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ORIGINAL ARTICLE

Occupational sedentariness and breast cancer risk

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ABSTRACT

Background: Epidemiological studies have indicated that physical activity reduces the risk of developing breast cancer. More recently, sedentary behavior has been suggested as a risk factor independent of physical activity level. The purpose of the present study was to investigate occupational sedentariness and breast cancer risk in pre- and postmenopausal women.

Materials and methods: In a population-based prospective cohort study (n = 29 524), working history was assessed by a questionnaire between 1990 and 1992. Participants were classified as having: (1) sedentary occupations only; (2) mixed occupations or (3) non-sedentary occupations only. The association between occupational sedentariness and breast cancer incidence was analyzed by Cox regression, adjusted for known risk factors and participation in competitive sports.

Results: Women with a working history of occupational sedentariness had a significantly increased risk of breast cancer (adjusted HR 1.20; 95% CI 1.05, 1.37) compared with those with mixed or non-sedentary occupations. The association was stronger among women younger than 55 years (adjusted HR 1.54; 95% CI 1.20, 1.96), whereas no association was seen in women 55 years or older. Adjustment for participation in competitive sports did not change the association.

Conclusions: We found that occupational sedentariness was associated with increased breast cancer risk, especially in women younger than 55 years. This may be a modifiable risk factor by planning breaks during the working day. Whether this reduces the risk of breast cancer needs to be further studied.

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Breast cancer is the most common type of cancer in women in Sweden. In 2014, 9730 women were diagnosed with breast cancer [1]. The incidence is associated with hormonal factors such as parity, age at birth of the first child, age at menarche, age at menopause, and use of oral contraceptives and hormone replacement therapy, as well as age, family history of breast cancer, body mass index (BMI), alcohol consumption [2] and low levels of physical activity [3].

Regardless of physical activity level, sedentariness has been associated with an increased risk of disease and illness, including several types of cancer [4]. Sedentary behavior is commonly characterized by prolonged sitting, which is distinct from a low level of physical activity [5]. Sedentary behavior, as well as physical activity, can occur in different contexts (domains), including sitting during transport, at work, at home and during leisure time.

Previous studies have shown an association between sedentary behavior and endometrial, colorectal and breast cancer [6–8]. The evidence is stronger for endometrial [relative risk (RR) 1.32] and colorectal cancer (RR 1.24–1.30) than for breast cancer (no association or RR 1.17). In a meta-analysis regarding the association between sedentary behavior and breast cancer incidence by Zhou et al., only occupational sedentary behavior was significantly associated with an increased risk of breast cancer (RR 1.10), whereas sedentary behavior during leisure time or in daily life was not. Subgroup analyses by menopausal status, which was performed in only three studies (all of them case-control design), did not change the results [8].

To our knowledge no previous cohort study has investigated associations between occupational sedentariness as a risk factor for breast cancer, stratified by menopausal status. In the present study, we used a large prospective population-based cohort including 29 524 women, aged 25–65 years, to further elucidate the associations between working history of occupational sedentariness and the occurrence of pre- and postmenopausal breast cancer. As physical activity is a protective factor against breast cancer we also included participation in competitive sports in the analyses.

Materials and methods

Participants

In this population-based cohort study, 40 000 women in the southern part of Sweden with no history of invasive cancer were invited by letter to answer a questionnaire about risk factors relevant to cancer development. The invitation was

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sent in 1990 to 1000 women from each yearly birth cohort, between 25 and 64 years of age, who were randomly chosen from the general population registry. One reminder was sent to non-responders. All participants signed a written informed consent. A follow-up questionnaire was sent in 2000. The Regional Ethical Review Board of Lund University approved the study (LU-34-92, LU 849-05).

Questionnaire

The first questionnaire in 1990 contained questions on, for example education, marital status, family history of cancer, smoking, age at menarche, age at menopause, parity, oral contraceptives and hormone replacement therapy (HRT). The occupational history was based on the following question: '*Do/did you have any occupation? Yes/No.* If the answer was yes: *Please, fill in all your occupations from your first until now*'. *One question about sports was included: 'Did you participate in competitive sports during adulthood or as an adult?'* The second questionnaire also included information about body height and weight.

