



Sedentary work and breast cancer risk: A systematic review and meta-analysis

Jongin Lee MD, PhD¹  | JaeYong Lee MD, PhD¹  | Dong-Wook Lee MD, MSc²  |
Hyoungh-Ryoul Kim MD, PhD¹  | Mo-Yeol Kang MD, PhD¹ 

¹Department of Occupational and Environmental Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

²Department of Preventive Medicine, College of Medicine, Seoul National University, Seoul, Republic of Korea

Correspondence

Mo-Yeol Kang, Department of Occupational and Environmental Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222, Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea.
Email: snaptoon@naver.com

Abstract

Objectives: This systematic review and meta-analysis aimed to assess sedentary work's contribution to breast cancer risk quantitatively using thorough research articles.

Methods: We performed a meta-analysis using a registered protocol in PROSPERO (registration number: CRD42020204629). Literature from PubMed, Embase, and Cochrane involving sedentary work and breast cancer risk was reviewed. We calculated the overall pooled risk ratios (RRs) and 95% CI with a random-effect model from the included studies. Furthermore, we performed stratified analyses by characteristics of studies.

Results: Thirty-one studies (13 cohort studies and 18 case-control studies) were included in the analysis. The overall effect of the pooled analysis was an RR of 1.16 (95% CI 1.08-1.23). The results were 1.20 (95% CI 1.10-1.30) and 1.12 (95% CI 1.02-1.23) for cohort and case-control studies. The effect of sedentary work did not seem to be consistently attenuated by controlling body mass index, menopausal status, or experience of hormone replacement therapy.

Conclusion: The results from this meta-analysis suggest that sedentary behavior within the occupational domain was associated with a 15.5% increased risk of breast cancer. It is essential to reduce the sedentary time spent at work and to secure time for leisure-time physical activity among sedentary workers as a primary preventive measure.

KEYWORDS

breast neoplasms, meta-analysis, sedentary behavior, sedentary work, systematic review

Both authors contributed equally to the study.

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1 | INTRODUCTION

Breast cancer is one of the most common cancers and the leading cause of cancer-related deaths in women worldwide. There were 2.93 million incident cases and an estimated 0.63 million deaths from breast cancer globally in 2018, which significantly burdened the public health system.¹ Although early detection and screening techniques have improved gradually, breast cancer incidence has been stable since 2004.

Previous epidemiological studies have shown that the incidence of breast cancer is associated with various risk factors, such as diet, obesity and weight gain, alcohol intake, tobacco smoke, prolonged hormone therapy after menopause, and use of oral contraceptives.² The aging world's population, a marked increase in life expectancy, and a rapid tendency to adopt a Westernized lifestyle, including low fertility rates, sedentarism, and short breastfeeding periods, contribute to the accumulation of risk factors known to be associated with breast cancer. These factors contribute to the continual increase in the global burden of this cancer.³ Therefore, a public health priority is to identify environmental or lifestyle factors whose modifications could reduce breast cancer incidence.

An increase in sitting time accompanied by a decrease in physical activity levels in adults. Sedentary behavior is more widespread in modern life, and hence, people spend 50%-60% of their waking time (7.7 h) sitting every day, and this number may continue to rise.⁴ Over the past decade, health consequences have been of increasing interest to the public. For example, it has been suggested that increased sitting time in daily life is associated with the risk of weight gain,⁵ obesity,⁶ Type 2 diabetes, coronary heart disease,⁷ and even cancer.⁸

Breast cancer is an obesity-related type of cancer, and sedentary behavior and physical inactivity are known risk factors for it. The results of a meta-analysis integrated from 21 observational studies with 34 reports showed that sedentary behavior was found to increase the risk of breast cancer (pooled odds ratio [OR] with a 95% confidence interval [CI] of 1.08 and 1.04-1.13).⁸ However, this meta-analysis only identified 12 studies on sedentary behavior in the occupation domain, and the evidence related to it has not been thoroughly assessed. Because the relatively larger proportion of time spent for occupation by working-aged adults, it is important to ascertain if and by how much sedentary behavior in occupational domains influence the risks of breast cancers. Given the missing studies in the previous meta-analysis and additional recent literature, an improved analysis needs a clear understanding of the effect of sedentary work on breast cancer risk. Therefore, this systematic review and meta-analysis aimed to assess the contribution of sedentary work to breast cancer risk quantitatively.

