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ORIGINAL ARTICLE

Elevated perceived stress scale (PSS) scores are associated with increased risk of poor sleep assessed by global PSQI scores: cancer and hypnotics-stratified analysis in an adult population-based study

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Abstract

Patients with cancer tend to have an increased risk of sleep disorders. The exact association between cancer and sleep disorders remains uncertain. We aimed to investigate whether elevated perceived stress is linked to a higher risk of sleep disorders in patients with and without cancer history respectively. A total of 941 adult individuals from the Midlife in the United States (MIDUS) study were included in this study. Multivariate analyses were used for assessing the association between Perceived Stress Scale (PSS) and Global Pittsburgh Sleep Quality Index (PSQI) Score. Adjusted for age, gender, BMI, blood pressure (BP), smoking and drinking status, exercise, disease history, and blood biomarkers, elevated PSS score was significantly associated with a higher PSQI score in the linear regression model (0.189 [0.154–0.224], $p < 0.001$; Model 2). The higher PSS score was still significantly associated with Poor sleep status (score > 5) in the logistic regression model (1.062 [1.036–1.090], $p < 0.001$; Model 2). Stratified analysis showed that the association between PSS and poor sleep status was affected by hypnotics use, but not by ever cancer history. Elevated PSS is linked with a higher risk of poor sleep status in the adult population from the United States. Elevated PSS might mediate the association of cancer and poor sleep quality. Future studies need to evaluate whether reducing PSS can improve sleep status in patients with cancer history.

Keywords Perceived stress · Sleep · Cancer · Ross-sectional study

Introduction

Sleep disorders are a global public health problem due to lifestyle and chronic diseases [1]. Existing evidence has suggested a close association between cancer and sleep disorders [2, 3]. Studies have demonstrated that patients with cancer tend to suffer from a higher risk of sleep disorders, as sleep disorders lead to poor treatment adherence [3, 4] and a high prevalence of cancer-related complications, such as cardiovascular diseases (CVDs) and all-cause mortality [5, 6]. However, compared with psychological well-being, however, sleep disorders in patients with cancer always receive less empirical attention [6, 7]. Emerging literature has shown that sleep disorders, including shorter or longer sleep times, poor sleep quality and others, have a higher prevalence among patients with cancer than in general populations [7, 8]. A recent study showed that approximately 2/3 of patients with cancer reported an increase in the severity of sleep difficulties [7]. These findings highlight the magnitude of sleep disorders in cancer patients. Furthermore, it was reported that cancer patients with poorer sleep quality have lower mental health and more bodily pain than those with improved sleep quality [9]. After controlling for sociodemographic, psychosocial, and medical covariates, one study showed that poor sleep quality still independently contributed to poorer prognosis among patients with cancer [9, 10]. Therefore, finding significant risk factors as sensitive markers or predictors for detecting sleep disorders is very important for treating cancer and alleviating the rate of cancer-related complications.

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Perceived stress is generally considered to be a result of disruptive physiology and psychology and a response to events that threaten the ability to cope [11, 12]. Perceived stress can lead to significant changes in the adrenal cortex and cortisol levels, which are linked to CVDs, respiratory diseases, immunological diseases, and other health issues [13–17] and may cause psychological distress such as anxiety and depression [18, 19]. The biopsychological consequences of perceived stress are also associated with poor sleep quality. Many studies have suggested that hyperarousal due to elevated cortisol levels increases heart rate and sympathetic activation in people with insomnia, which coincide with stress responses [20, 21]. Some psychological stressors, including anxious and depressive symptoms among patients with cancer, have been found to be directly related to poor sleep quality.

To date, few studies have comprehensively evaluated whether Perceived Stress Scale (PSS) scores are associated with global sleep quality. The Global Pittsburgh Sleep Quality Index (PSQI) score, which assesses seven sleep parameters, is a very valuable and practical measure for assessing global sleep quality in general populations. In the present study, we aimed to examine the association between perceived stress (assessed by the PSS) and global sleep quality (assessed by the PSQI) independent of related confounding factors, such as sociodemographic characteristics and lifestyle factors.

