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H. 知的財産権の出願・登録状況
なし

F. 健康危険情報
特になし

G. 研究発表

G-1. 論文発表

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Ⅲ．研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
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Ⅳ. 研究成果の刊行物・別刷

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Original Article

Effects of insomnia and sleep medication on health-related quality of life

Taeko Sasai [a,d,*], Yuichi Inoue [a,b], Yoko Komada [b], Takashi Nomura [c], Masato Matsuura [e], Eisuke Matsushima [d]

[a] Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan
[b] Department of Somnology, Tokyo Medical University, Japan
[c] Department of Neurology, Institute of the Neurological Sciences, Tottori University Faculty of Medicine, Tottori, Japan
[d] Section of Liaison Psychiatry and Palliative Medicine, Graduate School of Tokyo Medical and Dental University, Japan
[e] Department of Life Sciences and Bio-Informatics, Division of Biomedical Laboratory Sciences, Graduate School of Health Sciences, Tokyo Medical and Dental University, Japan

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ABSTRACT

Objective: This study, using Short-Form 8 (SF-8), was undertaken to assess the effects of insomnia and sleep medication use on quality of life (QOL) in 2822 people (ages 20–97 years) in a rural population. Factors associated with deterioration of the mental component summary (MCS) score and physical component summary (PCS) score were investigated.
Methods: Questionnaires asked participants' basic information and included assessments using SF-8, the Pittsburgh Sleep Quality Index (PSQI), and a 12-item version of the Center for Epidemiological Studies Depression scale. Results of PSQI supported the classification of subjects as good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication.
Results: Insomnia was associated with low scores of MCS and PCS. Nevertheless, sleep medication use was associated with low PCS scores only. Good sleepers using sleep medication had significantly higher MCS scores than either insomniacs or insomniacs using sleep medication, but lower scores than good sleepers. Similarly to insomniacs using sleep medication, good sleepers using sleep medication had significantly lower PCS scores than either good sleepers or insomniacs.
Conclusions: Sleep medication was useful to improve mental QOL. That usage, however, might degrade the physical QOL, possibly because of the medication's adverse effects.

1. Introduction

Insomnia is well known as a common disorder [1–3] with a prevalence of about 20% among the general population [4,5]. Major symptoms of insomnia are poor nocturnal sleep and impaired daytime functioning during wakefulness [6]. In the 2nd edition of International Classification of Sleep Disorders (ICSD-2) [7], daytime impairment as well as nighttime sleep difficulties – difficulty initiating sleep, difficulty maintaining sleep, waking up too early or sleep that is chronically nonrestorative or poor in quality – are emphasized among the diagnostic criteria.

Reports describing clinical populations show that patients with chronic insomnia commonly complain of subjective daytime impairments including mood disturbances, concentration problems, elevated fatigue, and sleepiness [6,8]. Regarding objective daytime impairments, these patients show impairments in tasks evaluating vigilance, working memory, and motor control [9,10]. These various daytime dysfunctions attributable to insomnia are presumed to degrade quality of life (QOL), an evaluation of general daytime functioning [11,12]. Reportedly, degradation of QOL, as evaluated using the standardized 36-item Short Form Health Survey of the Medical Outcomes Study (SF-36), is associated with insomnia's severity [13]. Because QOL is a complex and multidimensional term, it can reflect the lifestyle, health status, and socio-environmental background of subjects. Although such factors should be analysed when evaluating QOL, few reports have described an association between insomnia and QOL in a general population with due consideration of these demographic factors.

Results of previous studies revealed the use of sleep medication for insomnia by approximately 5–8% of the general population [1,14,15]. The relative frequency among the general population of people with at least occasional use of sleep medication is approximately 3–11% [1,16,17]. Several studies conducted in clinical settings have revealed that the use of sleep medication improves not only sleep quality but also daytime ability to function and a sense of physical well being of patients with insomnia [18,19]. In addition, long-term nightly pharmacologic treatment of primary insomnia with any hypnotic has been reported to enhance both

* Corresponding author. Address: Japan Somnology Center, Neuropsychiatric Research Institute, 1-24-10 Yoyogi, Shibuya-ku, Tokyo, Japan. Tel.: +81 3 3374 9112; fax: +81 3 3374 9125.
E-mail address: taeko_ssi@yahoo.co.jp (T. Sasai).

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mental QOL and physical QOL [20]. Contrary to those reports, others have described sleep medication as having no significant effect on next-day psychomotor performance or QOL [21,22]. Furthermore, differences in the effects of sleep medication between mental and physical QOL among the general population have not been clarified yet.

In the series of Daisen sleep health care studies, we first reported the prevalence of restless legs syndrome (RLS) among residents in rural areas and the negative impact of the disorder on QOL [23]. Secondly, we presented data related to the influence of insomnia and sleep medication use on depressive symptoms [unpublished observations]. For the present study, we used the 8-item Short Form Health Survey of the Medical Outcomes Study (SF-8) – a simpler version of SF-36 that is nevertheless as useful as SF-36 for evaluating QOL [24,25] – to clarify the above-described issue of the association between insomnia, sleep medication use, and QOL. This study was designed to evaluate QOL among the general population in a rural community using SF-8, particularly addressing the impact of insomnia and sleep medication use on the mental component summary (MCS) score and physical component summary (PCS) score.

2. Methods

2.1. Subjects and procedures

The ethics committees of Tottori University approved this study. All subjects gave their informed consent to take part in this investigation.

This survey was conducted as a part of the above-described Daisen sleep health care studies undertaken in a rural community in Tottori prefecture in western Japan [23]. The total population of the town was 6643 in 2004, with 5528 residents aged 20 years or older (2521 men and 3007 women). Major industries in this area are agriculture, farming, and tourism. The questionnaire survey was conducted during November 2005–January 2006. With the cooperation of local public health nurses, questionnaires were delivered to all residents who were 20 years of age or older.

The questionnaires requested information related to family circumstances, existence of family members who need home-based nursing care (home-based nursing care), existence of any currently treated disease, smoking habits, and drinking habits. We used SF-8 for assessing QOL [26], a Japanese version of the Pittsburgh Sleep Quality Index (PSQI) [27,28] for inferring sleep disturbances in the subjects, and a 12-item version of the Center for Epidemiological Studies Depression scale (CES-D) [29] for estimating depressive symptoms. The SF-8, consisting of domains including vitality, social function, mental health, role emotional, general health, physical function, role physical, and bodily pain, were calculated according to standard methods. The MCS scale of the SF-8 was evaluated as an index of mental QOL; the PCS subscale was evaluated as an index of physical QOL. General population averages for these scores were set at 50 points. Consequently, a subject with a score of less than 50 points was inferred to have deteriorated QOL [25,30].

The PSQI included sub-items evaluating sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), frequency of sleep disturbance (C5), use of sleep medication (C6), and daytime dysfunction (C7), of which C1–C5 indicate problems with nocturnal sleep [27,28]. After excluding items of C6, we used the total score of the Pittsburgh Sleep Quality Index as the score of insomnia and defined greater than one standard deviation (SD) of the mean sum score (6.4) as designating insomnia, using a similar method to that used in our previous report (in submission). Based on the answers to C6, we defined subjects who used sleep medications less than once a week as "not using sleep medication" and once or more a week as "using sleep medication." According to these PSQI sub-items, subjects were classified into four groups: good sleepers ($n = 2070$), good sleepers using sleep medication ($n = 95$), insomniacs ($n = 264$), and insomniacs using sleep medication ($n = 85$). In addition, the subjects were categorized based on the frequency of sleep medication use obtained from the answer to C6: no use ($n = 2300$), less than once a week ($n = 50$), 1–2 times a week ($n = 43$), and more than three times a week ($n = 137$).