2 | MATERIALS AND METHODS

The protocol for this systematic review with meta-analysis was registered in PROSPERO a priori. The review itself was conducted in accordance with the PRISMA statement guidelines.⁹

2.1 | Searching and selection of studies

Three authors (JL, JYL, MYK) and a trained librarian searched the literature in PubMed, Embase, and Cochrane Library on January 11, 2020, using the following keywords: ("occupational physical activity," "occupational physical inactivity," "sedentary work," "occupational sitting time," "light work," "occupational energy expenditure") AND ("cancer," "tumour," "malignant," "neoplasm," "carcinoma"). Among the preliminary results, articles reporting the effects of breast cancer in English were used in this study. Two authors (JL and JYL) screened eligible studies per titles and abstracts. Furthermore, they selected available studies using the following inclusion criteria by reviewing all the articles' full texts. Three authors (JL, JYL and MYK) also examined the articles' reference lists from retrieved studies; studies not included in the preliminary search results were also included in the analysis.

2.2 | Inclusion criteria

We included cohort and case-control studies on breast cancer reporting effect sizes and 95% CI of "sedentary work" as an exposure variable. All studies with different study populations, for example, articles of postmenopausal women only or carcinoma in situ, were also included.

2.3 | Extraction of data

From the included articles, we extracted the study name (first author and publication year), study design, country, the total number of participants, number of cases, sedentary work definition, comparison group definition, and effect sizes (odds ratios for case-control studies and relative risks/hazard ratios for cohort studies) with 95% CI. Most of the studies used multiple levels of occupational physical activity. The basic principle to select effect sizes was to compare the least active group with the most active group. Some studies reported effect sizes of the occupationally active group compared with the sedentary group. In this case, we used reciprocal numbers of the effect sizes and confidence intervals of the comparison.

2.4 | Quality assessment

The Newcastle-Ottawa Scale is a tool widely used in the quality assessment of the meta-analysis of observational studies.¹⁰ Three authors independently estimated the quality score using the Newcastle-Ottawa Scale. Afterward, they resolved disagreements by discussion. Studies were classified into two categories: fine (six stars or more) and coarse (five stars or less).

2.5 | Statistical analysis

We calculated the overall pooled risk ratios (RRs) and 95% CI with a random-effect model from the included studies. Furthermore, we performed stratified analyses by publication year, study location, quality assessment, sedentary work definition, and adjusted variables, including body mass index (BMI), recreational or leisure-time physical activity (LTPA), and experience of hormone replacement therapy (HRT). Some studies have reported divided results by menopausal status, estrogen/progesterone receptor, or stage (in situ vs invasive). We also performed subgroup meta-analyses using these stratified results.

The heterogeneity among the studies was assessed by I^2 statistics following these criteria: I^2 of <25%, 25%-50%, and <75% was set to low, moderate, and high, respectively. Begg's and Egger's tests were used to evaluate publication bias.^{11,12} A visual inspection was conducted using a funnel plot. We used R software (Vienna, Austria) with its "meta" package.¹³ All statistical tests were two-sided. A P -value of 0.05 and a 95% CI were considered statistically significant.

3 | RESULTS

3.1 | Study selection

Overall, we found 5381 studies regarding (occupational) physical activity and cancer by preliminary searching. We collected 136 studies eligible for the analysis between sedentary work and cancer after the removal of duplicates and screening of the abstract. Among them, 34 studies (16 cohort studies¹⁴⁻²⁹ and 18 case-control studies³⁰⁻⁴⁷) met our inclusion criteria. Because three and two studies were from the same cohort (European Prospective Investigation into Cancer [EPIC]^{20,27,29} and Black Women's Health Study,^{24,27} respectively), we selected studies that could represent the overlapped population.^{24,29} Finally, 31 studies (13 cohort studies and 18 case-control studies) were included in the analysis (Figure 1).

3.2 | Characteristics of the studies

Most of the selected studies did not use the same definition for sedentary work. Three main types of definitions were used: types of work, sitting time at work, and the metabolic equivalent of task (MET). We assessed five cohort studies and seven case-control studies of fine quality. Studies with fine quality tended to have fewer participants. However, this tendency was not absolute (Table 1).

3.3 | Overall analysis

The overall pooled estimates were an RR of 1.16 (95% CI 1.08-1.23). The effects were 1.20 (95% CI 1.10-1.30)