Materials and methods

Study population

The data were collected from 1255 American adults in the Midlife in the United States (MIDUS) study, including social, psychological, and behavioral factors [22]. Complete data and specific codebooks are also available at http://www.midus.wisc.edu/. In summary, the data for the present study are from the MIDUS II study, which was conducted between 2004 and 2006. The MIDUS II study included a self-administered survey of social, psychological, and behavioral variables. Data collection was conducted during a 2-day visit to a clinical research center (CRC) at the University of California-Los Angeles, University of Wisconsin or Georgetown University. Blood-related data were collected from 2004 to 2009 [23]. For research purposes, a total of 941 (75.0%) participants were included in our studies after 314 participants were excluded due to the lack of complete data (disease history, medications, blood biomarkers, sleep score, perceived stress score, depression score, etc.). Figure 1 shows a detailed flow chart of the participants included in the analysis.

In accordance with the Declaration of Helsinki guidelines, the Ethics Committee of three affiliated General Clinical Research Centers (University of California-Los Angeles, University of Wisconsin and Georgetown University) approved this prospective study, and all patients gave written informed consent.

Measurement of blood

Subjects underwent fasting blood draws prior to breakfast. The blood samples were sent to the MIDUS Biocore Lab for analysis. Hemoglobin A1c %, fasting glucose, fasting insulin levels, total cholesterol C-reactive protein, and other indexes were tested by using a Cobas Integra analyzer (Roche Diagnostics, Indianapolis, IN). Full details of the Biomarkers Project protocol from the MIDUS study are available elsewhere [32, 33]. Complete data and specific codebooks are also available at http://www.midus.wisc.edu/.

Global PSQI score

The global PSQI score was used for the evaluation of sleep quality. This 19-item index assesses the respondent's sleep quality over the past month [24, 25]. Items are mainly divided into 7 components, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction. After weighting the scores of 7 components ranging from 0 (no difficulty) to 3 (severe difficulty), we can obtain the global PSQI score by summing responses to each item. A higher global PSQI score indicates worse sleep quality. Poor sleep quality is usually indicated by a global PSQI score > 5 [24, 25].

Perceived Stress Scale

The Perceived Stress Scale (PSS) is a self-reported instrument with 10 items and is a widely used psychological instrument for measuring an individual's level of stress over the past month [26]. Responses options for each item (e.g., How often have you felt confident about your ability to handle personal problems?) range from 1 (never) to 5 (very often). Many studies have used PSS to examine the association between stress and quality of life, depression, and other parameters.

Depression score

The Center for Epidemiological Studies Depression (CESD) scale was used to assess depression [37]. The CES-D scale has been used widely in epidemiological studies and has been shown to be appropriate for use in studies with adult subjects [27, 28].

