JOMH
Journal of Men's Health

ORIGINAL RESEARCH

Sex-specific cancer risk associated with insomnia: a prospective cohort study using the Korean genome and epidemiology study (KoGES) data

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Abstract

The interaction effect of sex and insomnia on the risk of cancer remains unclear. Our study aimed to examine the association between insomnia and cancer development, and through stratified analysis, to determine if this association is modified based on sex. We used the Korean Genome Epidemiology Study (KoGES), which initiated two distinct prospective cohort investigations in 2001. The main exposure variable are sex and insomnia and the main outcome is cancer occurrence. The occurrence of cancer was considered the main outcome, and Cox regression analysis was utilized to estimate hazard ratios and 95% confidence interval. Additionally, stratified analysis was conducted to evaluate the interaction effect of sex and insomnia on cancer risk. In our study, the incidence of cancer per 1000 person-years was 5.23 in the insomnia group and 5.33 in the non-insomnia group, with no significant difference in adjusted hazard ratio (aHR: 1.01 (0.81–1.26)). Stratifying by sex, incidence rates were 4.86 for males and 5.72 for females per 1000 person-years, with females presenting a significantly higher aHR (1.30 (1.03–1.71)). No significant interaction was observed for both "insomnia × sex" and "sex × insomnia". Notably, females on insomnia medication had a substantially increased cancer risk (aHR: 4.06 (1.95–17.24)). Our study revealed that females, especially those undergoing insomnia medication treatment, exhibited a heightened cancer risk, though insomnia alone did not significantly influence this risk. These findings suggest a potential protective effect of male gender against cancer incidence.

Keywords

Cancer; Insomnia; Sex

1. Introduction

Cancer, one of the leading causes of mortality globally, represents a significant public health challenge [1]. The World Health Organization estimated that cancer was responsible for nearly 10 million deaths in 2020, a tole which is projected to rise with the aging and growth of the global population, as well as an increase cancer-inducing behavior, such a smoking, sedentary lifestyles and unhealthy diets [2]. Beyond the human cost, the economic impact is profound: the global cost of cancer care has soared beyond a staggering US$1.16 trillion annually [3]. This burden underscores the urgency for timely diagnosis, effective treatments, and preventive strategies, especially in low- and middle-income countries where health infrastructure is often under-sourced, and late-stage presentations are prevalent [4]. Cancer arises from a multifaceted interplay of genetic, environmental and lifestyle factors [5, 6]. Established risk factors for cancer include genetics and family history, age, chronic inflammation, exposure to certain chemicals and substances, certain viral and bacterial infections, ionizing radiation, hormone therapy, a weakened immune system, and lifestyle choices such as tobacco and alcohol consumption, poor diet, physical inactivity and excessive exposure to sunlight [7, 8]. However, in the evolving landscape of cancer research, other potential risks are continually being explored to gain a holistic understanding of the disease's etiology. Intriguingly, recent studies have begun to shed light on the potential link between sleep disturbances, particularly insomnia and an elevated risk of cancer [9, 10].

Insomnia, among other sleep disorders, represents a prevalent concern for many worldwide, with research increasingly highlighting its association with the risk of multiple diseases [11]. Beyond mere fatigue and decreased focus, insomnia can elevate the risk of conditions such as depression, anxiety, heart diseases and diabetes [12, 13]. Particularly concerning is the ongoing research into its correlation with cancer risk. Initial studies have suggested links between insomnia and various types of cancers, notably breast, lung and colorectal cancers [14, 15]. Some research proposes that disruptions in sleep cycles and melatonin production might influence the growth and spread of cancer cells. While these findings are still in their preliminary stages, and a clear causal link between insomnia

and cancer risk necessitates further research, these initial studies underscore the importance of sleep and maintaining healthy lifestyle habits for our overall health [16].

There are studies indicating that the relationship between insomnia and cancer risk can differ based on sex. Some research has found that women more frequently report symptoms of insomnia compared to men and notably, there seems to be a stronger association with breast cancer among women [17, 18]. Proposed reasons for this association include changes in female hormone levels and alterations in melatonin secretion, which affects sleep cycles. On the other hand, in men, there has been an emphasized correlation between insomnia and certain types of cancers, such as prostate or lung cancer [19]. These sex differences may be influenced by genetic, hormonal and lifestyle environmental factors. However, further studies are needed to gain a deeper understanding of the association between insomnia and cancer risk by sex. These investigations underscore the significance of sex-specific diagnostic, therapeutic and preventive strategies.