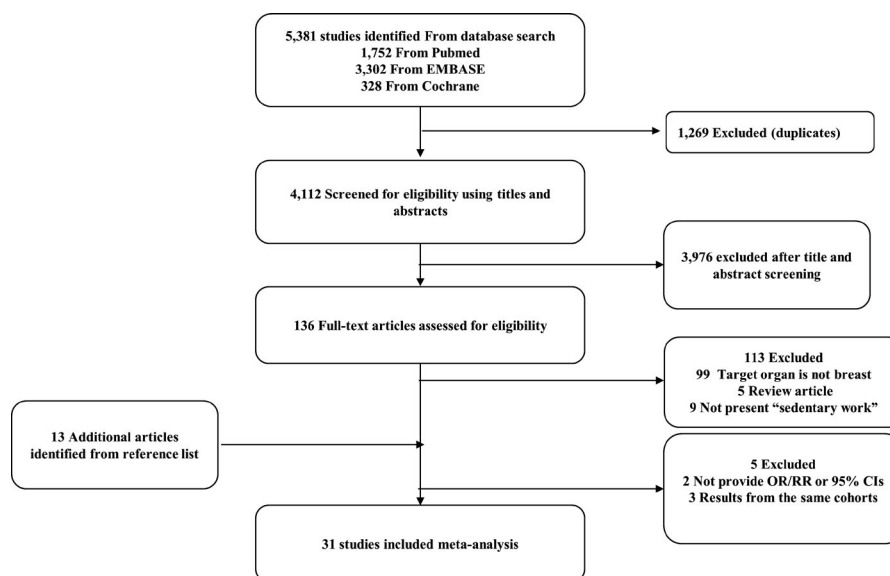


FIGURE 1 Flow diagram of processes for study selection in the meta-analysis

TABLE 1 Characteristics of studies included in the meta-analysis

| Study name | Design | Country | Number of participants | Number of cases | Comparison | Definition of sedentary work/ definition of comparison group | Adjustment of confounders | Quality assessment |
|-------------------------------|--------|-----------------|------------------------|-----------------|--------------|--|---|--------------------|
| Thune et al ¹⁴ | Cohort | Norway | 25 624 | 351 | Type | Four types of work: sedentary/ heavy manual labor | Age at entry, body mass index, height, county of residence, and number of children | Fine |
| Moradi et al ²² | Cohort | Sweden | 1 940 510 | 51 520 | Type | Five levels of physical activity: sedentary/high or very high | Age (by 5-year intervals), calendar year of follow-up by year, place of residence, socioeconomic status (in the analysis of occupational physical activity), or physical activity (in the analysis of socioeconomic status) | Coarse |
| Dirx et al ¹⁵ | Cohort | The Netherlands | 62 537 | 1208 | Sitting time | Sitting time per day (h): 6-8 h < 2 h | Age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol and energy intake | Coarse |
| Moradi et al ²³ | Cohort | Sweden | 9539 | 506 | Type | Three types of activity: sedentary/strenuous | Age | Fine |
| Rintala et al ²⁶ | Cohort | Finland | 680 000 | 5721 | Type | Five classes of tasks: sitting/ heavy task | Social class and reproductive factors | Coarse |
| George et al ¹⁷ | Cohort | United States | 97 039 | 3436 | Sitting time | Occupational activity: sitting all day/heavy lifting or carrying | Age, energy intake, recreational physical activity, parity, menopausal hormone, number of breast biopsies, smoking, alcohol intake, race, education | Coarse |
| Pronk et al ²⁵ | Cohort | China | 73 049 | 717 | Sitting time | Average sitting time: ≥ 4 h/day/ ≤ 1.2 h/day | Age, education, family history of breast cancer, age at first birth, and number of pregnancies | Fine |
| Steindorf et al ²⁸ | Cohort | Mixed (Europe) | 257 805 | 8034 | Type | Three types of activity: sedentary/manual and heavy manual | BMI, age at first period, age at first full-term pregnancy, number of full-term pregnancies, breastfeeding, ever oral contraceptive, menopausal status, age at menopause, use of hormone replacement therapy, alcohol consumption, smoking status, level of school attained; other types of physical activity | Coarse |
| Ekenga et al ¹⁶ | Cohort | United States | 47 649 | 1798 | Type | Occupational history: mostly sitting/active | Race/ethnicity, education, income, parity, age at menopause, BMI, recreational physical activity, and work at night | Coarse |
| Masala et al ²¹ | Cohort | Italy | 15 010 | 672 | Type | Three types of activity: sedentary/manual | Education, number of children, age at menarche, non-alcohol energy intake, current use of HRT, smoking status, and total vegetables consumption, physical activity, alcohol consumption, and anthropometric measures | Coarse |

(Continues)

TABLE 1 (Continued)

