Sleep Patterns and Total Mortality: A 12-Year Follow-up Study in Japan

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A population-based cohort study was conducted to assess the relationship between total mortality and self-reported sleep patterns as regards not only to sleep duration but also subjective sleep quality. A total of 5,322 inhabitants in Gifu Prefecture, Japan, completed a self-administered questionnaire on health status and lifestyles including habitual sleep patterns, and were followed-up for an average of 11.9 years. Relative risks were computed by using Cox proportional hazards models. Both longer and shorter sleep, compared to 7-8 hour-sleep, was related to significantly increased risk of total mortality in males (relative risk [RR] for ≥10 hours = 1.94, and RR for <7 hour = 1.90), but not in females. Females complaining of poor awakening state experienced a higher mortality risk compared to those who woke up normally (RR: 1.97). Males who usually fell asleep easily showed a marginally lower mortality risk compared to those who fell asleep normally (RR: 0.70). Female users of sleeping pills were at an elevated risk (RR: 1.89). These findings were almost unchanged after adjustment for sleep duration and other confounders. Poor self-reported quality of sleep seemed to be associated with an increased risk of mortality independently of sleep duration. *J Epidemiol*, 2000 ; 10 : 87-93

mortality, cohort study, sleep duration, quality of sleep

INTRODUCTION

Sleep is an essential activity of life, a reviving period of rest. Scientific analyses have confirmed the relationship between sleep and protein synthesis, growth and tissue restoration [1]. Sleep has also been related to the endocrine [2] and immune system [3]. Previous reports [4-7] have found that long and short sleep duration increased total mortality risk.

The relationship between sleep quality and mortality, however, has not been studied appropriately. Several studies [6-9] have examined the associations of sleep patterns including subjective sleep quality with mortality, but the findings are inconsistent. This is partly because there is no clear definition nor an established measure of quality of sleep. In this study, we analyzed the associations of mortality, with particular interest in the effect of sleep quality, in a general population cohort. We examined habitual patterns of falling asleep and awakening using a self-administered questionnaire to measure sleep quality.

MATERIALS AND METHODS

Subjects of this study were inhabitants aged 20 to 67 years in Shirakawa town, a rural area of Gifu prefecture, central Japan. At Shirakawa Municipal Health Center, the inhabitants underwent health check-ups supported by the town authority. They included urine analysis, blood cell counts, blood chemistry, measurement of blood pressure, electrocardiogram, and others. We enrolled residents who underwent the health examinations from 1982 to 1986, and followed them up by December 31,

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1996. Those who moved away from the town were treated as censored cases at the date of their move. When subjects underwent multiple health check-ups, the data from the first check-up were adopted for the present study. Vital status of the subjects was confirmed by resident registration records in the municipality. Causes of death were identified by death certificates in cooperation with Shirakawa Municipal Health Center. At the occasion of the health check-up, each participant was requested to complete a self-administered questionnaire that inquired about health status. To assess sleep patterns, the following questions were asked in the questionnaire.

Q(a): What time do you usually go to bed at night?

Q(b): What time do you usually wake up in the morning?

Q(c): Do you usually wake up feeling good in the morning (Four prepared answers: [1] good, [2] normal, [3] bad, and [4] awaking too early.)

Q(d): Do you usually fall asleep easily at night? (Four prepared answers: [1] easily, [2] normally, [3] with difficulty, and [4] wake up several times.)

Q(e) Do you use drugs for sleep? (Three prepared answers: [1] never, [2] sometimes, and [3] always)

Sleep duration was calculated from the answers to Q(a) and Q(b). Subjective sleep quality was evaluated according to Q(c) and Q(d). Subjects were also grouped by use of sleeping pills, the answer to Q(e). Answers [2] and [3] in Q(e) were combined because only small proportion of the subjects were pill users.

STATISTICAL ANALYSIS

The difference in mean sleep duration between males and females was tested by an unpaired t-test. To assess the association between sleep duration and age, Spearman rank correlation coefficients were computed. The gender difference in use of sleeping pills was examined by using Mantel extension test with adjustment for age category [10]. Chi-square tests with one degree of freedom were carried out to examine the trends of the associations between the subjective sleep quality and age and sleep duration [11]. The trends for answer [1] to [3] were examined separately from answer [4] in Q(c) and Q(d), because answer [4] is categorically different from the others and not ordinal.