We also used total scores of CES-D as parameters of depressive symptoms. The CES-D had four response options for each question: "never or rarely," "sometimes," "often," and "always," coded as 0–3. We divided responses into two categories: 0–11 as normal and 12–36 as depressive [29].

Of the 5528 eligible subjects, 2937 subjects (53.1%) responded to our questionnaires and 2822 (51.0%) completed the questionnaires (1222 male, 1600 female; ages 20–97 years; mean [SD]: 57.4 [17.7] years).

2.2. Statistical analyses

Student's *t*-test was used to compare the MCS scores and PCS scores between the insomniac group and the group of good sleepers. One-way analysis of variance (ANOVA) was used to compare respective MCS scores and the PCS scores among the four groups described above: good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication. In addition, ANOVA was used to compare these scores among the four groups, categorized based on the frequency of sleep medication use described above: no use, less than once a week, 1–2 times a week, and more than three times a week. When significant differences were found using ANOVA, a Bonferroni's *post hoc* analysis was used. The chi-square test and subsequent residual analysis were used to compare differences in the rates of insomniacs in the four groups categorized based on the frequency of sleep medication use. The factors associated with deterioration of the MCS score and those of the PCS score were examined using a series of logistic regression analyses. All variables were examined initially in univariate models. To control for confounding factors and to determine main correlates, we then performed multivariate logistic regression analyses for all variables that showed a significant correlation in univariate models. Statistical tests of the regression estimates' odds ratios (ORs) were based on Wald statistics. Odds ratios and their 95% confidence intervals (CIs) were presented to show the association. These statistical analyses were conducted using software (Statistical Package for the Social Sciences [SPSS], ver. 11.5J, SPSS Inc., Tokyo, Japan).

3. Results

3.1. Sample characteristics

Demographic characteristics of the sample population are presented in Table 1. The sample comprised 1222 men (43.3%) and 1600 women (56.7%) with mean [SD] age of 57.4 [17.7] years (range 20–97 years). The mean family size in this cohort was 4.6 [1.6]: 120 subjects (4.3%) lived alone and 1210 responders (43.9%) lived with more than five family members.

3.2. Differences in scores of MCS and PCS between the insomniac group and good sleepers group

Supplementary Fig. 1 (in online supplementary material) portrays comparisons between the MCS score and the PCS scores of the insomniac group's insomniacs and those using sleep medica-

Table 1
Demographic characteristics of the sample.

	n	%
Sex		
Male	1222	43.3
Female	1600	56.7
Age group		
20s	242	9.5
30s	266	10.4
40s	339	13.3
50s	574	22.5
60s	461	18.0
70s	444	17.4
80s	204	8.0
90s	25	1.0
Number of family members		
Alone	120	4.3
2 (with partner)	351	12.6
3 person	752	27.0
4 person	504	18.1
⩾5	1210	43.6
Habitual alcohol consumption		
Yes	1083	39.0
No	1697	61.0
Smoking habit		
Yes	609	21.9
No	2174	78.1

tion ($n = 365$) and comparisons of the good sleepers groups' good sleepers and those using sleep medication ($n = 2165$). Regarding these two values, significant differences were found between these two groups [MCS score, $t_{(2498)} = 14.5$, $p < 0.01$; PCS score, $t_{(2498)} = 9.9$, $p < 0.01$]. The insomniac group showed a significantly lower MCS score than the good sleepers group (45.3 ± 8.0 vs. 50.5 ± 5.9, $p < 0.01$). The insomniac group also showed significantly lower PCS scores than the good sleepers group (44.3 ± 8.6 vs. 48.3 ± 6.9, $p < 0.01$).

3.3. Factors associated with MCS score deterioration

The mean [SD] score of the MCS was 49.7 [6.6] in the total sample. We designated subjects whose scores were below those of the population average (50 points) as poor MCS. Results show that the mean [SD] score was 44.0 [5.3] in the group with poor MCS; the value was 54.4 [2.8] in the group with good MCS.

Univariate logistic regression analyses were performed for 10 independent variables: sex, age, smoking habit, habitual alcohol ingestion, living alone, home-based nursing care, existence of disease currently treated, depression, insomnia, and use of sleep medication (C6). Among these variables, five items (sex, age, home-based nursing care, depression, and insomnia) were significantly associated with MCS score deterioration in the univariate model. Multivariate logistic regression analysis revealed that MCS score deterioration was significantly associated with being female (OR = 1.52, 95%CI: 1.23–1.89), younger than the median age (<58 years, OR = 0.75, 95%CI: 0.61–0.92), having a family member requiring home-based nursing care (OR = 1.67, 95%CI: 1.31–2.12), depression (OR = 5.83, 95%CI: 4.60–7.38), and insomnia (OR = 2.29, 95%CI: 1.71–3.05) (Supplementary Table 2 in online supplementary material).

3.4. Factors associated with PCS score deterioration

The mean [SD] score of the PCS was 47.5 [7.4] in the total sample. We determined the subjects whose scores were below the general population averages (50 points) as poor PCS. The mean [SD] score of this value was 42.5 [6.3] in the group with poor PCS, although the value was 53.7 [2.2] in the group with good PCS.

Univariate logistic regression analyses were performed for the same 10 independent variables used for analysis of associated factors for MCS score deterioration. Among these variables, seven items (age, smoking habit, habitual alcohol ingestion, existence of disease currently treated, depression, insomnia, and use of sleep medication) showed significant correlations with deterioration of the PCS score. Multivariate logistic regression analysis revealed that PCS score deterioration was significantly associated with being older than the median age (⩾58 years, OR = 2.68, 95%CI: 2.21–3.25), existence of a disease currently treated (OR = 1.95, 95%CI: 1.59–2.39), depression (OR = 1.64, 95%CI: 1.31–2.05), insomnia (OR = 1.69, 95%CI: 1.27–2.24), and use of sleep medication (OR = 1.36, 95%CI: 1.16–1.61) (Supplementary Table 3 in online supplementary material).

3.5. Differences in MCS scores among the four groups categorized by both insomnia symptoms and sleep medication use

Fig. 1 presents a comparison of the MCS scores among the four groups: good sleepers, good sleepers using sleep medication, insomniacs, and insomniacs using sleep medication. Among the four groups, this value was significantly different ($F_{(3, 2496)} = 79.2$, $p < 0.01$), showing the following order: good sleepers (50.7 ± 5.8) > good sleepers using sleep medication (48.1 ± 7.7) > insomniacs (45.9 ± 7.8) > insomniacs using sleep medication (43.6 ± 8.7). Results of *post hoc* analyses show that the insomniacs using sleep medication had significantly lower MCS scores than those of the good sleepers ($p < 0.01$), the insomniacs ($p < 0.01$), or the good sleepers using sleep medication ($p < 0.01$). The insomniacs also had significantly lower scores than the good sleepers ($p < 0.01$). The good sleepers using sleep medication had significantly lower scores than the good sleepers ($p < 0.01$) but had significantly higher scores than those of the insomniacs ($p < 0.01$).