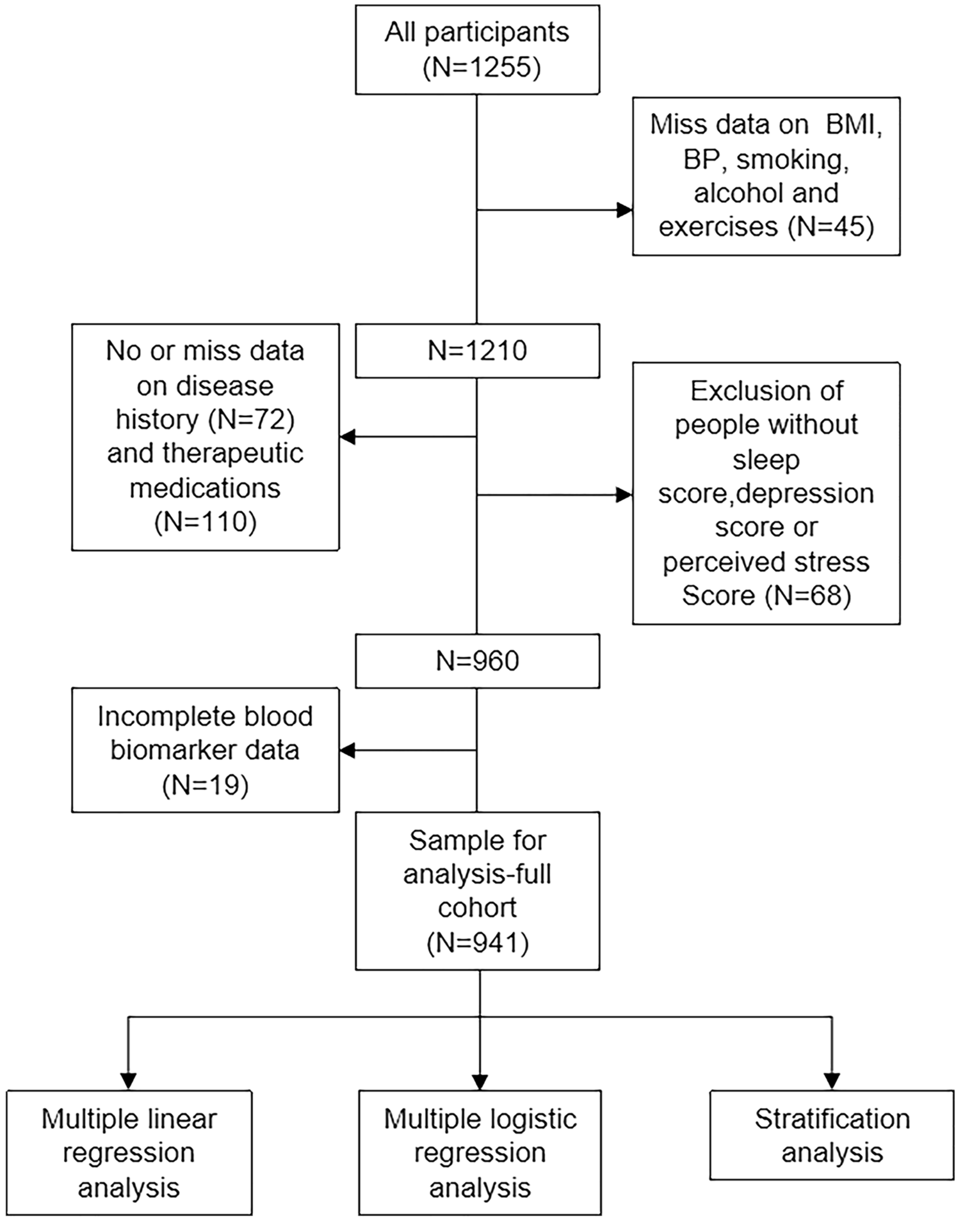

Fig. 1 A detailed flow chart of the participants included in the analysis

Statistical analysis

We used SPSS 25.0 for data analysis. The Kolmogorov–Smirnov test and Q-Q plots were used to determine the normality of the data. We used n (%) for the expression of categorical variables. The median (interquartile range [IQR]) was used for continuous variables with nonnormal distributions. The association between PSS and the global PSQI score was examined by multivariate linear regression. The relationship between PSS and poor sleep quality (global PSQI score > 5) was examined by logistic regression. The final calibration model (Model 2) adjusted for age, sex, BMI, blood pressure, smoking, alcoholism, exercise status, disease history (ever had depression, heart disease, high blood pressure, cholesterol problems, diabetes, emphysema/COPD), and blood biomarkers (hemoglobin A1c %, fasting glucose levels, fasting insulin levels, fasting IGF1, total cholesterol, HDL cholesterol, LDL cholesterol, serum IL-6, serum IL10 and C-reactive protein). Sensitivity analysis was performed by adding the CESD scale as a covariant to analyze the association between PSS scores and sleep quality. Stratified analyses were performed to investigate the effects of cancer and medications on the association between PSS scores and sleep quality: "Ever had cancer" and "hypnotic use" were treated as stratification variables. A P value (< 0.05) was considered statistically significant.