Associations of sleep duration and subjective sleep quality with total mortality risk were examined by using Cox proportional hazards models with the procedure PHREG in SAS (Statistical Analysis System) [12]. We computed relative risks adjusted for age at baseline alone, and also those adjusted for age, present and past medical history of hypertension, cerebrovascular, heart and renal diseases, and diabetes, smoking and drinking habits, sleep duration, and use of sleeping pills. Smoking and drinking habits were taken into account only in males, because there were very few smokers or drinkers among females.

RESULTS

A total of 5,322 residents (males: N=2,438, females: N=2,884) were registered as subjects, which corresponded to 68.9% of the total population (63.2% of males and 74.5% of females) aged from 20 to 67 in Shirakawa town, 1985. The age distribution of subjects at baseline was similar between males and females, as shown in Table 1. Mean age ± standard deviation (SD) at baseline was 46.9 ± 11.9 for males and 47.7 ± 11.2 for females. A total of 292 subjects (5.5% of enrolled persons), 135 men (5.5%) and 157 women (5.4%), moved away, and 258 deaths (4.8%), 149 men (6.1%) and 109 women (3.8%), were observed during the study period. The total observed person-years were 63,239, and the mean follow-up period was 11.9 years. Cancer accounted for about half of the total deaths in both sexes (47.0% in males and 47.7% in females).

Reported hours of sleep

Because of inconsistent answers (waking up at a time prior to the reported bed time), extreme values (less than 3 or 18 or more hours of sleep per day), or missing data, 24 subjects were excluded from the analysis for total sleep duration. Means ± SD of sleep duration were 7.7 ± 1.0 hours in males and 7.2 ± 1.0 hours in females (males vs. females: $p<0.001$). Age showed a strong correlation with sleep duration in both males and females; the elderly tended to report longer sleep hour (Spearman rank correlation coefficients $r=0.24$, $p<0.001$ in males, and $r=0.30$, $p<0.001$ in females).

Subjective sleep quality

Associations of age and sleep duration with subjective sleep quality are shown in Table 2. In males, shorter sleep tended to be associated with ease of falling asleep (trend $p=0.08$), while no significant association was observed between age and ease of falling asleep. A significant trend was observed between awakening state and age (trend $p<0.001$); the elderly tended to awake feeling good, but no significant association between awakening state and sleep duration was found. Both of the proportions of males who answered "awaking too early" and "waking up several times" increased with age (trend $p<0.001$

Table 1. Age distribution (at baseline) of the study population by sex.

	Males		Females	
Age	N	%	N	%
20-29	95	3.9	56	1.9
30-39	588	24.1	617	21.4
40-49	461	18.9	630	21.8
50-59	749	30.7	924	32.0
60-69	545	22.4	657	22.8
Total	2438	100.0	2884	100.0

Table 2. Associations of subjective sleep quality with age and sleep duration by sex.

Sex	Subjective sleep quality		Age					Sleep duration (hours/night)				
			20-39	40-49	50-59	60-69	Total	≤6	7	8	9≥	Total
			%	%	%	%	%	%	%	%	%	%
Males	Do you usually wake up feeling good ?	Good	24.6	33.8	41.4	43.2	35.6	40.2	35.9	33.6	38.6	35.6
		Normal	49.3	48.2	45.0	42.7	46.3	36.9	44.4	49.5	46.1	46.2
		Bad	23.6	12.2	7.4	6.3	12.6	11.2	13.6	13.2	9.6	12.6
		Awaking too early	2.5	5.9	6.3	7.9	5.5	11.7	6.1	3.8	5.8	5.5
	Do you usually fall asleep easily?	Easily	40.8	42.0	41.4	41.7	41.4	52.8	40.8	40.2	39.8	41.5
		Normally	45.0	45.2	43.0	43.0	44.0	31.3	44.4	45.7	45.4	43.9
		With difficulty	12.3	10.2	12.1	10.9	11.5	11.2	11.6	11.6	10.8	11.5
		Waking up several times	1.9	2.6	3.6	4.4	3.1	4.7	3.2	2.5	4.1	3.1
	Do you use drugs for sleep?	Never	99.4	98.2	97.5	95.9	97.8	97.2	98.5	98.2	95.9	97.9
		Sometimes or always	0.6	1.8	2.5	4.1	2.2	2.8	1.5	1.8	4.1	2.1
	N		683	461	749	545	2438	214	811	1052	346	2423
Females	Do you usually wake up feeling good ?	Good	18.0	24.2	28.8	36.0	26.9	26.6	25.3	28.1	35.0	27.0
		Normal	55.5	54.5	54.2	45.7	52.6	51.6	55.5	51.3	41.5	52.6
		Bad	25.2	15.9	9.7	4.7	13.5	16.0	13.2	12.1	13.0	13.5
		Awaking too early	1.3	5.4	7.4	13.6	6.9	5.8	6.0	8.6	10.5	6.9
	Do you usually fall asleep easily?	Easily	46.1	50.5	33.0	25.9	38.3	46.5	39.7	32.9	25.4	38.4
		Normally	44.5	41.4	47.1	48.2	45.5	42.7	45.9	47.2	44.3	45.4
		With difficulty	5.5	5.6	14.1	15.6	10.6	7.9	9.6	12.0	19.4	10.6
		Waking up several times	3.9	2.5	5.7	10.4	5.7	2.9	4.9	7.9	11.0	5.7
	Do you use drugs for sleep?	Never	99.3	98.4	96.5	92.2	96.6	98.4	97.4	95.6	88.9	96.6
		Sometimes or always	0.8	1.6	3.5	7.8	3.4	1.6	2.6	4.4	11.1	3.4
	N		673	630	924	657	2884	620	1306	748	201	2875