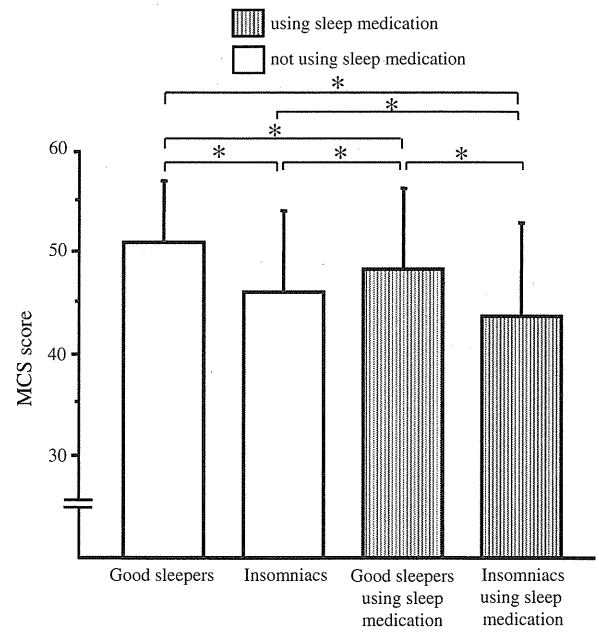

Fig. 1. Differences in MCS scores among four groups categorized by both insomnia symptoms and sleep medication use. MCS, mental component summary; good sleepers ($n = 2070$); insomniacs ($n = 280$); good sleepers using sleep medication ($n = 95$); insomniacs using sleep medication ($n = 85$); * $p < 0.01$, one-way ANOVA.

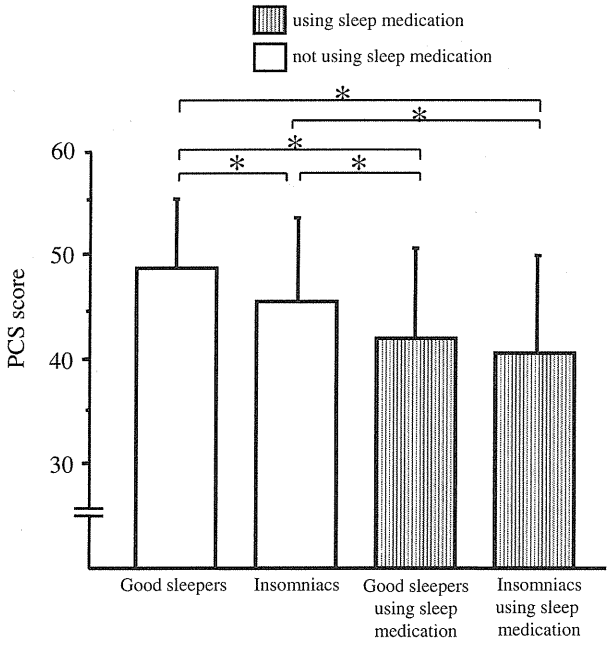

Fig. 2. Differences in PCS scores among four groups categorized by both insomnia symptoms and sleep medication use. PCS, physical component summary; good sleepers ($n = 2070$); insomniacs ($n = 280$); good sleepers using sleep medication ($n = 95$); insomniacs using sleep medication ($n = 85$); $p < 0.01$, one-way ANOVA.

3.6. Differences in PCS scores among the four groups categorized by both insomnia symptoms and sleep medication use

Fig. 2 presents a comparison of PCS scores among the four groups. A significant difference in this value was found among the four groups ($F_{(3, 2496)} = 72.7$, $p < 0.01$). The scores showed the following order: good sleepers (48.6 ± 6.6) > insomniacs (45.4 ± 8.0) > good sleepers using sleep medication (41.9 ± 8.5) > insomniacs using sleep medication (40.5 ± 9.2). *Post hoc* analyses revealed that the insomniacs using sleep medication had a significantly lower value than that of either the good sleepers or the insomniacs using sleep medication ($p < 0.01$, respectively). The insomniacs also had a significantly lower value than the good sleepers ($p < 0.01$). The good sleepers using sleep medication showed a significantly lower value than the good sleepers or the insomniacs ($p < 0.01$). No significant difference was found between the good sleepers using sleep medication and the insomniacs using sleep medication.

3.7. Differences in MCS and PCS scores among the four groups categorized by frequency of sleep medication use

Table 2 presents a comparison of the MCS and PCS scores among four groups categorized according to frequency of sleep medication use. Among the four groups, the MCS scores were significantly different ($F_{(3, 2496)} = 24.5$, $p < 0.01$). *Post hoc* analyses revealed that the group using sleep medication 1–2 times a week and that with sleep medication more than three times a week had significantly lower values than that with no sleep medication use ($p < 0.01$, respectively). For the PCS score, the value was significantly different among the four groups ($F_{(3, 2496)} = 64.5$, $p < 0.01$). *Post hoc* analyses revealed that the group using sleep medication 1–2 times a week and the group using sleep medication more than three times a week had significantly lower MCS scores than the group using no sleep medication ($p < 0.01$, respectively). The PCS scores were significantly different among the four groups ($F_{(3, 2496)} = 64.5$, $p < 0.01$). *Post hoc* analyses revealed that all three groups using sleep medication had significantly lower scores than the group of subjects using no sleep medication ($p < 0.01$, respectively). The group using sleep medication more than three times a week had a lower value than that using sleep medication less than once a week and 1–2 times a week ($p < 0.01$, respectively). The group using sleep medication 1–2 times a week had a significantly lower value than that using sleep medication less than once a week ($p < 0.01$). For respective groups, the numbers and rates of insomniacs were as follows: no use ($n = 264$, 11.5%), less than once a week ($n = 50$, 32.0%), 1–2 times a week ($n = 43$, 55.8%), and more than three times a week ($n = 137$, 44.5%). As Table 2 shows, significant differences were found in the rates of insomniacs among the four patient groups ($\chi^2_{(3)} = 188.9$, $p < 0.01$). The rest error test revealed that the two groups using sleep medication more than once a week showed higher rates of insomniacs than either the group with no medication use or the group using sleep medication once a week.

4. Discussion

Leger et al. reported that chronic insomniacs showed lower scores of SF-36 than good sleepers in all eight domains. The more severe the insomnia symptoms were, the worse the QOL [13]. Compatible with their results, our results showed that both the MCS scores and the PCS scores were significantly lower for insomniacs than for good sleepers in the study area population.

Results of multiple logistic analysis show that depression and age are associated with the deterioration of physical QOL and mental QOL. Younger age (<58 year) was associated with lower MCS scores, and older age (⩾58 year) was associated with lower PCS scores, as previous studies have also shown [31,32]. Being a woman and the presence of a family member needing home-based nursing care were also associated with lower mental QOL; the existence of currently treated diseases was associated with lower physical QOL. These results were compatible with those of previous reports [33–37]. In addition to these factors, insomnia was found to be a significant factor associated with deterioration of both the mental QOL and the physical QOL. Results of earlier reports have described that sleep loss deteriorates physical function such as postural sway [38], blood pressure elevation [39], glucose

Table 2
Differences in scores of MCS and PCS among four groups categorized by frequency of sleep medication use.