Results

The characteristics of the participants ($N=941$)

The 941 participants were divided into two groups by using "ever cancer" as a covariant, and 140 of them had a history of "ever cancer". The characteristics of the participants are presented in Table 1, which shows that cancer participants are generally older and have higher rates of chronic diseases, including CVDs, depression and respiratory diseases. Their blood levels of inflammatory biomarkers were higher than those in participants without a history of cancer. Furthermore, participants with a history of cancer were more likely to take anxiolytic sedatives, hypnotics, and antidepressants. Their sleep score, perceived stress score, and depression score did differ significantly from those of participants without a history of cancer ($p<0.05$).

Table 1 Characteristics of participants

Variables	All $N=941$	Ever cancer $N=140$	No-ever cancer $N=801$
Age (years)	55 (47–64)	62 (54–70)	54 (46–62)
Gender (male), n (%)	395 (42)	51 (36.4)	344 (42.9)
BMI	28.61 (25.27–33)	28.19 (24.98–32.25)	28.74 (25.32–33.37)
Average BP (sitting) systolic	131 (119–144)	130 (120–145)	131 (118–143)
Average BP (sitting) diastolic	75 (68–83)	77(20–83.75)	75 (68–82)
Ever smoked regularly, n(%)	430 (45.7)	64 (45.7)	366 (45.7)
Ever had alcoholism, n(%)	28 (3)	5 (3.6)	23 (2.9)
Frequency of exercise ≥ 3 times/week, n (%)	720 (76.5)	111 (79.3)	609 (76)
Ever diseases			
Ever had depression, n (%)	238 (25.3)	40 (28.6)	198 (24.7)
Ever had heart disease, n (%)	116 (12.3)	21 (15)	95 (11.9)
Ever had high blood pressure, n (%)	379 (40.3)	68 (48.6)	311 (38.8)
Ever had cholesterol problems, n (%)	436 (46.3)	70 (50)	366 (45.7)
Ever had diabetes, n (%)	121 (12.9)	22 (15.7)	99 (12.4)
Ever had emphysema/COPD, n (%)	28 (3)	8 (5.7)	20 (2.5)
Medication			
Anxiolytics sedatives and hypnotics, n (%)	127 (13.5)	23 (16.4)	104 (13)
Antidepressants, n (%)	150 (15.9)	26 (18.6)	124 (15.5)
Global PSQI score	5 (4–8)	7 (5–11)	3 (1–5)
CESD Scale	7 (5–11)	8 (6–13)	5 (2–8)
PSS	22 (15–24)	25 (17–26)	18 (12–20)
Biomarker blood sample status			
Hemoglobin A1c % (mg/dL)	5.86 (5.6–6.242)	5.92 (5.63–6.35)	5.81 (5.6–6.2)
Fasting Glucose levels (mg/dL)	96 (90–105)	96 (90–105)	96 (90–104)
Fasting Insulin levels (μIU/mL)	10 (6–17)	10 (6–16)	10 (6–17)
Fasting IGF1 (ng/mL)	118 (87–157.5)	109.5 (85–139.75)	118 (88–160)
Total Cholesterol (mg/dL)	183 (160–211)	184 (160–206.5)	183 (160–212)
HDL Cholesterol (mg/dL)	53 (43–66)	53 (43.25–67)	53 (43–66)
LDL Cholesterol (mg/dL)	101 (80–127)	101.5 (81–126.25)	101 (80–127.5)
Serum IL-6 (pg/mL)	2.14 (1.36–3.46)	2.59 (1.59–4.15)	2.07 (1.34–3.39)
Serum IL10 (pg/mL)	0.22 (0.17–0.33)	0.24 (0.17–0.37)	0.22 (0.17–0.32)
C-Reactive Protein (ug/mL)	1.51 (0.74–3.745)	1.87 (0.83–3.67)	1.46 (0.73–3.76)

M (IQR) for non-normally distributed variables, and n (%) for categoric variables

