 84% of cases and 93% of controls had worked before in their lifetime. The mean value for MET-hours/week per year for occupational activities for cases and controls were 37.6 and 36.2 respectively. There was no significant difference between cases and controls for occupational physical activities. Relatively small number of women, both cases and controls, in Kelantan were engaged in sports or recreational activities. Although there is a significant difference between the mean MET-hours/week per year for cases (3.3) and controls (2.13) the amount were very small relative to the total mean of 120.2 and 132.9 of MET-hours/week per year respectively. The number of respondents engaging in these activities was small. Those who we engaged sports and recreational activities at moderate and vigorous intensities were negligible.

Highest mean MET-hours/week per year value were recorded for both cases and controls among the respondents between age 22 to 34 years old compared to other age groups. There were no significant difference between the mean MET-hours/week per year values for cases and controls between puberty to 21 years as well as age between 22 to 34 years. However, the controls seemed to be more physically active compared to cases from age 35 years and above. Notably from age 51 onwards, higher physical activities were recorded among controls is not a surprise as most cases were already diagnosed with breast cancer which have resulted in lower physical activities. A marked difference between the MET values for cases and controls can also be seen over the last 12 months from the time of the survey.

Logistic regression estimated the odds of being diagnosed with breast cancer across tertiles of lifetime physical activity based on different age groups and types of activities are shown in table 2 and table 3 respectively. The association between total lifetime physical activity and breast cancer was examined between cases and control and adjusted for current age, menopausal status, secondary smoke exposure and 6-month history of breastfeeding.

Table 2 shows the odds ratio for lifetime total physical activity and total physical activity based on different periods for cases and controls. Higher lifetime total physical activity seemed to reduce breast cancer risk. There were significant difference between controls and cases for those in tertiles 2 and 3 groups (tertile 1 is used as referent) who recorded greater than 102.0 mean MET-hours/week per year. This outcome is also true for the age-adjusted and the multivariable adjusted models.

We decided to evaluate physical activity between menarche to 21 years old, 22-34 years old and 35-50 years old. The reason for excluding the age group between 51-65 years old is the small number of observations. As shown in table 2, more cases were in tertile 1 compared to the controls in all the age groups. Between menarche and 21 years old there was a significant association of risk reduction for those in tertile 3. Associated risk reduction was also shown in those in tertile 2 between 22 and 34 years old. A more distinctive relationship was recorded for physical activity between 35 and 50 years old which indicate significant difference in tertile 2 and 3 when compared to tertile 1.

This study finds no associations between lifetime occupational and recreational/sports physical activities with breast cancer risk reduction among the Kelantanese women. As shown in table 3, only lifetime household physical activity that indicate a significant difference in the mean MET-hours/week per year value between cases and controls. Higher intensity lifetime household activities seemed to have significant risk reduction of breast cancer.

Discussion

Development in the form of industrialization, urbanization and automation, has resulted in the population's lifestyle becoming increasingly sedentary. Sedentary behaviors such as watching television and using the computer or mobile phone are possible causes for weight gain, overweight and obesity. Overweight has been identified as one of the risk factors for breast cancer (McCullogh et al., 2012; Friedenreich, 2011; Brown et al., 2009; Fair and Montgomery, 2009). Automation in many workplace practices has now classified jobs as sedentary. These jobs may have previously required significantly more energy expended through light or moderate intensity activity. For example, in the USA between 1965 and 2009 total sedentary time increased by 43 % (Ng and Popkin, 2012). Technological changes have also substantially reduced the intensity levels of household activities over the last three to four decades particularly in the developing nations. For example, in Malaysia, especially in the rural areas, not many households owned washing machines way back in 1970s or even 1980s. Household activities then involved much higher intensity levels of physical activities.

The objective of this study was to examine whether there is a critical time period for physical activity or a specific type of physical activity that influence breast cancer risk. Our result indicated that higher intensity in the total lifetime physical activity was recorded among controls. In general, more controls were also recorded with higher MET values during the period before the cases were diagnosed with breast cancer. As shown in our study, controls recorded significantly higher MET values between menarche and 21 years old and also between 22 and 34 years old. Thus, indicating that to a certain extent, higher intensity lifetime physical activity was associated with breast cancer risk reduction. Between 35 and 50 years old there was a more distinctive difference between the intensity of physical activity between controls and cases. Most cases were diagnosed within this age group and usually patients will slow down or reduce the intensity of their physical activities.

Our findings shows that occupational and recreational/sports physical activities do not have significant risk reduction for breast cancer among women in Kelantan. Although the most consistent associations have been found for recreational physical activity, especially strenuous activity, uncertainties remain regarding how breast cancer risk is affected by household, outdoor, or occupational activities, especially if light and moderate

ranges of activities are involved (McTiernan et al., 2003). However, overall, women in Kelantan have recorded too low MET values for recreational/sports physical activity to have any distinctive impact. Similar to some other studies occupational, particularly, the sedentary types have no significant impact on breast cancer risk (Lynch et al., 2013). In this study there is a breast cancer case that is worth noting with a very high MET value for occupational physical activity, it turned out that she was working at a tobacco factory for a substantial number of years.

The main proportion of the lifetime physical activities among Kelantanese women consist of household activities. Breast cancer risk reduction was indicated among those who recorded high MET values in their lifetime household physical activity. Almost all the respondents in this study were married or had been married. Main household chores were childcare, cooking, washing clothes and cleaning. More strenuous household chores were recorded during younger age when most chores where carried out manually.

About one in four breast cancers is diagnosed before the age of 50, therefore, breast cancer prevention efforts must begin early in life. Breast cancer prevention efforts that focus on lifestyle, food intake and physical activity will have the greatest effect when initiated at an early age and continued over a lifetime.

The setback of this study is the limited sample size. A more accurate analysis should be carried out based on a case-control study of both pre- and postmenopausal breast cancer. Other limitations include imprecise recall of lifetime physical activities among respondents, and predefined categories of the activities (eg, heavy household chores), or preset categories of occupational activities, might also introduce some exposure misclassification.

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