Frequency of sleep medication use (/week)	No use ($n = 2300$)	<1 ($n = 50$)	1⩽, 2⩽ ($n = 43$)	⩾3 ($n = 137$)
MCS	50.1 ± 6.2	48.2 ± 7.2	46.4 ± 7.4*	45.8 ± 8.8*
PCS	48.3 ± 6.8	46.8 ± 8.3*	44.0 ± 6.7*,a	40.4 ± 9.3*, a,b
Number of insomniacs (%)c	264 (11.5)	16(32.0)	24 (55.8)	61 (44.5)

MCS, mental component summary; PCS, physical component summary.
[a] $p < 0.01$ compared to the value in the group using sleep medication less than once a week.
[b] $p < 0.01$ compared to the value in the group using sleep medication 1–2 times a week.
[c] $\chi^2 = 188.9$ (df = 3), chi-square test.
* $p < 0.01$ compared to the value in the no use group.

intolerance [40], and immunological dysfunction [41]. Regarding mental function, insomnia has been identified as a risk factor for developing depression or anxiety disorder [42]. Furthermore, insomniacs undergo psychomotor performance degradation, including impairment of both cognitive function and short-term memory [9,43]. These physiological and/or psychological dysfunctions brought about by sleep loss and/or subjective insomnia might contribute to deterioration of mental QOL and physical QOL.

The most remarkable finding of this study was the different influences of sleep medication use on mental QOL and physical QOL: multiple logistic analyses revealed that sleep medication use is a significant factor associated with deterioration of physical QOL, but not mental QOL. To our knowledge, few reports in the relevant literature have described evaluation of the association between sleep medication use and physical QOL, especially in a large general population. Zammit et al., however, reported that no differences in SF-36 domains were observed between insomniac subjects receiving treatment for the disorder versus those who were untreated in a general population [12]. Inconsistent with their result, the present study showed that insomniacs using sleep medication have lower physical QOL than those not using sleep medication. More strikingly, good sleepers using sleep medication showed significantly lower PCS scores than insomniacs not using sleep medication, and the scores in this group were almost equal to that of insomniacs using sleep medication. Consequently, sleep medication use was thought to affect physical QOL negatively, irrespective of the improvement of insomnia symptoms. Benzodiazepine/non-benzodiazepine hypnotics are known to be effective for treatment of chronic non-organic insomnia. Nevertheless, many reports have described adverse effects of such medications on physical function, e.g., myorelaxant effects, amnesia, or next-day hangover effects [44–46]. It is possible, therefore, that the adverse effects of sleep medication contribute to deterioration of physical QOL in the subject population. Adverse effects would interfere with physical QOL improvement after the dissolution of insomnia if this were the case.

In contrast, sleep medication use was proven not to be a significant factor for deterioration of mental QOL. This fact might be reflected in the results showing that good sleepers using sleep medication showed a significantly higher MCS value than insomniacs who did not use sleep medication. As described above, several clinical studies have revealed that sleep medication has positive effects not only on sleep parameters, but also on daytime consequences of insomnia [20,47]. Given this fact, our results suggest that dissolution of insomnia symptoms with sleep medication can improve mental QOL, even in the general population.

Regarding the impact of the frequency of sleep medication use on QOL, for the MCS scores, the group using sleep medication 1–2 times a week and that using medication more than three times a week had significantly lower scores than that using no sleep medication use. For the PCS score, all groups with sleep medication had significantly lower scores than the group with no sleep medication use. These findings imply that the frequency of sleep medication use adversely affects both physical QOL and mental QOL. But the rate of incidence of insomniacs in each of the two groups using sleep medication more than once a week was higher than in either the group using sleep medication less than once a week or the group using no sleep medication. Therefore, the lack of a significant association between sleep medication use and the deterioration of mental QOL in our logistic regression analysis results was explainable by the greater negative impact of insomnia on mental QOL than that of frequency of sleep medication use.

This study has several limitations. First, it was impossible to obtain detailed information about medication usage, e.g., the kind and dosage of medication or the duration of usage. Future examination of the information described above related to sleep medication usage would clarify the influence of its adverse effects on QOL. Secondly, the differences in PCS scores among the four groups might reflect other causes which might bias the findings, i.e., individuals with insomnia or medical disease are more likely to have lower PCS scores because of disease processes and are more likely to take sleep medication because they are receiving medical attention. Our results, however, showed that the use of sleep medication use appeared as a significant factor for the deterioration of PCS independent of the existence of insomnia or any currently treated disease. Thirdly, we used six items of the PSQI after excluding items related to sleep medication use (C6). Therefore, different from standard scoring, the cut-off value of insomnia was set at 1 SD of the mean sum score (6.4). Doi et al. developed a Japanese version of PSQI and showed a mean score of each component for both their control and primary insomnia groups [28]. In their report, the mean sum score [SD] of the PSQI (C1 – C5 + C7) in the control group was 3.78 [1.78]; it was 7.86 [2.77] in the group with primary insomnia. The mean sum scores obtained in this study were, respectively, 3.95 [2.40] in the group without insomnia and 8.33 [2.19] in the insomniac group. Therefore, the cut-off value used for this study was considered reasonable. In addition, the results in this rural cohort study might differ from those for urban areas in Japan: they might not be representative of the Japanese general population.

Conclusively, results of this study demonstrate that insomnia is closely associated with deterioration of both mental QOL and physical QOL in this rural cohort. Sleep medication might be associated with improvement of mental QOL. Nevertheless, such medication might adversely affect physical QOL through disadvantageous effects. This finding underscores the importance of appropriate use of sleep medication for patients with insomnia.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.sleep.2009.09.011.

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Insomnia as a Risk for Depression: A Longitudinal Epidemiologic Study on a Japanese Rural Cohort

Isa Okajima, PhD; Yoko Komada, PhD; Takashi Nomura, MD, PhD; Kenji Nakashima, MD, PhD; and Yuichi Inoue, MD, PhD

ABSTRACT

Objectives: To determine (1) whether insomnia is a factor related to the presence or persistence of depression for 2 years in the Japanese population and (2) which component of insomnia is associated with the presence of depression for 2 years in a rural cohort.

Method: This is a community-based longitudinal study. Two thousand eight hundred twenty-five people aged 20 years or older were evaluated at baseline, and of those participants, 1,577 (56%) were reevaluated after 2 years. During both surveys, the participants were asked to describe demographic variables and to fill out self-rating scales of insomnia (Pittsburgh Sleep Quality Index [PSQI]) and depressive symptoms (Center for Epidemiologic Studies Depression Scale).

Results: The results of a multiple logistic regression analysis showed that depression (OR = 6.0; 95% CI, 4.4–8.0) and insomnia (OR = 2.1; 95% CI, 1.5–2.8) at baseline were significantly associated with the presence of depression at the follow-up. Most of the PSQI subscales, except for sleep duration and habitual sleep efficiency, were significantly associated ($P < .01$) with the presence of depression at the follow-up. In addition, the new appearance and repeated existence of depression at the follow-up were related to persistent insomnia (adjusted ORs = 7.0 and 3.3 [$P < .001$], respectively). A result of the receiver operating characteristic curve showed that persons with insomnia whose PSQI scores exceeded 8 points at the baseline were most likely to still have insomnia at the follow-up (cutoff point = 7.5).