BMI body mass index, *BP* blood pressure, *COPD* chronic obstructive pulmonary disease, *PSQI* Pittsburgh Sleep Quality Index, *CESD* Center for Epidemiologic Studies Depression Scale, *PSS* perceived stress score, *IGF1* insulin-like growth factor-1, *HDL* high density lipoprotein, *LDL* low density lipoprotein, *IL* interleukin

Table 2 Multiple linear regression analysis for relationship between PSS and sleep score

Variables	B	Sβ	B 95% CI	*P* Value
Crude				
Global PSQI score	0.211	0.365	0.177–0.246	< 0.001
Subjective Sleep Quality	0.035	0.327	0.029–0.042	< 0.001
Sleep Latency	0.033	0.217	0.023–0.042	< 0.001
Sleep Duration	0.015	0.125	0.007–0.023	< 0.001
Habitual Sleep Efficiency	0.025	0.153	0.015–0.036	< 0.001
Sleep Disturbances Range	0.027	0.292	0.021–0.033	< 0.001
Sleeping Medication	0.029	0.162	0.017–0.040	< 0.001
Daytime Dysfunction	0.047	0.453	0.041–0.053	< 0.001
Model 1				
Global PSQI score	0.193	0.334	0.158–0.228	< 0.001
Subjective Sleep Quality	0.033	0.306	0.026–0.040	< 0.001
Sleep Latency	0.030	0.196	0.020–0.039	< 0.001
Sleep Duration	0.013	0.108	0.005–0.021	0.001
Habitual Sleep Efficiency	0.021	0.126	0.010–0.032	< 0.001
Sleep Disturbances Range	0.025	0.274	0.020–0.031	< 0.001
Sleeping Medication	0.026	0.150	0.015–0.038	< 0.001
Daytime Dysfunction	0.045	0.431	0.039–0.051	< 0.001
Model 2				
Global PSQI score	0.189	0.327	0.154–0.224	< 0.001
Subjective Sleep Quality	0.033	0.302	0.026–0.039	< 0.001
Sleep Latency	0.028	0.183	0.018–0.037	< 0.001
Sleep Duration	0.013	0.108	0.005–0.021	0.001
Habitual Sleep Efficiency	0.020	0.121	0.009–0.031	< 0.001
Sleep Disturbances Range	0.025	0.269	0.019–0.031	< 0.001
Sleeping Medication	0.026	0.146	0.014–0.037	< 0.001
Daytime Dysfunction	0.045	0.433	0.039–0.051	< 0.001

Crude: Adjusted for age and gender

Model 1: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise and disease history

Model 2: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise, disease history and blood biomarkers

PSS perceived stress score, *PSQI* sleep quality index, *BMI* body mass index, *BP* blood pressure

Associations between PSS and global PSQI scores by multivariate linear regression analysis

The regression coefficient (β = 0.193, 95% CI 0.158–0.228, $p < 0.001$) in Model 1 (Table 2) indicates that PSS scores were significantly associated with global PSQI scores after adjusting for age, gender, BMI, BP, smoking, and drinking status, exercise, and disease history. Moreover, after adjusting for the indicators above, blood biomarkers of glucose metabolism (hemoglobin A1c, fasting glucose levels, fasting insulin levels, and fasting IGF1), lipids (total cholesterol, HDL cholesterol, and LDL cholesterol) and inflammation (IL-6, IL-10, and C-reactive protein), PSS scores were still positively related to global PSQI scores. Strong associations were also found between PSS scores and each dimension of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance range, sleeping medication, daytime dysfunction). These results suggested that high PSS scores are closely associated with poor sleep quality after controlling for related confounding factors, including sociodemographic characteristics and lifestyle factors.