Thus, we hypothesized that there is an association between insomnia and the risk of cancer, and that this relationship may vary according to sex. The purpose of our study was to elucidate the association between insomnia and cancer development, and through stratified analysis, to determine if this association is modified based on sex.

2. Methods

2.1 Study design and data sources

The Korean Genome Epidemiology Study (KoGES) initiated two distinct prospective cohort investigations in 2001. These were executed in two separate regions: Ansung, a countryside location housing approximately 176,000 residents as of 2010, and Ansan, an urban locale with nearly 715,000 inhabitants during the same year. Both cohorts consist of Korean individuals, male and female, aged between 40 to 69, all sharing a consistent ethnic background. Detailed methodologies, including sampling plans and selection criteria for these ongoing studies, are available in previous publications. Between 2001 and 2002, 7129 eligible individuals were pinpointed in Ansung, and 10,957 in Ansan. Collectively, 5018 participants in Ansung (2239 men and 2779 women) and 5020 in Ansan (2523 men and 2497 women) partook in preliminary examinations in their designated areas. Each participant underwent periodic evaluations up to the cohort study's endpoint, which was the 9th assessment spanning 2019 to 2020. Interviewers, adhering to a consistent guideline, receive retraining every alternate year. Cohort participants have been observed at regular intervals, with structured site visitations every two years [20].

2.2 Study population and definition of cancer

KoGES data included biennial follow-up assessments of patient information, beginning with the baseline survey in 2001–2002. For the analysis, we excluded participants who were reported physician diagnosed cancer and who were not reported insomnia history at the time of baseline survey. Participants who did not have a history of cancer at the time of the baseline survey, and during the biennial follow-up surveys commencing from 2003–2004, and those who reported being diagnosed with a cancer were classified as having a cancer.

2.3 Insomnia and other potential risk factors

During the 2001–2002 survey period, participants underwent an interview where they answered a structured questionnaire. A pivotal aspect of this questionnaire was the question, "Have you been diagnosed with insomnia?" to determine insomnia history. In addition, we collected data on the use of insomnia medications through self-report from participants. In our methodology, participants were queried regarding their use of insomnia medications, without specifying particular drugs. This information was gathered independently of the participants' responses to questions related to their insomnia diagnosis. We defined an insomnia case as any participant who either reported receiving an insomnia diagnosis or responded positively to using insomnia medications. Furthermore, participants provided standard demographic information such as age, sex, marital status and education years. Their socioeconomic status (SES) was determined by their household income, with those in the lower 50% of the cohort being classified as having a low SES. Health conditions, including comorbidities like hypertension, diabetes mellitus and dyslipidemia, were identified based on participants' self-reported doctor-diagnosed conditions. The Body Mass Index (BMI) was calculated from measured weight and height, offering insights into their physical health. Lifestyle behaviors, including alcohol consumption, smoking habits and physical activity, were documented using standardized questions about their frequency, duration and type. Depression status was determined based on participants' self-reported history of receiving a diagnosis or treatment for depression. Additionally, participants' serum levels of C-reactive protein (CRP) were ascertained following a standard laboratory assay protocol. For the handling of missing data in our analyses, any missing values related to the main exposure and outcome were excluded. For all other variables, missing data were coded and treated as "no". The missing data of all variables were less than 2%.

2.4 Statistical analysis

We calculated descriptive statistics for the baseline characteristics of study participants by sex and insomnia. Baseline characteristics of KoGES participants were compared using the Wilcoxon rank sum test for continuous variables and using the chi-square test for categorical variables. The crude 19-year (2001 to 2020) incidence rates of cancer were calculated as the number of risk cases per 1000 person-years based on the sex and insomnia. Thereafter, hazard ratios (HRs) and 95% confidence interval (CIs) from Cox proportional hazard regression models with fixed covariates were used to estimate relative risks for 19-year cumulative cancer incidence based on sex and insomnia. Three models were adjusted for different covariates: Model 1 adjusted for age and sex; Model 2 further adjusted for comorbidities including hypertension, diabetes mellitus and dyslipidemia; and Model 3 was additionally adjusted for smoking, alcohol intake, physical activity, marital

status, socioeconomic status and body mass index. We employed a stratified analysis by sex and insomnia using the Cox proportional hazard regression model to estimate the influence of sex on study outcomes, specifically in relation to insomnia status. Moreover, a sensitivity analysis was conducted focusing on individuals with insomnia who were on medication.