Conclusions: On the basis of our results in a Japanese population, insomnia with high severity level could be a risk factor for the presence/persistence of depression in the long-term prognosis.

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Corresponding author: *Yuichi Inoue, MD, PhD, Department of Somnology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan (inoue@somnology.com).*

Insomnia is well-known as a common disorder with an extremely high prevalence,[1–3] and it has been reported that one-fifth of the general population in Japan has symptoms related to insomnia.[4] In addition, insomnia is suspected to be a risk factor for the development of other psychiatric disorders (eg, anxiety disorders, depressive disorders, and substance abuse),[5,6] and particularly, its association with depression has been widely accepted.[7,8]

The results of previous longitudinal epidemiologic studies[5,7,9] have revealed that people who had suffered from persistent insomnia from the baseline to a follow-up survey conducted several years later had a markedly increased risk for developing depression at the follow-up compared to people who had not suffered from insomnia. This finding was consistent in studies of young adults[6,10] and of older adults.[11,12] Therefore, insomnia is considered an important risk factor for the development of depression. However, thus far, no longitudinal study has been performed in Japan regarding this issue. In addition, previous studies have not yet elucidated which of the insomnia symptoms (eg, sleep quality, sleep onset latency, sleep duration, sleep efficiency, and daytime dysfunction) becomes a risk factor for developing depression. Moreover, the relationship between the occurrence and persistence/disappearance of insomnia symptoms in a long-term interval and the development of depression has not been sufficiently confirmed, especially in the Asian population. In addition, if the chronicity of insomnia is actually involved in the development of depressive symptoms, it still remains unclear as to what level of insomnia severity leads to chronic morbidity of insomnia.

In order to clarify these issues, we conducted a longitudinal study on the basis of an anonymous self-rating questionnaire survey over a 2-year interval on a rural population cohort in Japan.

METHOD

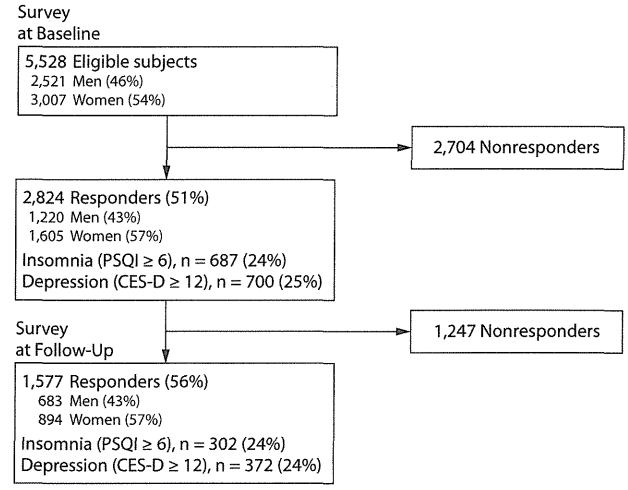
Participants and Procedure

The Ethics Committee of Tottori University, Tottori, Japan, approved this study. Two-point epidemiologic surveys with a 2-year interval were performed on the same adult cohort in the town of Daisen in Tottori Prefecture, Japan. In 2004, the total population of the town was 6,643, and there were 5,528 residents aged 20 years or older (2,521 men, 3,007 women, mean age = 55.2 years). The questionnaire survey was conducted from November 2005 to January 2006 as the first survey (baseline) and from November to December 2007 as the second survey (follow-up). With the cooperation of local public health nurses, questionnaires with individual code numbers were delivered to all residents aged 20 years and older at baseline and at follow-up. All the participants gave their written informed consent to participate in this study at the time of questionnaire delivery. Response to the questionnaire was obtained from 2,825 people anonymously at the baseline survey (responder rate, 51%; 1,220 men, 1,605 women; mean [SD] age = 57.4 [17.7] years). Two years later, a follow-up survey was conducted of the people who had submitted responses for the baseline survey, and 1,577 of them responded to the questionnaire (responder rate, 56%; 683 men, 894 women; mean [SD] age = 58.6 [16.1] years; Figure 1). The respondents of the 2 surveys were matched using code numbers.

Clinical Points

- Patients with chronic insomnia are highly likely to develop and sustain depression.
- Current evidence best supports the position that early intervention for insomnia patients with 7.5 or higher score on the Pittsburgh Sleep Quality Index can be helpful for the prevention, onset, and relapse of depression.

Figure 1. Participants Flowchart



Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, PSQI = Pittsburgh Sleep Quality Index.

Measures

The contents of the questionnaire were as follows:

(1) Demographic variables—The participants were asked about their age, gender, disease currently treated ("What kind of disease you are currently being treated for?"), family constitution ("Do you currently live with your family?"), smoking habits ("Do you currently smoke?"), and alcohol habits ("Do you currently have a drinking habit?").

(2) The Japanese version of the Pittsburgh Sleep Quality Index (PSQI)[13]—We used the scale for estimating sleep disturbance. The PSQI included subitems evaluating sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbance (C5), use of sleeping medication (C6), and daytime dysfunction (C7). The cutoff score of PSQI for insomnia was already determined to be 5.5 points.[13] Therefore, in this study, responders with PSQI scores of 6 or higher were considered to have insomnia.

(3) Twelve-item version of the Center for Epidemiologic Studies Depression Scale (CES-D)[14]—We used the scale for estimating depressive symptoms similar to the report by Kaneita et al.[15] The scale had 4 response options, namely, "never or rarely," "sometimes," "often," and "always," which were coded 0 to 3, respectively. We used the total scores of CES-D as parameters of depression, and the scores were divided into 3 categories: 0 to 11 as normal, 12 to 20 as moderate, and 21 to 36 as severe.[14] On the basis of these criteria, we classified the participants into a nondepression group (CES-D score < 12) and a depression group (CES-D score ≥ 12).

Statistical Analysis

All statistical and receiver operating characteristic (ROC) analyses were performed using SPSS (version 11.5, SPSS Japan, Inc, Tokyo) unless otherwise stated.

Using the above-mentioned standard cutoff score of PSQI and CES-D, we classified the participants on the basis of the presence/absence of insomnia and depression in both surveys. Using this classification, we performed a univariate and multivariate logistic regression analysis with the presence/absence of depression during the follow-up as a dependent variable and the above-mentioned demographic variables (gender, age, disease currently treated, drinking habit, smoking habit, and living alone) and the presence/absence of insomnia and depression as independent variables. In addition, to determine the insomnia symptom component associated with the presence of depression at the follow-up, we conducted univariate and multivariate logistic regression analyses with the presence/absence of depression at the follow-up as a dependent variable and the scores of PSQI subscales as independent variables.