Associations between PSS scores and poor sleep quality (global PSQI score > 5) by multivariate logistic regression analysis

Participants were considered to have poor sleep quality when their global PSQI score was > 5 [24, 25]. The crude model (1.084 [1.059–1.109]) shows a statistically significant relationship between elevated PSS scores and poor sleep quality in Table 3. After adjusting for age, sex, BMI, BP, smoking and drinking status, exercise, and disease history, the adjusted association (OR = 1.063, 95% CI 1.037–1.090, $p < 0.001$; Model 1) between PSS scores and poor sleep quality was still statistically significant. In addition, after blood biomarkers of glucose metabolism, lipids and inflammation were added for the correction, the final association (OR = 1.062, 95% CI 1.036–1.090, $p < 0.001$; Model 2) showed that participants with higher PSS scores had significantly worse sleep quality. Sensitivity analysis suggested the association of PSS scores with poor sleep quality

Table 3 Multiple logistic regression analysis for relationship between PSS and poor sleep status (global PSQI score > 5)

Variables	Crude	Model 1	Model 2
Poor sleep status	1.084(1.059–1.109)	1.063(1.037–1.090)	1.062(1.036–1.090)
P Value	< 0.001	< 0.001	< 0.001

Crude: Adjusted for age and gender

Model 1: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise,and disease history

Model 2: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise,disease history and blood biomarkers

PSS perceived stress score, *PSQI* sleep quality index, *BMI* body mass index, *BP* blood pressure

(OR = 0.963 95% CI 0.929–0.999, p = 0.046; Model 2) still existed after adjusting for age, sex, BMI, BP, smoking and drinking status, exercise, disease history, blood biomarkers and CESD scale (Table 4).

Associations between PSS scores and poor sleep quality (global PSQI score > 5) by stratified analysis

To further investigate the correlation between PSS scores and poor sleep quality (global PSQI score > 5), "ever cancer" and "hypnotic use" were used to stratify the sample, and then the data were analyzed by multivariate logistic regression analysis, as shown in Table 5. An independently significant correlation still existed in both participants with and without a history of cancer, but the OR was higher among the participants with a history of cancer (OR = 1.128, 95% CI 1.036–1.227; Model 2) than among participants without a history of cancer (OR = 1.053, 95% CI 1.025–1.082; Model 2), which suggested that elevated PSS scores were more strongly associated with a higher risk of poor sleep quality among in participants with a history of cancer than in participants without a history of cancer, consistent with our research hypothesis. Additionally, we found a significant association in participants without "hypnotic use" (OR = 1.065, 95% CI 1.034–1096; $p < 0.001$; Model 2) but not in participants with "hypnotic use" (OR = 1.038, 95% CI 0.968–1.114; $p = 0.298$; Model 2), which suggested that the independent association between PSS scores and poor sleep quality was also significantly affected by "hypnotic use".

Table 4 Sensitivity analysis for depression score between PSS and poor sleep status (global PSQI score > 5) by Multiple logistic regression analysis

Variables	Crude	Model 1	Model 2
Poor sleep status	0.968(0.934–1.003)	0.966(0.931–1.001)	0.963(0.929–0.999)
P Value	0.073	0.057	0.046

Crude: Adjusted for age, gender and CESD scale

Model 1: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise, disease history and CESD scale

Model 2: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise,disease history, blood biomarkers and CESD scale

PSS perceived stress score, *PSQI* sleep quality index, *BMI* body mass index, *BP* blood pressure, *CESD* Center for Epidemiologic Studies Depression

Discussion

Previous studies have mainly focused on the impacts of stress-related variables on sleep quality in noncancer patients [29–31]. Only a few studies have attempted to investigate the association of stress variables with sleep quality in patients with cancer [32]. It has been reported that cancer patients' stress status could play a role in their sleep quality. For instance, patients with cancer tend to have an increased risk of sleep disorders [3, 4]. Stress in social interactions was found to be associated with poor sleep quality among an adult population [33]. However, the exact association between cancer and sleep disorders in cancer populations remains uncertain. Finding reliable risk factors or predictors for identifying sleep disorders, therefore, is very significant for early cancer treatment and alleviating the risk of cancer-related complications in patients with cancer.