| Study name | Design | Country | Number of participants | Number of cases | Comparison | Definition of sedentary work/ definition of comparison group | Adjustment of confounders | Quality assessment |
|-------------------------------------|--------------|-----------------|------------------------|-----------------|--------------|--|---|--------------------|
| Nomura et al ²⁴ | Cohort | United States | 46 734 | 2041 | Sitting time | Sitting time/day (h): 5+ h/day < 1 h/day | Age, geographic region of residence, BMI, education, recreational physical activity, caloric intake, parity, age at menarche, menopausal hormone use, oral contraceptive use, family history of breast cancer, mammogram, smoking | Coarse |
| Johnsson et al ¹⁹ | Cohort | Sweden | 29 524 | 1506 | Type | Three types of baseline occupation data: sedentary/non-sedentary | Age at inclusion, occupation, competitive sports, family history of breast cancer, age at birth of first child, age at menarche, HRT, BMI | Fine |
| Ihira et al ¹⁸ | Cohort | Japan | 33 307 | 3807 | Sitting time | Occupational sitting time: ≥ 7 h/day/1-3 h/day | Age, area, history of diabetes, smoking status, alcohol intake status, body mass index, coffee, walking time at work, strenuous time at work, moderate-to-vigorous physical activity time in leisure time, type of job, and total working hours | Fine |
| Coogan et al ³³ | Case-control | United States | 11 646 | 4863 | Type | Four types of work: sedentary/heavy | Age, state, BMI, benign breast disease, family history of breast cancer, menopausal status, age at menarche, parity, age at first birth, education, physical activity during ages 14-22, and alcohol consumption | Fine |
| Levi et al ³⁸ | Case-control | Switzerland | 620 | 246 | Type | Three grades of intensity of work: low/high | Age, education, age at menarche, age at first birth, number of births, menopausal status, age at menopause, calorie intake, previous benign breast disease, and history of breast cancer in first-degree relatives | Coarse |
| Coogan and Aschengrau ³² | Case-control | United States | 903 | 233 | Type | Exclusively sedentary work/exclusively medium/heavy | Vital status, education, and total duration of working years. | Fine |
| Verloop et al ⁴⁵ | Case-control | The Netherlands | 1836 | 918 | Type | >80% sedentary work/ $\leq 80\%$ sedentary work | Family history of breast cancer, education, smoking, occupational activity, and the other recreational physical activity variables | Coarse |
| Moradi et al ⁴¹ | Case-control | Sweden | 6802 | 3347 | Type | Five levels of physical activity: sedentary/high or very high | Age, age at menarche, parity and age at first birth, BMI, height, use of hormone replacement therapy, age at menopause, and use of oral contraceptives | Fine |
| Matthews et al ⁴⁰ | Case-control | China | 3015 | 1459 | Sitting time | Longest sitting time/short sitting time | Age, education, household income, first-degree family history of breast cancer, history of breast fibroadenoma, age at menarche, age at first live birth, and age at menopause | Fine |

(Continues)

TABLE 1 (Continued)

| Study name | Design | Country | Number of participants | Number of cases | Comparison | Definition of sedentary work/ definition of comparison group | Adjustment of confounders | Quality assessment |
|----------------------------------|--------------|---------------|------------------------|-----------------|------------|--|--|--------------------|
| Friedenreich et al ³⁵ | Case-control | Canada | 2470 | 1233 | MET | MET-h/week/year/≥61.8 | Current age, waist-hip ratio, educational level, ever use of hormone replacement therapy, ever diagnosed with benign breast disease, first-degree family history of breast cancer, ever alcohol consumption, current cigarette smoker, and other types of activity | Coarse |
| Dorn et al ³⁴ | Case-control | United States | 1550 | 740 | MET | Percent of work years/ moderate + jobs: 0%/100% | Age, education, age of menarche, relative with breast cancer, benign breast disease, BMI and age first pregnancy | Coarse |
| Steindorf et al ⁴⁴ | Case-control | Germany | 1246 | 360 | Type | MET-h/week in occupation: 0.0/35.1-170.5 | First-degree family history of breast cancer, number of full-term pregnancies, height, change in body mass index between age 20 and 30 years, total months of breastfeeding, and mean daily alcohol consumption | Coarse |
| Kruk et al ³⁷ | Case-control | Poland | 822 | 257 | Type | Three types of activity: sedentary/medium | BMI, age at menarche, sport and recreational activities, intake of vegetables and fruits and experience of stress | Coarse |
| Yang et al ⁴⁶ | Case-control | United States | 1095 | 501 | Type | Job category: sedentary only/ active blue collar | Education, migration history, parity, family history of breast cancer, menopausal status, average MET h/week for all recreational activities, and soy intake during adolescence and adult life | Coarse |
| Sprague et al ⁴³ | Case-control | United States | 15 710 | 8080 | MET | MET-h/week: 0/>100 | Age, state, mammography, menopausal status, family history of breast cancer, parity, age at first birth, age at menarche, age at menopause, postmenopausal hormone use, education, alcohol, BMI, and weight change since age 18 | Fine |
| Peplonska et al ⁴² | Case-control | Poland | 4502 | 2176 | MET | MET-h/week of lifetime: <11.3/>47.8 | Age, study site, education, BMI, age at menarche, menopausal status, age at menopause (in postmenopausal women), number of full-term births, age at first full-term birth, breastfeeding, family history of breast cancer, and previous screening mammography | Coarse |

(Continues)