Registries

Breast cancer cases were identified through Swedish personal identification numbers, linked to the Swedish National Cancer Registry and the Swedish National Cause of Death Registry. The ICD-7 classification was applied.

Data processing

Reported occupations, were classified with a three-digit code into different categories, according to the Nordic classification of occupations (NYK) 1978 (Arbetsmarknadsstyrelsen, 1978), by a secretary of the epidemiological department. Two physiotherapists (AJ and ÅT) classified the different occupations as sedentary or non-sedentary. Each person registered up to a maximum of seven different occupations, and the participants were classified as having (1) *sedentary occupations*, if all of their occupations were sedentary; (2) *mixed occupations,* if their occupations were both sedentary and non-sedentary and (3) *non-sedentary occupations,* if their occupations were not sedentary.

Statistical analysis

Data were analyzed by Cox regression to estimate the hazard ratio (HR), with 95% confidence intervals (CIs). All analyses were conducted using the survival package in R [9]. The association between occupational sedentariness and time to breast cancer was analyzed in univariate and multivariate models. In the two variable models, an individual variable was tested after adjustment for age. In the multivariable model, adjustment for established risk factors selected a priori and age at entry was performed. The risk factors included family history of breast cancer in first relatives (yes/no), age at birth of the first child ($<30, \geq 30$ years), age at menarche (>13 years/≤ 13 years), use of oral contraceptives (never/ever), smoking status (never/ever), education (<9, 9–12, >12 years), marital status (unmarried/married/divorced/widow), participation in competitive sports (yes/no), use of HRT (never/ever) and BMI (<25/25–29/<29).

Subjects with missing information regarding a variable were generally excluded from the calculations. However, missing information regarding family history of breast cancer and participation in competitive sports was coded as 'No'. Furthermore, BMI included missing information as a separate category.

The time from enrollment in the study to breast cancer diagnosis, death or the end of follow-up, 31 December 2013, whichever occurred first, was calculated.

Breast cancer events were analyzed for the entire cohort and were also stratified by age at diagnosis, with a cutoff of 55 years. In women younger than 55 years, the time at risk was calculated from the date of enrollment in the study to the date of breast cancer diagnosis or was censored at the age of 55 years or death. In older women, the time at risk was calculated from 55 years to the end of the study period (31 December 2013) or death.

Results

The study period consisted of the interval from the distribution of the first questionnaires between 1990 and 1992 until 31 December 2013, thus yielding a follow-up time of 583 293 person-years and a maximum of 24 years (average: 19.8 years). A total of 1506 cases of breast cancer occurred during the study period, among which 423 were diagnosed before 55 years, and 1083 occurred in women 55 years or older. During the follow-up period, 3677 women died. At the end of the follow-up, the age of the included women ranged from 48 to 87 years. Of the 40 000 women who were invited to participate in the study, 29 524 (74%) responded to the first questionnaire; among those, 24 097 women (82%) also completed the second questionnaire. In the first questionnaire, 29 129 answered the question about occupation, and 27 525 of those declared an occupation, whereas 1604 had no occupation. Of the 27 525 with an occupation, 5220 had only sedentary occupations, 6988 had a mixture of sedentary and non-sedentary occupations, and 15 317 had only non-sedentary occupations. The most frequent sedentary occupations were office workers, office secretaries, community administrators, and shop and restaurant cashiers.

We found a significantly increased risk of breast cancer in women with a working history of occupational sedentariness compared to those who had mixed occupations or only non-sedentary occupations. A risk increase was found, both when adjusted for age (HR 1.21; 95% CI 1.06, 1.38) and when adjusted for other known risk factors such as family history of breast cancer in first relatives, age at birth of the first child, age at menarche, use of oral contraceptives, education, participation in competitive sports and BMI (HR 1.20; 95% CI 1.05, 1.37) (Table 1). The association between occupational sedentariness and breast cancer risk was stronger among women younger than 55 years (HR 1.54; 95% CI 1.20, 1.96) (Table 2), whereas no association was seen in women 55 years

Table 1. Hazard ratio for breast cancer incidence.