We tested the multi-collinearity between co-variables in the model. All statistical analyses were performed using SAS-version 9.4 software (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1 Demographic findings

Of the total 10,030 participants from the KoGES registry, we finally conducted our study on a total of 9036 participants, excluding those who had already been diagnosed with cancer at the time of cohort enrollment (n = 854) and those whose insomnia status was unknown (n = 140).

During the 18 years of follow-up, we documented 690 cases of new-onset cancer (5.39 cases per 1000 person-years). The characteristics of the study participants according to history of insomnia are presented in Table 1. The group with insomnia tended to be younger and female, with a lower socioeconomic status (SES). They also had higher rates of hypertension and diabetes mellitus, but lower rates of alcohol intake and current smoker. Depression was more frequently observed in those with insomnia, though no significant difference in cancer incidence was found. The characteristic of the study participants according to sex are presented in Table 2. Female had a significantly higher prevalence of hypertension, while there was no difference in diabetes mellitus between sexes. Male had notably higher rates of alcohol intake and current smoker. Both insomnia and depression were significantly more common in female, there was no sex difference in the incidence of cancer.

3.2 Main outcomes

Table 3 shows the association of sex and insomnia with the risk of developing cancer. The incidence of cancer per 1000 person-years was 5.23 for the group with insomnia and 5.33 for the group without insomnia; however, after adjusting for all potential confounders, there was no significant difference in the HR (aHR: 1.01 (0.81–1.26)). When stratified by sex, the incidence was 4.86 for males and 5.72 for females per 1000 person-years, with females showing a significantly higher aHR (1.30 (1.03–1.71)). In the stratified analysis by sex and insomnia, neither the stratification by insomnia within each sex nor by sex within insomnia status showed a significant interaction. However, when considering insomnia medication usage, females taking insomnia medication exhibited a significantly increased risk of cancer (aHR: 4.06 (1.95–17.24)) ($p < 0.05$) (Table 4).

4. Discussion

Our study aimed to examine the independent effect and potential interactions of sex and insomnia on cancer risk. While insomnia alone did not significantly elevate the risk of cancer, being male appeared to offer some protective effect, as

females, especially those on insomnia medication, exhibited a heightened risk. In our stratified analysis examining whether the effect of sex on cancer risk varied depending on the presence of insomnia, there was no significant association between insomnia status and sex. However, when considering the use of insomnia medication, females on such medication demonstrated a significantly increased risk of cancer. This finding underscores the potential nuanced relationship between insomnia, its treatment, and cancer risk, particularly among females. These results provide a foundation for further discussions on the multifaceted interactions and implication observed in our study.

Emerging Studies underscore sex-specific variances in both incidence and fatality rates of several cancers. In the U.S, prostate, lung and colorectal cancers are most prevalent in male, whereas women predominantly face breast, lung and colorectal cancers [21]. Beyond cancers specific to gendered organs like the prostate or ovary, there are noted differences in the prevalence of cancers such as colon, lung and liver between the sexes [22, 23]. Thyroid cancer, for instance, has a notably higher incidence in female [22], while cancers of the colorectal, stomach and liver are more frequent in male [24]. Notably, bladder cancer and leukemia diagnoses are predominantly found in male [25]. Even the location of cancer manifestation differs; women with colorectal cancer often exhibit right-sided malignancy, whereas it tends to appear on the left side in male, with the former being associated with more severe prognosis [26]. The variance in manifestation might be attributed to estrogen level disparities between sexes [27]. Building on this, our study primarily analyzed overall cancer risk and, contrasting with previous studies, indicated a higher cancer risk in females compared to males [28–30].

In comparing existing studies on the relationship between insomnia and cancer risk with our own findings, there are some discrepancies. Previous research has presented varying conclusions regarding the association between insomnia and heightened cancer risk. For instance, Kao *et al.* [31] found a stronger association between insomnia and an increased risk for lung cancer, while Zhang *et al.* [32] indicated only a mild correlation across specific types of cancer. Jiao *et al.* [33] reported an elevated risk of breast cancer among female insomniacs. However, our study found no significant correlation between insomnia and an increased risk of cancer. Several reasons might explain these divergent results. Differences in study populations, methodologies and definitions of insomnia can introduce variability [34]. Moreover, other confounding factors, such as lifestyle habits, comorbid conditions or medication usage, may not have been consistently accounted for across all studies. It's also worth considering the duration and severity of insomnia, which may differ substantially among individuals and influence outcomes.