On the basis of the results of the 2 surveys, the participants were divided into 4 insomnia subcategories (ie, i-category 1, the category without insomnia symptoms during both surveys; i-category 2, the category in which participants did not have insomnia symptoms at the baseline but had them at the follow-up; i-category 3, the category in which the participants had insomnia symptoms at the baseline but did not have the symptoms at the follow-up; and i-category 4, the category with insomnia symptoms during both surveys). The participants were also divided into 4 depression subcategories (ie, d-category 1, the category without depressive symptoms at both surveys; d-category 2, the category in which participants did not have depressive symptoms at the baseline but had them at the follow-up; d-category 3, the category in which participants had depressive symptoms at the baseline but did not have them at the follow-up; and d-category 4, the category with depressive symptoms during both surveys). In order to elucidate the association between the changes in the status of insomnia and depression symptoms on the basis of these classifications, we conducted a logistic regression analysis controlling for demographic variables by using the "new appearance of depression at the follow-up" (d-category 1 vs d-category 2) and the "repeated existence of depressive symptoms" (d-category 3 vs d-category 4) as dependent variables and the course patterns of insomnia (i-categories 1, 2, 3, 4) as an independent variable.

Receiver operating characteristic curves[16] were plotted and the mean (95% confidence interval) estimated area under the curve (AUC) for the PSQI score at the baseline was calculated targeting the repeated existence of insomnia at the follow-up. When the slope of the tangent line of the

Table 1. Descriptive Statistics of Demographic Data, the Scores on CES-D and PSQI, and Frequency of Medication Use Among the Participants

	Insomnia Negative at Baseline (n = 879)		Insomnia Positive at Baseline (n = 299)	
Characteristic	Insomnia Negative at Follow-Up (i-category 1, n = 762)[a]	Insomnia Positive at Follow-Up (i-category 2, n = 117)[b]	Insomnia Negative at Follow-Up (i-category 3, n = 128)[c]	Insomnia Positive at Follow-Up (i-category 4, n = 171)[d]
Gender, n				
Male	357	47	52	72
Female	405	70	76	99
Age, mean (SD), y	58.6 (15.8)	60.3 (16.2)	58.1 (15.8)	62.5 (15.9)
Disease currently treated, n (%)				
Baseline	273 (23.2)	41 (3.5)	49 (4.2)	80 (6.8)
Follow-up	295 (25.0)	56 (4.8)	43 (43.7)	94 (8.0)
Drinking habit, n (%)				
Baseline	300 (25.6)	48 (4.1)	50 (4.3)	55 (4.7)
Follow-up	218 (18.6)	41 (3.5)	39 (3.3)	37 (3.1)
Smoking habit, n (%)				
Baseline	143 (12.2)	24 (2.0)	26 (2.2)	31 (2.6)
Follow-up	131 (11.1)	22 (1.9)	25 (2.1)	32 (2.7)
Living alone, n (%)				
Baseline	23 (2.0)	2 (0.2)	4 (0.3)	9 (0.8)
Follow-up	25 (2.2)	4 (0.3)	5 (0.4)	9 (0.8)
CES-D score, mean (SD)				
Baseline	7.1 (4.0)	9.1 (4.4)	10.5 (5.1)	11.9 (5.1)
Follow-up	7.3 (4.0)	11.5 (4.3)	8.9 (3.9)	12.4 (5.1)
PSQI score, mean (SD)				
Baseline	2.7 (1.4)	3.6 (1.3)	7.1 (1.4)	8.4 (2.3)
Follow-up	2.8 (1.4)	7.3 (1.5)	3.6 (1.2)	8.2 (2.3)
Sleeping medication use score, mean (SD)[e]				
Baseline	0.0 (0.1)	0.0 (0.3)	0.4 (1.0)	1.0 (1.3)
Follow-up	0.0 (0.2)	0.7 (1.2)	0.1 (0.4)	1.0 (1.3)

[a]Includes subjects without insomnia symptoms at both surveys.
[b]Includes subjects who did not have insomnia symptoms at the baseline but had symptoms at the follow-up.
[c]Includes subjects who had insomnia symptoms at baseline but did not have symptoms at the follow-up.
[d]Includes subjects with insomnia symptom at both surveys.
[e]Frequency of medication use was rated on C6 on PSQI (0, not during the past month; 1, less than once a week; 2, once or twice a week; 3, 3 or more times a week).
Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, PSQI = Pittsburgh Sleep Quality Index.

ROC curve was statistically equal to 1 (ie, AUC = 0.5), computed by the SPSS software, the ROC curve was regarded as inaccurate for prediction. The best cutoff value for the repeated existence of insomnia was determined on the basis of sensitivity, specificity, and positive likelihood ratio and negative likelihood ratio. In accordance with the authorized method, the cutoff score was assessed as adequate when positive likelihood ratio was 2.0 or higher and negative likelihood ratio was 0.5 or less.[17]

RESULTS

When the demographic data pertaining to the responders who answered only at the baseline (n = 1,247) and those who responded at both the baseline and the follow-up (n = 1,577) were compared, the result showed a significant difference in age ($t_{2394} = -3.56$, $P < .01$; mean [SD] age = 55.9 [19.6] vs 58.6 [16.1] years), but the difference between the 2 groups was only 2.7 years. No gender difference was found. Of the 687 responders who were assessed as having insomnia at baseline, 385 (56.0%) responded at the follow-up. A comparison between the responders who answered only at the baseline and those who responded at both the baseline and the follow-up showed a statistical difference in age ($t_{471} = -2.20$, $P = .02$; mean [SD] age = 56.9 [19.5] vs 60.1 [16.0] years), but the difference between the 2 groups was only 3.2 years. No gender difference was found (men/women, n/n = 113/143 vs n/n = 154/231; $\chi^2_1 = 1.09$; $P = .3$). The comparison of the percentages of participants with insomnia or depression at each survey showed that the percentages were almost similar in both surveys ([insomnia] baseline, 24.0%; follow-up, 24.3%; [depression] baseline, 24.9%; follow-up, 24.4%). The participants who belonged to i-category 1 accounted for 64.2%; i-category 2, 9.9%; i-category 3, 10.9%; and i-category 4, 14.5%. Table 1 shows the demographic data of each survey, the CES-D scores, PSQI total scores, and frequency of the use of sleep medication manifested as C6 score of the PSQI scale. The number of participants taking sleep medication 3 days a week or more (C6 score = 3) was 82 (5.6%) at baseline and 105 (7.0%) at follow-up. A total of 161 participants (10.6%) answered that they had received treatment for insomnia in the period between the 2 surveys.

Association Between the Baseline Data and the Presence/Absence of Depression at the Follow-Up

To examine the risk factors on the presence of depression at the follow-up, we conducted univariate and multivariate logistic regression analyses. The results of both analyses revealed that CES-D score ≥ 12 and PSQI score ≥ 6 at the

Table 2. Logistic Regression Analysis on the Associated Factors for the Existence of Depression (CES-D score ≥ 12) at the Follow-Up Among the Descriptive Variables[a]

Baseline	Total Sample, N	Positive for Depression at the Follow-Up, n (%)	Univariate Relative Risk (95% CI)[b]	*P*	Multivariate Relative Risk (95% CI)	*P*
Gender						
Male	664	148 (22.3)				
Female	871	224 (25.7)		NS		NS
Age[c]						
<60	666	169 (25.4)				
≥60	868	203 (23.4)		NS		NS
Disease currently treated						
No	933	218 (23.4)				
Yes	602	154 (25.6)		NS		NS
Drinking habit						
No	955	225 (23.6)				
Yes	563	243 (43.2)		NS		NS
Smoking habit						
No	1,247	288 (23.1)				
Yes	272	79 (29.0)	1.4 (1.0–1.8)	.04		NS
Living alone						
No	1,493	348 (24.0)				
Yes	66	22 (34.4)		NS		NS
CES-D score						
<12	1,131	168 (14.9)				
≥12	320	180 (56.3)	7.4 (5.6–9.7)	<.001	6.0 (4.4–8.0)	<.001
PSQI score						
<6	1,052	188 (17.9)				
≥6	376	160 (42.6)	3.4 (2.6–4.4)	<.001	2.1 (1.5–2.8)	<.001

[a]The analyses within this table were conducted on the subset with complete data for each variable.
[b]Relative risks approximated with odds ratios.
[c]The age category was divided at the median age (=60 years old).
Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, NS = nonsignificant, PSQI = Pittsburgh Sleep Quality Index.