	Women without breast cancer (n = 28 018) n (%)	Women with breast cancer (n = 1506) n (%)	Hazard ratio (95% CI)	
			Age-adjusted	[a]Multivariate
Baseline data				
Occupation				
Non-sedentary (ref)	14 556 (95)	761 (5)	1.0	1.0
Mixed	6656 (95.2)	332 (4.8)	1.01 (0.89, 1.15)	0.98 (0.86, 1.12)
Sedentary	4904 (94.1)	316 (6.1)	**1.21 (1.06, 1.38)**	**1.20 (1.05, 1.37)**
Missing information	1902 (95.1)	97 (4.9)		
Competitive sports[b]				
Yes (ref)	2481 (94.4)	148 (5.6)	1.0	1.0
No	25 537 (95.0)	1358 (5.0)	0.95 (0.80, 1.13)	0.97 (0.81, 1.16)
Family history of breast cancer[b]				
No (ref)	25 984 (95.1)	1326 (4.9)	1.0	1.0
Yes	2034 (91.9)	180 (8.1)	**1.61 (1.38, 1.88)**	**1.62 (1.38, 1.91)**
Age at birth of first child				
<30 years (ref)	20 480 (95.0)	1084 (5.0)	1.0	1.0
≥30 years	7288 (94.6)	414 (5.4)	**1.16 (1.04, 1.30)**	**1.15 (1.02, 1.30)**
Missing information	250 (96.9)	8 (3.1)		
Age at menarche				
≤13 years	15 524 (94.9)	835 (5.1)	**1.12 (1.01, 1.25)**	1.10 (0.98, 1.23)
>13 years (ref)	11 900 (94.9)	643 (5.1)	1.0	1.0
Missing information	594 (95.5)	28 (4.5)		
Use of oral contraceptives				
No (ref)	9689 (94.4)	577 (5.6)	1.00	1.0
Yes	18 237 (95.2)	926 (4.8)	**1.22 (1.08, 1.38)**	**1.17 (1.03, 1.33)**
Missing information	92 (96.8)	3 (3.2)		
Marital status				
Unmarried (ref)	2457 (95.9)	106 (4.1)	1.0	
Married	21 835 (94.9)	1176 (5.1)	0.99 (0.81, 1.21)	
Divorced	2523 (94.6)	144 (5.4)	1.01 (0.78, 1.30)	
Widow	1081 (93.8)	72 (6.2)	0.90 (0.66, 1.23)	
Missing information	122 (93.8)	8 (6.2)		
Smoker				
Never	11 332 (94.7)	636 (5.3)	1.0	
Ever	16 480 (95.0)	866 (5.0)	1.06 (0.96, 1.18)	
Missing information	206 (98.1)	4 (1.9)		
Education (years)				
<9 (ref)	11 076 (94.5)	640 (5.5)	1.0	1.0
9–12	8568 (95.5)	405 (4.5)	1.10 (0.96, 1.26)	1.04 (0.90, 1.19)
>12	8077 (94.9)	438 (5.1)	**1.20 (1.06, 1.12)**	1.14 (1.00, 1.31)
Missing information	297 (92.8)	23 (7.2)		
Data from second survey				
BMI				
<25 (ref)	12 360 (95.1)	633 (4.9)	1.0	1.0
25–29	5538 (94.5)	323 (5.5)	1.02 (0.89, 1.17)	1.04 (0.90, 1.20)
>29	3033 (94.1)	189 (5.9)	1.09 (0.92, 1.28)	1.12 (0.94, 1.33)
Missing information	7087 (95.2)	361 (4.8)	0.99 (0.87, 1.13)	1.06 (0.92, 1.23)

Results in bold indicate $p < 0.05$.
[a]BMI: body mass index; CI: confidence interval.
[a]Multivariate analyses adjusted for age at inclusion and all the variables in table simultaneously (except marital status and smoking).
[b]Missing values were classified as 'No'.

or older (HR 1.03; 95% CI 0.88, 1.22) (Table 3). Participation in competitive sports did not affect the risk of breast cancer in any age group. Among the other previously established risk factors, a significantly increased risk of breast cancer in the multivariate analyses was found for family history of breast cancer, age ≥30 years at the birth of the first child, use of oral contraceptives and use of HRT (only >55 years) (Tables 1–3).