There are several studies that report the impact of insomnia on the risk of developing various disease varies by sex. In previous studies reporting that the risk of insomnia in relation to specific disease incidence varies by sex, insomnia increased incidence of cardiovascular disease [35], depression [36], and metabolic syndrome [37], with a more pronounced effect in females. Also, insomnia raised the risk of all-cause mortality, and this risk was also higher in females [38]. In meta-analysis

T A B L E 1. Baseline characteristics of patients according to insomnia.

Variables	All	Insomnia		
	N (%)	Yes	No	*p*-value
All	9036 (100.0)	1467 (100.0)	7569 (100.0)	
Age, year, mean (SD)	56.1 (8.84)	58.8 (8.69)	55.6 (8.77)	<0.001
Sex, female	4753 (52.6)	996 (67.9)	3757 (49.6)	<0.001
Married, yes	6560 (72.6)	964 (65.7)	5596 (73.9)	<0.001
Educational period >9 years	3087 (34.2)	335 (22.8)	2752 (36.4)	<0.001
Socioeconomic status, low	4561 (50.5)	922 (62.8)	3639 (48.1)	<0.001
Comorbidity				
Hypertension	1905 (21.1)	375 (25.6)	1530 (20.2)	<0.001
Diabetes mellitus	839 (9.3)	166 (11.3)	673 (8.9)	<0.001
Dyslipidemia	215 (2.4)	42 (2.9)	173 (2.3)	0.181
Body mass index				
<18.5 (underweight)	1747 (19.3)	314 (21.4)	1433 (18.9)	
18.5–24.9 (normal weight)	4061 (44.9)	643 (43.8)	3418 (45.2)	0.088
>25.0 (overweight)	3228 (35.7)	510 (34.8)	2718 (35.9)	
Health-related behavior				
Alcohol intake, yes	3505 (38.8)	481 (32.8)	3024 (40.0)	<0.001
Smoking				
Current smoker	1403 (15.5)	165 (11.2)	1238 (16.4)	
Former smoker	1396 (15.4)	160 (10.9)	1236 (16.3)	<0.001
Never smoker	6237 (69.0)	1142 (77.8)	5095 (67.3)	
Physical activity, vigorous	2689 (29.8)	394 (26.9)	2295 (30.3)	<0.001
Depression, yes	2668 (29.5)	756 (51.5)	1912 (25.3)	<0.001
Serum level of CRP (mg/dL), mean (SD)	1.61 (3.67)	1.81 (4.52)	1.57 (3.48)	<0.001
Total cancer cases	680 (7.5)	105 (7.2)	575 (7.6)	0.562
Gastrointestinal	230 (2.5)	38 (2.6)	192 (2.5)	
Pulmonary	175 (1.9)	31 (2.1)	144 (1.9)	
Liver	110 (1.2)	13 (0.9)	97 (1.3)	
Other	165 (1.8)	23 (1.6)	142 (1.9)	

SD: standard deviation; CRP: C-reactive protein.

concerning insomnia and cancer risk, the risk of developing cancer was significantly higher in studies conducted in female (HR: 1.24 (1.01–1.53), but not in male (1.28 (0.90–1.80) [39]. However, in contrast to previous studies, our study found no significant interaction effect between sex and insomnia (and insomnia and sex) in terms of disease risk, suggesting that the combined impact of these factors may not be as pronounced or consistent as previously thought. Additionally, in our study, elevated CRP levels were observed in males, which is deemed significant in the context of chronic inflammation being recognized as a pivotal factor in cancer incidence. On the other hand, despite the observed increased risk of cancer in females, a direct association with CRP levels was not confirmed.

When categorizing insomnia patients based on medication use and analyzing the interaction with sex, males demonstrated relatively protective effects, whereas the cancer risk was significantly higher in females with medicated insomnia.

In previous studies regarding insomnia medications including zolpidem and benzodiazepines have been shown to increase the risk of cancer [31, 40]. However, there hasn't been any established research indicating that zolpidem or benzodiazepines pose a greater risk to females or increase the risk of other diseases specifically in female [41]. Possible explanations for our study findings can be multifaceted. The interaction between insomnia medication and increased cancer risk in females might be rooted in biological or hormonal differences between the sexes [28]. While males might exhibit resilience to certain risks due to these biological differences, females may metabolize or respond to certain medications differently than males, potentially leading to varying side effects or interactions [30]. Additionally, the severity or type of insomnia might differ between genders, influencing the necessity and type of medication prescribed [29]. It's also plausible that underlying health conditions, lifestyle factors, or other medications

TABLE 2. Baseline characteristics of patients according to sex.