TABLE 1 (Continued)

| Study name | Design | Country | Number of participants | Number of cases | Comparison | Definition of sedentary work/ definition of comparison group | Adjustment of confounders | Quality assessment |
|---------------------------|--------------|---------------------|------------------------|-----------------|--------------|--|---|--------------------|
| Kruk ³⁶ | Case-control | Poland | 1943 | 858 | Type | Four activity level: sedentary/high | 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 | Coarse |
| Cohen et al ³¹ | Case-control | United States | 2730 | 546 | Sitting time | Sitting at work, h/day: >3/none | Age, race, menopausal status, education, household income, BMI at age 21, cigarette smoking, ever use of hormone replacement therapy, parity, age at menarche, first-degree family history of breast cancer, and having health insurance | Coarse |
| Lynch et al ³⁹ | Case-control | Canada | 2452 | 1222 | Sitting time | Occupational sitting time (h/week/year): $\geq 7.3/0$ | Current age, educational level, lifetime total physical activity, caloric intake, ever alcohol consumption, smoking status, waist-hip ratio, menopausal status, total number of mammograms, first-degree family history of breast cancer, ever use of hormone replacement therapy, number of children breastfed | Fine |
| Yen et al ⁴⁷ | Case-control | Malaysia | 243 | 121 | MET | MET-h/week/year: <102.0/>140.2 | Current age, menopausal status, secondary smoke exposure and 6-month history of breastfeeding | Coarse |
| Boyle et al ³⁰ | Case-control | Australia Canada | 4294 | 1762 | Type | Sit-JEM: sedentary/sit-JEM75 | Age, study location, education, ethnicity, recreational physical activity in early adulthood, body mass index in early adulthood, number of births, breastfeeding status, shift work status. and years worked in an active occupation | Fine |

and 1.12 (95% CI 1.02-1.23) for cohort and case-control studies, respectively (Figure 2). The pooled estimates were almost the same between the two design groups, as no difference was observed between them (P for difference = 0.31). The overall I^2 score was 68%, which showed high heterogeneity ($P < .01$). The I^2 scores by study design were 69% and 53% for cohort studies and case-control studies, respectively, with high heterogeneity ($P < .01$).

The visual inspection of the funnel plot showed asymmetry (Figure 3). The P -values for Begg's and Egger's tests were 0.03 and 0.04, respectively. This publication bias was diluted in the sensitivity analysis limited to the studies of high quality, although visual asymmetry was still seen in the sensitivity analysis limited to fine-quality studies (Figure 4). However, the P -values for Begg's and Egger's tests were 0.78 and 0.96, respectively. Because of the differences in study design, we also generated funnel plots by study design (cohort and case-control, Figures S1 and S2). The P -values for Begg's and Egger's tests were 0.46 and 0.31, respectively, for cohort studies and 0.16 and 0.34, respectively, for case-control studies.

3.4 | Subgroup analysis

All the studies assessed sedentary work using the following three methods (Table 2): classifying types of work, assessing daily sitting time at work, and calculating METs. Studies that assessed the type of work and METs showed significantly increased RRs (1.18 95% CI [1.09-1.27] and 1.21 95% CI [1.04-1.40], respectively). However, studies with sitting time did not (RR, 1.07; 95% CI, 0.91-1.25). Studies with METs, which were all case-control designs, showed low heterogeneity ($I^2 = 30.7%$, $P = .22$).

All studies from Europe and Asia showed significantly increased RRs (1.17 95% CI [1.03-1.32] and 1.21 95% CI [1.03-1.42], respectively). However, studies from America did not (RR, 1.08; 95% CI, 0.95-1.23). All pooled RRs by publication year showed significant RRs (1.19 95% CI [1.11-1.28] and 1.12 95% CI [1.00-1.25], respectively). Pooled RR from coarse-quality studies showed significant RR (1.20 95% CI [1.11-1.30]), while the RR did not meet statistical significance among fine-quality studies (1.08 95% CI [0.97-1.20]).

All studies that adjusted BMI, LTPA, or HRT showed significant RRs. However, results from the subgroup analyses