Discussion

The present study showed an increased risk of breast cancer in women with a working history of occupational sedentariness compared with women with a mixture of sedentary and non-sedentary occupations or only non-sedentary occupations (HR 1.20; 95% CI 1.05, 1.37), especially for women younger than 55 years (HR 1.54, 95% CI 1.20, 1.96). These findings are in line with a meta-analysis conducted by Zhou et al. showing a moderate but statistically significant association between occupational sedentary behavior and breast cancer risk [odds ratio (OR) 1.10, 95% CI 1.02, 1.18) [8]. Three previous case-control studies have analyzed the interaction between occupational sedentariness and menopausal status with respect to the risk of developing breast cancer [10–12]. Kruk et al. reported a non-significantly increased risk of postmenopausal breast with occupational sedentary behavior and a decreased risk of premenopausal breast cancer in a case-control study including 858 breast cancer cases [11]. In another case-control study including 1222 breast cancer cases, Lynch et al. found a decreased risk of both pre- and postmenopausal breast cancer in women with occupational sedentary behavior [12]. A third case-control study showed

Table 2. Hazard ratio for breast cancer incidence in women younger than 55 years.

	Women without breast cancer (n = 20 602) n (%)	Women with breast cancer (n = 423) n (%)	Hazard ratio and 95% CI	
			Age-adjusted	[a]Multivariate
Baseline data				
Occupation				
Non-sedentary (ref)	10 564 (98.2)	196 (1.8)	1.0	1.0
Mixed	5284 (98)	109 (2)	1.10 (0.87, 1.39)	1.08 (0.85, 1.37)
Sedentary	3655 (97.3)	100 (2.7)	**1.53 (1.20, 1.95)**	**1.54 (1.20, 1.96)**
Missing information	1099 (98.4)	18 (1.6)		
Competitive sports[b]				
Yes (ref)	1867 (98.2)	35 (1.8)	1.0	1.0
No	18 735 (98.0)	388 (2.0)	1.05 (0.74, 1.49)	1.07 (0.74, 1.55)
Family history of breast cancer[b]				
No (ref)	19 136 (98.1)	379 (1.9)	1.0	1.0
Yes	1466 (97.1)	44 (2.9)	**1.61 (1.18, 2.20)**	**1.55 (1.12–2.15)**
Age at birth of first child				
<30 years (ref)	14 855 (98.1)	286 (1.9)	1.0	1.0
≥30 years	5531 (97.7)	131 (2.3)	1.17 (0.95, 1.45)	1.18 (0.95, 1.46)
Missing information	216 (97.3)	6 (2.7)		
Use of oral contraceptives				
No (ref)	4461 (98.5)	66 (1.5)	1.0	1.0
Yes	16 110 (97.8)	357 (2.2)	1.19 (0.91, 1.55)	1.19 (0.90, 1.58)
Missing information	31 (100.0)	0		
Age at menarche				
≤13 years	12 389 (97.8)	278 (2.2)	1.15 (0.93, 1.40)	1.13 (0.92, 1.40)
>13 years	7810 (98.2)	141 (1.8)	1.0	1.0
Missing information	403 (99.0)	4 (1.0)		

Results in bold indicate $p < 0.05$.
CI: confidence interval.
[a]Multivariate analyses adjusted for age at inclusion, and all variables in the table simultaneously
[b]Missing values were classified as 'No'.

Table 3. Hazard ratio for breast cancer incidence in women 55 years or older.