Table 3. Logistic Regression Analysis on the Associated Factor for the Existence of Depression (CES-D score ≥ 12) at the Follow-Up Among PSQI Variables

PSQI Subitem	Univariate Relative Risk (95% CI)[a]	*P*	Multivariate Relative Risk (95% CI)	*P*
C1: sleep quality	2.6 (2.1–3.2)	<.01	1.6 (1.3–2.1)	<.01
C2: sleep latency	1.7 (1.5–2.0)	<.01	1.2 (1.0–1.5)	<.01
C3: sleep duration	1.1 (1.0–1.3)	NS	1.1 (0.9–1.3)	NS
C4: habitual sleep efficiency	1.5 (1.3–1.8)	<.01	1.1 (0.9–1.3)	NS
C5: sleep disturbance	2.5 (2.0–3.1)	<.01	1.3 (1.0–1.7)	<.01
C6: use of sleeping medication	1.5 (1.3–1.8)	<.01	1.2 (1.0–1.4)	<.01
C7: daytime dysfunction	2.3 (1.9–2.8)	<.01	1.8 (1.4–2.2)	<.01

[a]Relative risks approximated with odds ratios.
Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale, NS = nonsignificant, PSQI = Pittsburgh Sleep Quality Index.

baseline were factors significantly associated with the presence of depression at the follow-up ([CES-D] univariate OR = 7.4; 95% CI, 5.6–9.7; multivariate OR = 6.0; 95% CI, 4.4–8.0; [PSQI] univariate OR = 3.4; 95% CI, 2.6–4.4; multivariate OR = 2.1; 95% CI, 1.5–2.8; respectively [Table 2]). The same result was obtained from the multivariate logistic regression analysis when the item for insomnia was excluded from the total CES-D score and item C7, which may assess depressive thought, was excluded from the total PSQI ([CES-D] OR = 4.5; 95% CI, 3.3–6.2; [PSQI] OR = 1.6; 95% CI, 1.1–2.2).

Since it was revealed that the existence of insomnia at baseline was associated with the presence of depressive symptoms at follow-up, we conducted univariate and multivariate logistic regression analyses to examine which of the insomnia symptom components were associated with depression at the follow-up. The results showed that poor quality of sleep (C1, OR = 1.6), sleep latency (C2, OR = 1.2), sleep disturbance (C5, OR = 1.3), use of sleeping medication (C6, OR = 1.2), and daytime dysfunction (C7, OR = 1.8) at the baseline were factors significantly related to the presence of depression at the follow-up (Table 3). However, sleep duration (C3) and habitual sleep efficiency (C4) did not appear to be significantly associated factors.

Examining the Association Between Symptoms of Insomnia and Depression Through the 2 Surveys

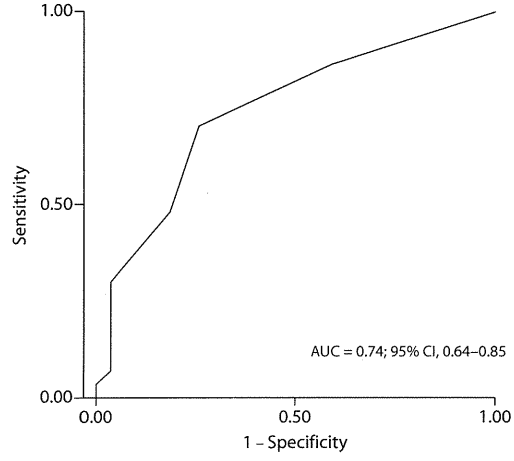
The results of the logistic regression analysis showed that i-category 2 (OR = 10.0) and i-category 4 (OR = 7.0) were significantly associated factors for the new appearance of depression at the follow-up in comparison to i-category 1. In addition, it was revealed that i-category 4 (OR = 3.3) was

Table 4. Associated Risk for the New Appearance of Depression at Follow-Up or the Repeated Existence of the Symptom at 2 Surveys in Relation to the Variations of Insomnia Course Pattern Categories[a]

Variable	i-Category 1 (n = 762)	i-Category 2 (n = 117)	i-Category 3 (n = 128)	i-Category 4 (n = 171)
New appearance of depressive symptom at follow-up, n (%)	48 (6.3)	39 (33.3)	10 (7.8)	29 (17.0)
Unadjusted odds ratio (95% CI)	...	10.1 (6.0–16.8)*	1.8 (0.9–3.7)	6.3 (3.6–10.9)*
Adjusted odds ratio (95% CI)[b]	...	10.0 (5.9–16.7)*	1.8 (0.9–3.7)	7.0 (3.9–12.2)*
Repeated existence of depressive symptom, n (%)	40 (5.3)	16 (13.7)	16 (12.5)	54 (31.6)
Unadjusted odds ratio (95% CI)	...	2.3 (1.0–5.9)	0.7 (0.4–1.6)	2.8 (1.5–5.4)*
Adjusted odds ratio (95% CI)[b]	...	2.5 (0.9–6.8)	0.7 (0.3–1.6)	3.3 (1.6–6.6)*

[a]i-Category 1: the category of subjects without insomnia symptoms at both surveys; i-category 2: the category in which subjects did not have insomnia symptoms at the baseline but had symptoms at the follow-up; i-category 3: the category in which subjects had insomnia symptoms at baseline but did not have symptoms at the follow-up; i-category 4: the category of subjects with insomnia symptoms at both surveys.
[b]Odds ratio adjusted for the factors including gender, age, disease currently treated, habitual alcohol ingestion, smoking habit, and living alone, with i-category 1 as the reference.
*$P < .001$.

Figure 2. Cutoff Point of the Pittsburgh Sleep Quality Index for the Repeated Existence of Insomnia Estimated With Receiver Operating Characteristic Curve



Cutoff Point	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio
5.0	1.00	0.00	1.00	...
6.5	0.86	0.41	1.45	0.34
7.5	0.70	0.74	2.70	0.40
8.5	0.48	0.81	2.61	0.63

Abbreviation: AUC = area under the curve.

a factor significantly associated with the repeated existence of depression (Table 4).