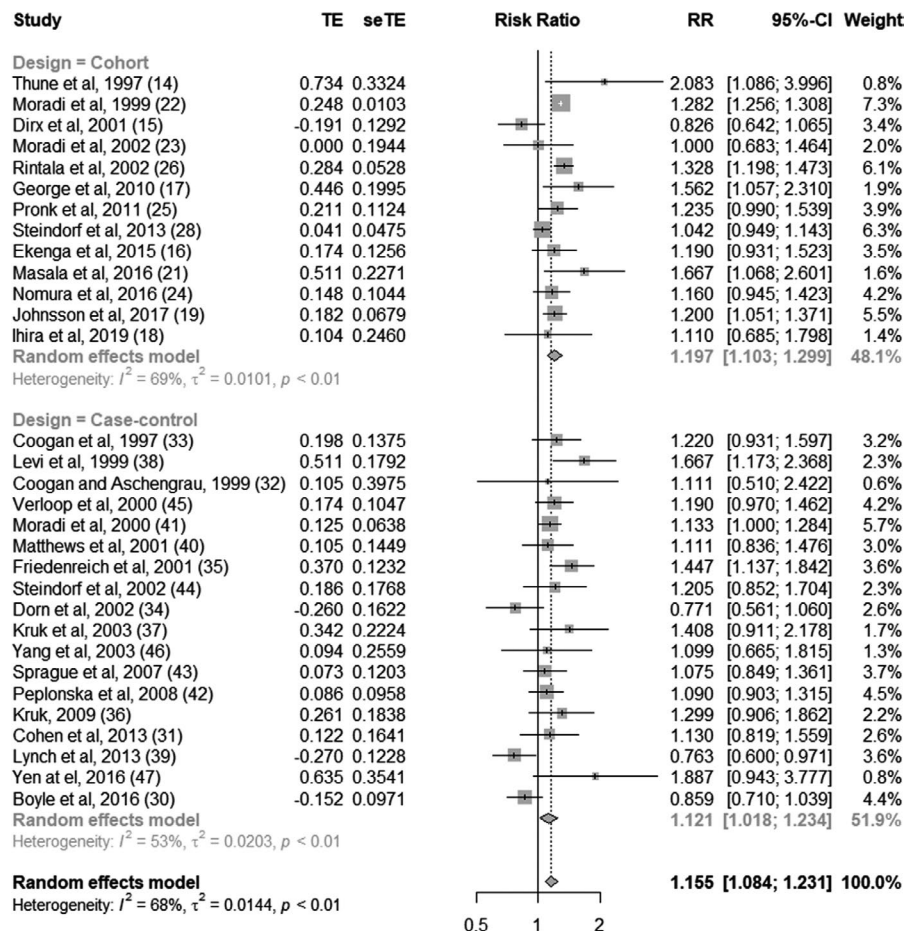


FIGURE 2 Forest plot of risk ratios between sedentary work and breast cancer, divided by study design

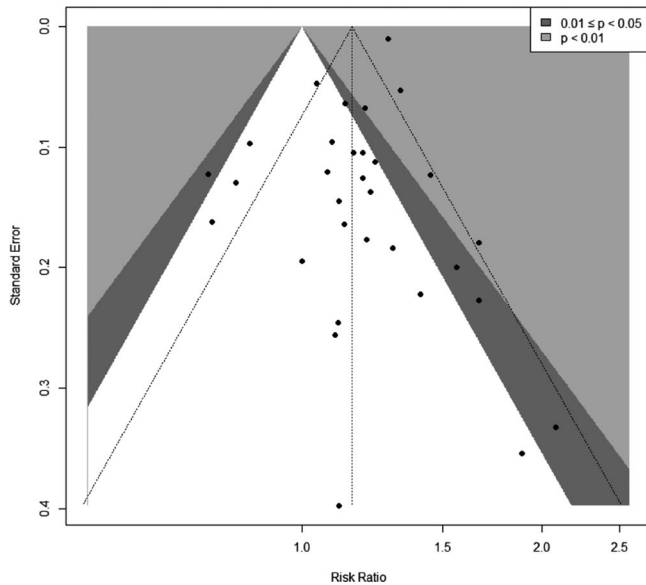


FIGURE 3 Funnel plot for the studies between sedentary work and breast cancer

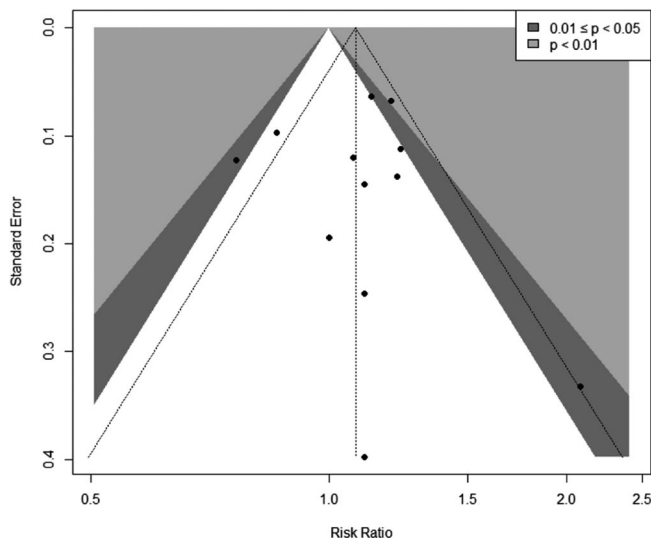


FIGURE 4 Funnel plot for the studies between sedentary work and breast cancer, fine-quality studies only

based on menopausal status ($n = 10$ for premenopausal and $n = 11$ for postmenopausal) or cancer characteristics ($n = 3$ for carcinoma in situ only, $n = 2$ for estrogen receptor-positive only, and $n = 2$ for estrogen receptor-negative only) did not yield significant results at all. The pooled result from studies that have not mentioned about menopausal status showed significantly increased risk (RR, 1.21 95% CI [1.14-1.29]).