We provided the first evidence that there is an independent association between PSS scores and global PSQI scores in participants with cancer. We found that the median global PSQI score was 8, which exceeded the threshold of the normal sleep quality score (global PSQI score = 5) in participants with cancer, as shown in Table 1. This suggests that the sleep quality of cancer patients is significantly worse

Table 5 Multiple logistic regression analysis for relationship between PSS and poor sleep status (score > 5) stratified by cancer and hypnotics use respectively

Variables	Crude	Model 1	Model 2
Ever had cancer	1.145(1.069–1.227)	1.134(1.048–1.227)	1.128(1.036–1.227)
P Value	< 0.001	0.002	0.005
No cancer	1.075(1.048–1.102)	1.054(1.026–1.083)	1.053(1.025–1.082)
P Value	< 0.001	< 0.001	< 0.001
Hypnotics use	1.061(1.006–1.119)	1.041(0.976–1.112)	1.038(0.968–1.114)
P Value	0.028	0.222	0.298
No hypnotics use	1.082 (1.053–1.111)	1.066 (1.036–1.096)	1.065 (1.034–1096)
P Value	< 0.001	< 0.001	< 0.001

Crude: Adjusted for age and gender

Model 1: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise and disease history

Model 2: Adjusted for age, gender, BMI, BP, smoking and drinking status, exercise, disease history and blood biomarkers

PSS perceived stress score, *PSQI* sleep quality index, *BMI* body mass index, *BP* blood pressure than that of general populations, consistent with previous studies [2–9]. A recent study also suggested that about 2/3 of cancer patients reported an increased severity in sleep difficulties [7], which is consistent with our conclusion that OR was stronger among the participants with a history of cancer than among participants without a history of cancer. The high prevalence of poor sleep quality in cancer patients highlights the importance of understanding the correlation between sleep quality and cancer. In this study, the independent association between PSS and poor sleep quality was also significantly affected by "hypnotic use". Elevated PSS scores tend to be more strongly associated with a higher risk of poor sleep quality in participants without hypnotic use than in participants without hypnotic use. The simplest and reasonable explanation for this difference is that improved sleep quality by hypnotic use made this significant correlation disappeared. The use of hypnotics reduced the sleep score of cancer patients, making the consistent perceived stress not proportional to sleep quality. Certainly, future studies are necessary to investigate other social relationship variables that contribute to sleep quality in participants with cancer.

This study has several obvious advantages. First, although many studies have reported that increased social stress is closely associated with CVDs and other inflammatory diseases [3], few studies have comprehensively focused on the association between PSS scores and sleep disorders in patients with cancer. To our knowledge, this study is the first to suggest that PSS scores are significantly associated with global PSQI scores among patients with cancer independent of relevant confounding factors, including sociodemographic characteristics, lifestyle factors, and biochemical parameters. Additionally, perceived stress was evaluated by the PSS, and global sleep quality was evaluated by the PSQI in this study [24–26]. These two measurement tools have been used widely in epidemiological studies and have been shown to be appropriate for use in our study [24–26]. Finally, the sample in this study is large and comes from multiple centers, so the results are relatively reliable. Of course, our results also had some limitations. First, the data are from a cross-sectional survey. Future studies need to replicate our findings using longitudinal designs in cancer patients. Second, we only used self-report measurements, which may cause some bias to the actual results. Third, the specific types of tumors in our study are not clear. Different tumors and their related treatment and prognosis may affect the relationship between PSS scores and sleep quality. Fourth, self-selection bias in participation with cancer might limit the generalizability of the findings. Fifth, sleep quality can vary across patients with different cancer stages and treatment statuses [3]. It is possible that the target variables should be adjusted when designing interventions for different populations.

Conclusions

Our results comprehensively showed that perceived stress is independently associated with an increased risk of poor sleep quality among adults with cancer and that the independent association can be affected by hypnotic use. Elevated PSS scores might be a valuable landmark for detecting poor sleep in patients with cancer. These findings can help clinicians pay attention to sleep disorders in cancer patients and further improve the prognosis of patients with cancer by improving sleep quality.

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Declarations

Conflict of interest The authors declare that they have no competing interests.

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