	Women without breast cancer (n = 22 051) n (%)	Women with breast cancer (n = 1083) n (%)	Hazard ratio and 95% CI	
			Age-adjusted	[a]Multivariate
Baseline data				
Occupation				
Active (ref)	11 550 (95.5)	541 (4.5)	1.0	1.0
Mixed	4956 (95.8)	215 (4.2)	0.98 (0.83, 1.14)	0.96 (0.82, 1.13)
Sedentary	4057 (95.1)	207 (4.9)	1.06 (0.90, 1.24)	1.03 (0.88, 1.22)
Missing information	1488 (92.6)	120 (7.4)		
Competitive sports[b]				
Yes (ref)	2372 (95.4)	115 (4.6)	1.0	1.0
No	19 679 (95.3)	968 (4.7)	1.01 (0.83, 1.24)	0.95 (0.77, 1.17)
Family history of breast cancer[b]				
No (ref)	20 318 (95.5)	947 (4.5)	1.0	1.0
Yes	1733 (92.7)	136 (7.3)	**1.56 (1.29, 1.87)**	**1.53 (1.26, 1.85)**
Age at birth of first child				
<30 years (ref)	16 743 (95.6)	769 (4.4)	1.0	1.0
≥30 years	5210 (95.1)	267 (4.9)	**1.19 (1.04, 1.37)**	1.14 (0.99, 1.33)
Missing information	98 (67.6)	47 (32.4)		
Age at menarche				
≤13 years	11 629 (95.6)	534 (4.4)	1.13 (1.00, 1.28)	**1.17 (1.03, 1.34)**
>13 years (ref)	9970 (95.4)	482 (4.6)	1.0	1.0
Missing information	452 (87.1)	67 (12.9)		
HRT				
Never (ref)	14 670 (96.3)	556 (3.7)	1.0	1.0
Ever	7152 (95.7)	479 (6.3)	**1.40 (1.24, 1.58)**	**1.45 (1.27, 1.66)**
Missing information	229 (82.7)	48 (17.3)		
Data from second survey				
BMI				
<25 (ref)	9332 (93.5)	170 (6.5)	1.0	1.0
25–29	4634 (95.8)	408 (4.2)	1.06 (0.90, 1.24)	1.03 (0.87, 1.21)
>29	2526 (95.0)	244 (5.0)	1.09 (0.89, 1.34)	1.05 (0.86, 1.28)
Missing information	5559 (95.5)	261 (4.5)	0.93 (0.79, 1.09)	0.94 (0.79, 1.12)

Results in bold indicate $p < 0.05$.
BMI: body mass index; CI: confidence interval; HRT: hormone replacement therapy.
[a]Multivariate analyses adjusted for age at inclusion, and all the variables in the table simultaneously.
[b]Missing values were classified as 'No'.

an increased risk of both pre- and postmenopausal breast cancer, but the association was not statistically significant [10]. Although occupational sedentariness is associated with increased breast cancer risk, the results are inconsistent when stratified by menopausal status. In a recently published prospective cohort study including women with a family history of breast cancer, Ekenga et al. found an association between occupational physical activity and decreased breast cancer risk. When analyzed by menopausal status, the risk reduction was shown for only postmenopausal breast cancer [13]. This finding is inconsistent with ours.

Thus, there are discrepancies between our results and those of previous studies. Three of them were retrospective case-control studies, which may have been affected by recall bias regarding risk factors. Our study was a cohort study, in which information regarding risk factors was collected prior to cancer diagnosis, thus eliminating the risk of recall bias. The study by Ekenga et al. included only women with a sister who had breast cancer, for example a high-risk population, whereas our cohort was randomly selected from the general population. Whether these differences in study design may explain the outcome discrepancies is unclear.