and p<0.01, respectively). Sleep duration was negatively related to complaints of "awaking too early" (trend p<0.01), but a consistent trend was not observed with those of "waking up several times". In females, both age and sleep duration showed significant associations with awakening state (age: trend p<0.001, sleep duration: trend p<0.01) and with difficulty of falling asleep (age: trend p<0.001, sleep duration: trend p<0.01). Older females tended to have better feeling at awakening, but have more difficulty to fall asleep than younger female subjects. Longer sleep was positively associated with good feeling at awakening, but negatively with ease of falling asleep. Both of the complaints of "awaking too early" and "waking up several times" increased with increasing age (trend p<0.001, for both) and sleep duration (trend p<0.01 and p<0.001, respectively).

Use of sleeping pills

More females used sleeping pills than males (Table 2, females 3.4% vs. males 2.2%, p<0.05). Pill takers were more frequent with increasing ages in both males and females (trend p<0.001), and with longer duration of sleep in females (trend p<0.001).

Sleep patterns and total mortality

Table 3 presents the results of the multivariate analysis for sleep duration and total mortality. In males, both longer and shorter duration of sleep, compared with the duration of 7-8 hours, was associated with an increased risk of total mortality. Such an increased mortality risk remained after controlling for present and past medical history, use of sleeping pills, smoking and drinking habits. In females, there was no material association between sleep duration and total mortality.

Associations of subjective sleep quality with total mortality are summarized in Table 4. In males, those who reported to fall asleep "easily" showed a slightly lower risk compared with those who reported to fall asleep "normally". This relation was almost unchanged after adjustment for sleep duration and other potential confounders, such as major present and past medical history, use of sleeping pills, smoking and drinking habits. No increased mortality was seen among men who had complained of troubles in either awakening nor falling asleep. In females, those who complained of poor awakening state showed an increased risk compared to those who reported normal awakening, and this increase remained significant after controlling for the potential confounding factors. Ease of falling asleep was not measurably associated with total mortality risk. Sleeping pill users tended to have increased risk of mortality, and the increased mortality risk was marginally significant in females.

Table 3. Associations between sleep duration and total mortality: relative risks derived from Cox proportional hazards models by sex.

Sex	Sleep duration (hours/night)	Subjects: Observed person-years	Subjects: Number of deaths	Adjusted1[b)] Relative risk (95% CI)	Adjusted2[c)] Relative risk (95% CI)
Males	-6.9	2375.4	15	1.90 (1.10-3.29) *[a)]	1.93 (1.12-3.35) *
	7.0-8.9	22115.6	95	1.00	1.00
	9.0-9.9	3551.0	27	1.13 (0.73-1.74)	1.15 (0.74-1.77)
	10.0-	603.0	10	1.94 (1.01-3.76) *	1.77 (0.88-3.54)
Females	-6.9	7369.4	15	0.92 (0.53-1.62)	0.90 (0.50-1.61)
	7.0-8.9	24518.5	80	1.00	1.00
	9.0-9.9	2050.6	13	1.10 (0.61-2.00)	1.07 (0.58-1.95)
	10.0-	378.4	1	0.42 (0.06-3.02)	0.40 (0.06-2.92)

a) *: $p<0.05$.
b) Adjusted1: relative risk with adjustment for baseline age.
c) Adjusted2: relative risk with adjustment for baseline age, present and past history of hypertension, cerebrovascular, heart and renal diseases and diabetes, and use of sleeping pills (smoking and drinking habits only in males).