The PSQI Cutoff Score for Predicting the Existence of Depression at the Follow-Up

The results described above revealed that the repeated existence of insomnia (i-category 4) has an influence on both the new appearance of depression and the repeated existence of depression at the follow-up. Therefore, we used the ROC curve to examine the cutoff value of the PSQI scores at the baseline for participants who repeatedly had insomnia at the follow-up. As a result, AUC of the ROC curve was 0.74 (95% CI, 0.64–0.85), and it was statistically larger than 0.50. The cutoff value of the PSQI at baseline was estimated at 7.5 points. This cutoff value's sensitivity was 70%, specificity was 74%, positive likelihood ratio was 2.70, and negative likelihood ratio was 0.40 (Figure 2).

DISCUSSION

We conducted a longitudinal study over a 2-year interval on a rural population cohort in Japan to examine whether persistent insomnia was a risk factor for the existence of depression at the follow-up using a multivariate logistic regression analysis. The results revealed that the risk of depression at the follow-up was high, with an OR of 2.1 for people with insomnia at the baseline. This finding is compatible with the reports in Western countries.[5,7] In addition, OR values between 2 and 4 reported in previous cohort studies for the later existence of depression relating to the presence of insomnia at the baseline[7,12,18] were equivalent to the results of this study (OR = 2.1).

This is the first study examining the relationship between each insomnia symptom component at the baseline and the presence of depression at the follow-up from a prognostic viewpoint. As a result, poor quality of sleep (C1), sleep latency (C2), sleep disturbance (C5), use of sleeping medication (C6), and daytime dysfunction (C7) were significantly associated with the presence of depression at follow-up. Few studies have examined the symptom components of insomnia associated with depression. In the report by Chang et al,[19] people's poor quality of sleep and less than 7 hours of sleep during their university days were associated with the occurrence of depression in the later years. Because their study showed the association between insomnia and depression occurring 30 or more years later, a simple comparison with our study results is not possible, although the findings of our study and those of Chang's study[19] are congruent with respect to the fact that poor quality of sleep was involved in the risk factors of later occurrence of depression. Early morning awakening has been believed to be a pathognomonic symptom of depression.[20] Recently, however, cross-sectional surveys[15,21] have shown that difficulty in initiating sleep is a factor associated with the presence of depressive symptoms. In particular, a study by Kaneita et al[15] conducted on a community sample of persons aged 20 years or older in a cross-sectional survey revealed that, among the symptoms of insomnia, difficulty in initiating sleep had the highest odds of association with depression (difficulty initiating sleep,

OR = 1.56; difficulty maintaining sleep, OR = 1.49; early morning awakening, OR = 1.34). Interestingly, our result showed that difficulty in initiating sleep at the baseline was indicated as a possible long-term risk factor for the presence (development or persistence) of depression. In other words, from the prophylactic viewpoint, clinicians treating patients who complain of difficulty in initiating sleep should consider the possibility of future development of depression.

The results of the relationship between the successive changes in the status of both insomnia and depression have shown that the new appearance and the repeated existence of insomnia are significantly associated with the new appearance of depression during the follow-up, and that the repeated existence of insomnia is significantly associated with the repeated existence of depression in both surveys. Previous studies have shown that the existence of insomnia that persisted for 2 weeks or more sometime during the survey period was significantly predictive of developing a major depressive episode.[10] In addition, it has been reported that, in people who were affected with persistent insomnia for 1 year, the risk of developing depression 1 year later was high, with an OR in a subsequent survey of about 40.[9] The results of this study showed that for people whose insomnia lasted for 2 years, the ORs of a new appearance of depression at the follow-up and of the repeated existence of depression were 7 and 3, respectively. These findings indicate that persistent insomnia is strongly related to the development and prolongation of depression, although there was a difference in the odds ratio between the studies, possibly because of a difference in terms of target populations and survey methods. Therefore, from the perspective of the prevention of depression, it would be clearly important to prevent chronicity and development of insomnia.

It is noteworthy that the results of the ROC curve revealed that, in the 2-year prognosis, insomnia was highly likely to appear repeatedly in people whose PSQI score exceeded 8 points at the baseline. The PSQI cutoff score for the chronicity of insomnia in the participants examined in this study (7.5 points) was unexpectedly lower than the general average PSQI score of patients with chronic insomnia examined in a clinical setting (range of mean scores: 10–12 points).[22,23] However, undoubtedly, the patients in clinical settings who seek treatment for insomnia experience a higher severity of the symptom than the general population. In addition, while the majority of patients with chronic insomnia in a clinical setting use sleep medication,[24] the frequency of the use of sleep medication by the participants examined in this study was extremely low (baseline C6 mean score, 0.23; the number of participants who used medication for 3 days a week or more, 89 [5.6%]; follow-up C6 mean score, 0.27; the number of participants who used medication for 3 days a week or more, 105 [7.0%]), and this might have played a role in the low score of PSQI in the participants with insomnia in our study. Thus, in order to prevent the subsequent development of depression, intensive treatment would presumably be necessary for the cases with PSQI scores of 8 or above if they do not take any sleep medication.

Limitations

First, we used the cutoff value of an established questionnaire-based rating scale to define insomnia and depression in this study. To obtain an accurate diagnosis, it might be necessary to diagnose through structured interviews. The findings of our study, which showed that insomnia at the baseline is a factor related to the long-term development of depression, are relatively consistent with previous studies in which participants were diagnosed using a structured interview.[7,10] Therefore, the results of this study regarding this issue are unlikely to deviate much from the actual conditions.

Second, the 12-item version of CES-D we used includes an item inquiring the severity of insomnia, and item C7 of PSQI may assess depressive thought (the problem of keeping up enough enthusiasm to get things done). However, we confirmed that the same results were obtained after excluding these items from the CES-D and the PSQI.

Third, we classified the successive changes in the status of insomnia and depression into 4 categories on the basis of survey scores obtained at 2 points in time, but because the 2 surveys were separated by a long interval of 2 years, the changes in insomnia and depressive symptoms may not have been assessed accurately. Therefore, it is unclear whether insomnia actually precedes or follows the occurrence of depression in the participants. In other words, our categorization does not apply to the cases wherein symptom levels have changed several times during the survey period, and this point cannot be elucidated through this study. To clarify this issue, future studies should use more frequent assessments with monthly or longer reference periods to obtain more reliable data about insomnia, as indicated by Morin et al.[25]

Finally, the response rate was approximately 50% at both survey points in this study. However, a sampling bias was considered to be relatively small, because a significant but small difference was observed only in age when demographic variables of the responders who answered only at the baseline and of those who responded to both the surveys were compared.

CONCLUSION

Our results revealed that insomnia is a risk factor for the development and persistence of depression in Japan, and insomnia symptoms, especially poor quality of sleep, difficulty in initiating sleep, and daytime dysfunction, are factors significantly related to depression. In addition, the results suggested that persistent insomnia is likely to increase the risk of new appearance or repeated existence of depression in the long-term prognosis. In particular, insomnia is highly likely to become chronic in people with untreated insomnia with PSQI scores of 8 or higher, and this outcome may lead to the risk of development and persistence of depression. These results emphasize that insomnia needs to be treated cautiously to prevent the occurrence of depression.

Author affiliations: Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo (Drs Okajima and Inoue); Department of Somnology, Tokyo Medical University (Drs Okajima, Komada, and Inoue); and Department of Neurology, Institute of the Neurological Sciences, Tottori University Faculty of Medicine, Tottori (Drs Nomura and Nakashima), Japan.
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