4 | DISCUSSION

In this study, we quantitatively reviewed the existing observational epidemiologic evidence on the relationship between

sedentary work and breast cancer risk. Compared with the previous meta-analysis,⁸ we included 19 additional studies and explored the influence of the occupational domain of sedentary behavior in more depth. The findings from this systematic review and meta-analysis suggest that sedentary behavior within the occupational domain was associated with a 15.5% increased risk of breast cancer, while previous meta-analysis reported only showed 10% increased risk of breast cancer associated with occupational sedentary behavior.⁸ This may be because recently published studies have produced relatively higher risk estimates.^{16,18,19,21,24,47}

Several plausible biological mechanisms have been proposed to explain how sedentary behavior increases the risk of breast cancer, including the possible effect of sedentarism on adiposity, insulin resistance, systemic inflammation, sex hormones, and breast density. These are thought to contribute to the development and progression of breast cancer.⁸ Most of the available evidence implies the role of reducing energy expenditure with weight gain over time, leading to cancer development. Adiposity can promote carcinogenesis through several pathways, including elevated estrogen in postmenopausal women, insulin resistance, perturbation of the insulin-like growth factor axis, and low-grade systemic inflammation.⁴⁸ In our meta-analysis, however, the effect of sedentary work did not seem to be consistently attenuated by controlling BMI. Accumulating epidemiological evidence suggests that higher physical activity levels may lower the risk of certain types of cancers independent of BMI.⁴⁹ For example, Reeves et al reported that overweight, the most apparent consequence of sedentary behavior, was an independently-related breast cancer risk in postmenopausal women, suggesting that fat accumulated through sedentary behavior is an independent contributor to breast cancer and a mediator in other pathways.⁵⁰ Nevertheless, the impact of sedentary behavior on cancer incidence, especially obesity-related cancer, does not seem to be entirely adiposity-independent to date. The potential role of the adiposity-independent pathway on this association requires further clarification, as this knowledge can help provide a better interpretation of current knowledge in this specific area of interest.

Sex hormones, including estrogens, are associated with an increased risk of pre- and postmenopausal breast cancer.⁵¹ Sedentary behavior and physical inactivity have been hypothesized to influence the endogenous production of sex steroid hormones by altering menstrual cycle patterns and increasing body fat.⁵² However, adjustments for menopausal status or HRT did not significantly attenuate the association between sedentary work and breast cancer in our subgroup analyses, suggesting that sedentary work does not wholly exert its biological effects hormonal mechanisms.

We noted that the positive association between sedentary work and breast cancer was less pronounced among fine-quality studies than others. The stronger association in

| Subgroup | Number of studies included | Pooled RR | I^2 | P -value for heterogeneity |
|---|----------------------------|----------------------|-------|------------------------------|
| Assessment for comparison | | | | |
| Type of work | 18 | 1.178 [1.090; 1.273] | 70.0% | <.0001 |
| Sitting time | 8 | 1.069 [0.914; 1.250] | 60.1% | .0143 |
| MET | 5 | 1.208 [1.042; 1.402] | 30.7% | .2168 |
| P value for subgroup difference = .4789 | | | | |
| Region | | | | |
| Europe | 15 | 1.168 [1.030; 1.324] | 55.1% | <.0001 |
| America | 12 | 1.079 [0.945; 1.231] | 61.7% | .0025 |
| Asia | 4 | 1.207 [1.029; 1.416] | 0.0% | .5572 |
| P value for subgroup difference = .2427 | | | | |
| Publication year | | | | |
| Before 2010 | 19 | 1.187 [1.105; 1.275] | 53.8% | .0026 |
| After 2010 | 12 | 1.120 [1.004; 1.249] | 61.6% | .3389 |
| P value for subgroup difference = .3814 | | | | |
| Quality assessment ^a | | | | |
| Fine | 12 | 1.081 [0.974; 1.200] | 51.6% | .0192 |
| Course | 19 | 1.202 [1.113; 1.297] | 65.1% | <.0001 |
| P value for subgroup difference = .1092 | | | | |
| Adjustment of confounder ^b | | | | |
| BMI | 18 | 1.114 [1.025; 1.210] | 54.0% | .0034 |
| LTPA | 14 | 1.163 [1.068; 1.267] | 68.9% | <.0001 |
| HRT | 10 | 1.144 [1.033; 1.267] | 61.8% | .0051 |
| Menopausal status | | | | |
| Premenopausal | 10 | 1.099 [0.968; 1.247] | 10.7% | .3444 |
| Postmenopausal | 11 | 1.105 [0.968; 1.263] | 67.8% | .0006 |
| Not mentioned | 19 | 1.212 [1.138-1.290] | 47.6% | .0113 |
| P value for subgroup difference = .9487 | | | | |
| Cancer characteristics | | | | |
| Carcinoma in situ only | 3 | 1.045 [0.959; 1.139] | 0.0% | .9527 |
| Estrogen receptor positive | 2 | 1.102 [0.971; 1.252] | 0.0% | .8435 |
| Estrogen receptor negative | 2 | 1.162 [0.843; 1.602] | 42.5% | .1874 |

Abbreviations: BMI, body mass index; HRT, hormone replacement therapy; LTPA, leisure-time physical activity; MET, metabolic equivalent of task.