The association between physical activity and breast cancer incidence has been more extensively investigated. Several studies have suggested an inverse association between physical activity and the risk of developing breast cancer [3]. Data from our cohort study did not show any risk reduction in women participating in competitive sports, but our questionnaire contained only one question on this subject ('Have you participated in competitive sports during adolescence or adulthood?'). Unfortunately, we did not have any other questions in this field, so we could not perform an analysis on the possible risk reduction by leisure time physical activity. It may be possible to compensate for occupational sedentariness with physical activity during leisure time as Biswas et al. found that the association between sedentary time and cancer incidence decreased with higher levels of physical activity [4]. In a meta-analysis, Wu et al. reported an association between physical activity and reduced breast cancer risk of 12%; this association was strongest in women with a high BMI, premenopausal women and women with estrogen and progesterone receptor-negative breast cancer [3]. This is in line with our findings showing that the risk increase with occupational sedentariness was most pronounced in women younger than 55 years, whereas breast cancer was not linked to occupational sedentariness in postmenopausal women.

The mechanisms by which occupational sedentariness and sedentary behavior are associated with an increased risk of cancer are unclear, and may be others than those responsible for the protective effect of physical activity.

Sedentary behavior may lead to increased intraabdominal fat mass [14]. Pedersen and Febbraio suggested a link between sedentariness and cancer development via chronic inflammation induced by visceral adipose tissue [15]. Others have shown that inflammatory factor levels are increased with prolonged sitting [16]. Visceral abdominal fat is also associated with metabolic dysfunction, for example elevated levels of insulin, IGF-1 and glucose, factors that may be associated with cancer development [17,18].

Sex hormone levels play an important role in breast cancer development. In a meta analyses including studies on healthy women, Ennour-Idrissi et al. found that physical activity reduces circulating sex hormones (standardized mean difference (SMD) 0.12, 95% CI −0.20–0.03), regardless of menopausal status [19]. In a small study, premenopausal women at high risk for breast cancer had lower total estrogen exposure (18.9%) and total progesterone exposure (23.7%) by high-intensity aerobic exercise (Kossman et al., 2011). Physical activity leads to loss of body fat mass [19,20], and visceral fat mass influences estrogen production [21]. Whether sedentariness affects the levels of sex hormones is unclear [22], but sedentariness does increase the amount of body fat mass [14], and body fat mass influences estrogen production [21].

Fat metabolism is affected by sedentary behavior. Sedentariness leads to decreased lipoprotein lipase (LPL) activity, and LPL is involved in the production of high-density lipoprotein (HDL) cholesterol [23]. High levels of HDL-C have been shown to reduce the risk of premenopausal breast cancer [24]. Studies have shown that training leads to lower levels of LDL and higher levels of HDL; in high-intensity aerobic training, a 25% increase was seen [25].

The strengths of our study were its prospective design and large ethnically homogeneous population, high response rate and long follow-up. The women in the cohort were aged between 25 and 65 years at enrollment. We did not have reliable data regarding actual menopausal status, but stratification of the cohort at 55 years age should be a reasonably valid division into pre- and postmenopausal subtypes.

Another advantage of our study was that we had information about working histories, from the first occupation until the occupation at baseline, enabling us to group women into three levels of occupational sedentariness, rather than analyzing occupations at only one time point.

Analyses regarding conventional risk factors did not change the results, suggesting that occupational sedentariness is an independent risk factor for breast cancer.

There were limitations to our study. Occupation was classified based on job title, a classification used in several previous studies. However, this method may have limitations such as misclassification, as well as difficulties in distinguishing sedentary behavior from time spent engaged in light physical activity. The study would have been strengthened with the inclusion of leisure time physical activity in the analyses, but we did not have information regarding physical activity other than participation in competitive sports. Another limitation was that data on BMI were not included in the first questionnaire and thus were obtained via the second questionnaire collected 10 years later.

In conclusion, we found that sedentariness at work was associated with an increased risk of breast cancer in women younger than 55 years and participation in competitive sports did not affect the risk. Sedentariness at work may be a modifiable risk factor by planning moments of physical activity during work or possibly by compensating with an adequate level of leisure time physical activity. Whether

this reduces the risk breast cancer needs to be further studied.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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