Variables	All	Sex		
	N (%)	Male	Female	*p*-value
All	9036 (100.0)	4283 (100.0)	4753 (100.0)	
Age, year, mean (SD)	56.1 (8.84)	55.6 (8.69)	56.5 (8.94)	<0.001
Married, yes	6560 (72.6)	3385 (79.0)	3175 (66.8)	<0.001
Educational period >9 years	3087 (34.2)	1912 (44.6)	1175 (24.7)	<0.001
Socioeconomic status, low	4561 (50.5)	1839 (42.9)	2722 (57.3)	<0.001
Comorbidity				
Hypertension	1905 (21.1)	804 (18.8)	1101 (23.2)	<0.001
Diabetes mellitus	839 (9.3)	425 (9.9)	414 (8.7)	0.233
Dyslipidemia	215 (2.4)	129 (3.0)	86 (1.8)	<0.001
Body mass index				
<18.5 (underweight)	1747 (19.3)	822 (19.2)	925 (19.5)	
18.5–24.9 (normal weight)	4061 (44.9)	2024 (47.3)	2037 (42.9)	<0.001
>25.0 (overweight)	3228 (35.7)	1437 (33.6)	1791 (37.7)	
Health-related behavior				
Alcohol intake, yes	3505 (38.8)	2498 (58.3)	1007 (21.2)	<0.001
Smoking				
Current smoker	1403 (15.5)	1310 (30.6)	93 (2.0)	
Former smoker	1396 (15.4)	1361 (31.8)	35 (0.7)	<0.001
Never smoker	6237 (69.0)	1612 (37.6)	4625 (97.3)	
Physical activity, vigorous	2689 (29.8)	1381 (32.2)	1308 (27.5)	<0.001
Depression, yes	2668 (29.5)	747 (17.4)	1921 (40.4)	<0.001
Serum level of CRP (mg/dL), mean (SD)	1.61 (3.67)	1.78 (4.22)	1.44 (3.07)	<0.001
Insomnia, yes	1467 (16.2)	471 (11.0)	996 (21.0)	<0.001
Medication	440 (4.9)	214 (5.0)	226 (4.8)	0.341
Total cancer cases	680 (7.5)	291 (6.8)	389 (8.2)	0.088
Gastrointestinal	230 (2.5)	82 (1.9)	148 (3.1)	
Pulmonary	175 (1.9)	77 (1.8)	98 (2.1)	
Liver	110 (1.2)	57 (1.3)	53 (1.1)	
Other	165 (1.8)	75 (1.8)	90 (1.9)	

SD: standard deviation; CRP: C-reactive protein.

TABLE 3. Risk of cancer in relation to sex and insomnia.

Potential risk factors	Numbers at risk	Cancer events	Person-years	Incidence rate per 1000 PYS	Model 1	Model 2	Model 3
					aHR (95% CI)	aHR (95% CI)	aHR (95% CI)
Insomnia							
No	7569	575	107,925.4	5.33	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	1467	105	20,058.8	5.23	1.01 (0.81–1.27)	1.01 (0.81–1.26)	1.01 (0.81–1.26)
Sex							
Male	4283	291	59,925.1	4.86	1.00 (reference)	1.00 (reference)	1.00 (reference)
Female	4753	389	68,059.20	5.72	1.11 (0.94–1.30)	1.12 (0.95–1.31)	1.30 (1.03–1.71)

PYS: person-years; HR: hazard ratio; CI: confidence interval.
Model 1: adjusted for age and sex.
Model 2: Model 1 + hypertension, diabetes mellitus, and dyslipidemia.
Model 3: Model 2 + Smoking, alcohol, physical activity, Marital status, Socioeconomic status, and Body mass index.

TABLE 4. Stratified analysis between the insomnia and sex (sex and insomnia) on the cancer occurrence.

	Insomnia	
	No	Yes
		aHR (95% CI)
Male	ref.	1.06 (0.72–1.56)
Female	ref.	1.08 (0.81–1.42)
	Sex	
	Male	Female
Non-insomnia	ref.	1.21 (0.94–1.68)
Insomnia	ref.	1.53 (0.75–3.19)
Medication (−)	ref.	1.28 (0.94–1.67)
Medication (+)	ref.	4.06 (1.95–17.24)

HR: Hazard ratio; CI: confidence interval.

commonly taken by females might interact with insomnia medications, enhancing their risks. A combination of these factors, alongside individual genetic predispositions, could contribute to the observed heightened risk in medicated female insomnia patients.