^aThe cutoff value for quality assessment with Newcastle-Ottawa Scale was six stars: fine (six stars or more) and coarse (five stars or less).

^bSubgroups of studies that had used confounders listed in the table were analyzed independently.

low-quality studies could arise from biases, such as selection bias, recall bias, misclassification, and confusion, which may have obliterated the true relationship in those studies. However, pooled estimates were almost the same between cohort and case-control studies (1.20 and 1.12, respectively), although prospective cohort studies are less prone to healthy

worker selection bias and recall bias than case-control studies. In addition, we could not find statistical differences by assessment for comparison, publication year, and menopausal status. Likewise, the difference by study region was statistically insignificant, but studies from Asian countries showed slightly stronger associations of breast cancer risk

TABLE 2 Pooled risk of breast cancer according to sedentary work derived from subgroup analysis

with sedentary work, compared with that from American regions. We assumed that most of the population within these areas are of similar race and ethnicity. There may be inequities regarding social structure, cultural norms, or economic obligations across the study region. Based on the above findings, we propose that race and ethnicity should be considered important effect modifiers in the analysis while investigating the associations between risk of breast cancer and sedentary work in future studies.

This systematic review and meta-analysis on the relationship between sedentary work and breast cancer risk is extensive and comprehensive. All existing scientific evidence from 31 epidemiological studies was included. Therefore, the results of meta-analyses provide sufficiently reliable estimates of breast cancer risk associated with sedentary work. However, some methodological limitations of this study must be considered. First, there were variations across studies in the methods used to ascertain sedentary work as exposure, and categorization of sedentary work was highly heterogeneous; therefore, it was difficult to make direct comparisons between the included studies. Moreover, there are concerns regarding the validity and reliability of job title-based and self-reported engagement in sedentary work, which was likely to cause a recall bias and exposure misclassification. A recent Japanese research demonstrated that without real-time feedback of individuals' current activity levels, subjective sedentary time might be underestimated compared with objective measurement of sedentary time.⁵³ Hence, it is expected that these possibilities would bias the results toward the null. Even though there was moderate heterogeneity throughout the study, our subgroup analysis of study characteristics identified some causes of this heterogeneity, such as publication year and study region. Second, due to the limited number of studies reporting information for potential confounding factors (eg gender, race/ethnicity, following a healthy diet, having regular medical check-ups, and hormone receptor status), we were unable to perform subgroup analyses based on most of these factors. Third, because we used the extreme categories of highest and lowest sedentariness levels as exposure measures, we were not able to investigate a dose-response relationship. Finally, it is suspected that the associations observed in the meta-analysis of published studies may suffer from publication bias because studies with null results tend not to be published. However, contour-enhanced funnel plots showed that many insignificant results were included in our meta-analysis, and there was no evidence for a separate test by study design and sensitivity analysis limited to fine-quality studies. Furthermore, we only selected literature written in English, which may have resulted in a language or cultural bias.

In summary, this systematic review and meta-analysis of observational epidemiologic studies with the most up-to-date evidence showed that sedentary work is significantly associated with breast cancer risk. This finding indicates that it is

essential to reduce the sedentary time spent at work and to secure time for LTPA among sedentary workers as a primary preventive measure.

DISCLAIMER

None.

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DISCLOSURE

Approval of the research protocol: Ethics approval for the present study was not required because this was a review of articles that is free of personally identifiable information. *Informed Consent:* N/A. *Registry and the Registration No. of the study/trial:* N/A. *Animal Studies:* N/A. *Conflict of Interest:* N/A.

AUTHOR CONTRIBUTIONS

J. Lee: Methodology, software, formal analysis, data curation and writing—original draft preparation. JY Lee: Methodology, validation, data curation. DW Lee: Interpretation and validation. HR Kim: Conceptualization, validation, and interpretation. MY Kang: Conceptualization, methodology, validation, interpretation, writing—original draft preparation.

ORCID

Jongin Lee  <https://orcid.org/0000-0003-4337-8444>

JaeYong Lee  <https://orcid.org/0000-0002-1062-658X>

Dong-Wook Lee  <https://orcid.org/0000-0002-4023-3269>

Hyoung-Ryoul Kim  <https://orcid.org/0000-0001-7535-3140>

Mo-Yeol Kang  <https://orcid.org/0000-0002-1682-865X>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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