In our study, we sought to understand the implications of sex and insomnia on cancer risk, with a specific focus on potential interaction effects. We found that insomnia alone did not significantly increase cancer risk. However, females taking insomnia medications demonstrated a notably increased risk of cancer, while male did not show any significant difference in cancer risk. These findings underscore the importance of understanding sex-specific responses and risks associated with insomnia and its treatments.

Our study has several limitations. Firstly, the data might not wholly encapsulate the wider Korean population due to potential biases in specific age groups, regions or subsets. Furthermore, the longitudinal nature of our study introduces biases, as changes might transpire during the data collection or follow-up periods. Our analysis was also bounded by the variables provided in the KoGES dataset, potentially excluding significant covariates that could influence outcomes. A significant limitation was our inability to differentiate between various types of cancers and the wide array of insomnia medications. Both cancer and insomnia medications present with a myriad of categories and effects, which our study might not have adequately captured. Second, one notable limitation of our study is the characterization of exposure. The definition of insomnia employed in our research is relatively inclusive, potentially encompassing a broader range of sleep disturbances. Consequently, the identified cases may not entirely encapsulate the classic chronic insomnia disorder, which is typically associated with more significant mental and physical health implications. This broad definition of insomnia in our study should be considered when interpreting the results, as it may dilute the specific effects of chronic insomnia on cancer risk. Further research with a more precise insomnia definition is warranted to explore its impact more comprehensively. Third, although the impact of insomnia on cancer might be influenced by factors like the severity of insomnia, which could vary by sex, our study did not collect data on insomnia severity, representing a limitation. Fourth, one limitation of our study is the low prevalence of certain comorbidities like chronic obstructive pulmonary disease (COPD), asthma and heart diseases within our dataset. Furthermore, due to constraints in our survey items, we were unable to present a comprehensive analysis incorporating these conditions or the Charlson Comorbidity Index. This restricts the scope of our findings, especially in understanding how specific comorbidities might influence sleep patterns and subsequent health outcomes. Fifth, one of the limitations of our study pertains to the duration of follow-up. Considering the latency period associated with many cancers, our study's follow-up duration may not be sufficiently long to capture the full spectrum of potential effects of insomnia on cancer risk. As certain risk factors or oncogenes can take an extended period to manifest as clinical diseases, the relationships we observed may only reflect short- to mid-term associations, and longer follow-up periods may provide different insights. Sixth, another limitation of our study is the lack of data collection regarding variables such as estrogen levels and menopausal status. This limitation prevents us from providing direct research findings on the differences in estrogen levels between genders and their association with cancer incidence. Additionally, it should be noted that this age group includes both pre-menopausal and peri-/post-menopausal women, potentially leading to variations in estrogen levels. Considering these limitations, further research is warranted, and a more comprehensive understanding of the relationship between female hormones and cancer incidence requires additional data and investigation. Seventh, one of the limitations of our study pertains to the handling of missing data. For questions left unanswered by the participants, we treated them as "no" responses. While this method simplifies the analysis process, it may introduce some level of bias. However, the proportion of such data was not substantial, and we believe that its impact on the overall results is minimal. Nevertheless, this approach should be taken into consideration when interpreting our findings. Eighth, the dependence on self-reported data within KoGES, such as lifestyle habits or medical histories, introduces possible recall or reporting biases. There is also an inherent risk of unaccounted external factors influencing the results. The KoGES dataset might not be reflective of recent advances in research, technological changes, or socio-economic alterations. Additionally, in areas with sparse cases, our study might lack the statistical power to discern nuanced outcomes. These constraints should be considered when interpreting and generalizing our findings.

5. Conclusions

Our study revealed that females, especially those undergoing insomnia medication treatment, exhibited a heightened cancer risk, though insomnia alone did not significantly influence this risk. This underlines the importance of understanding the potential protective mechanisms in males and the sex-specific risks associated with insomnia and its treatments.

AVAILABILITY OF DATA AND MATERIALS

AUTHOR CONTRIBUTIONS

EJ and HHR—conceptualization; data curation; formal analysis, supervision; investigation, software, writing original draft, writing review and editing. EJ—methodology. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was reviewed and approved by the Institutional Review Board of Chonnam National University Hospital (CNUH-2018-297). The requirement for informed consent from patients was waived because the study was a retrospective analysis of existing data.

ACKNOWLEDGMENT

FUNDING

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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