Table 4. Associations between subjective sleep quality and total mortality: relative risks derived from Cox proportional hazards models by sex.

Sex	Subjective sleep quality		Subjects: Observed person-years	Subjects: Number of deaths	Adjusted1[b)] Relative risk (95% CI)	Adjusted2[c)] Relative risk (95% CI)
Males	Do you usually wake up feeling good ?	Good	10435.6	60	0.94 (0.66-1.34)	1.01 (0.70-1.45)
		Normal	13245.7	64	1.00	1.00
		Bad	3578.4	12	1.12 (0.60-2.07)	1.13 (0.60-2.12)
		Awaking too early	1488.7	12	1.24 (0.67-2.30)	1.10 (0.58-2.07)
	Do you usually fall asleep easily?	Easily	12110.1	51	0.70 (0.49-1.01) #[a)]	0.72 (0.50-1.04) #
		Normally	12459.8	71	1.00	1.00
		With difficulty	3337.3	20	1.04 (0.64-1.71)	0.95 (0.57-1.59)
		Waking up several times	852.6	6	0.94 (0.41-2.17)	0.88 (0.38-2.06)
	Do you use drugs for sleep?	Never	27691.2	139	1.00	1.00
		Sometimes or always	588.6	8	1.70 (0.83-3.48)	1.28 (0.60-2.77)
Females	Do you usually wake up feeling good ?	Good	9162.1	36	1.17 (0.75-1.80)	1.21 (0.77-1.88)
		Normal	18242.8	48	1.00	1.00
		Bad	4525.4	14	1.97 (1.08-3.61) *	2.03 (1.10-3.74) *
		Awaking too early	2422.9	11	1.05 (0.54-2.03)	0.93 (0.46-1.86)
	Do you usually fall asleep easily?	Easily	13173.3	39	1.28 (0.84-1.97)	1.37 (0.89-2.11)
		Normally	15653.5	47	1.00	1.00
		With difficulty	3588.6	16	1.17 (0.66-2.07)	0.96 (0.52-1.78)
		Waking up several times	1976.0	7	0.87 (0.39-1.94)	0.81 (0.36-1.80)
	Do you use drugs for sleep?	Never	32759.4	95	1.00	1.00
		Sometimes or always	1099.4	10	1.89 (0.98-3.64) #	1.81 (0.92-3.56) #

a) #: $p<0.10$, *: $p<0.05$.
b) Adjusted1: relative risk with adjustment for baseline age.
c) Adjusted2: relative risk with adjustment for baseline age, present and past history of hypertension, cerebrovascular, heart and renal diseases and diabetes, sleep duration, and use of sleeping pills (smoking and drinking habits only in males).

DISCUSSION

We observed strong associations between age and sleep patterns in both sexes, in concordance with previous studies [6, 13-19]. However, a significant association between subjective awakening state and reported sleep duration was observed only in females in our study. These results may support the findings by Hoch et al. [20] who explored the association of self-reported sleep patterns with laboratory records among healthy elderly subjects without insomnia. They demonstrated higher and more stable associations between subjective and objective measures in females than in males.

Previous studies [4-7], though not all [8], reported that both long and short sleep duration increased mortality risk. Our findings that men sleeping 10 hours or more and less than 7 hours per day each had higher mortality than those sleeping 7-8 hours corroborate previous findings. However, we cannot explain why only male subjects showed a significant association of sleep duration with mortality risk. The relative risks reported by former studies [4-7] for long or short sleep duration have generally been lower in females than in males; possibly implying that the relationships of sleep duration with mortality may be much stronger in males.

Several explanations for the associations between sleep duration and mortality have been postulated. Prolonged sleep deprivation was confirmed to cause severe pathological changes and deaths by an experimental study with rats [21, 22]. Short sleep may reflect overwork and difficulty in having enough rest. Failure to restore physical and mental fatigue would invite somatic disorders and early deaths. Extended sleep is also suggested to be a debilitating and fatiguing process [23]. Oversleeping may disturb normal circadian rhythm and induce some health abnormalities. However, there are not enough biological explanations for the associations between long sleep and mortality. Long sleep may not necessarily mean sufficient sleep, and it may simply reflect sleep of poor quality. Further investigations would be required to resolve its mechanism.

In the present study, poor awakening state in females and ease of falling asleep in males were associated with risks of mortality independently of sleep duration. These results indicated that both quantity and quality of sleep is important for health. Several studies [6-9] addressed the association between sleep quality and mortality, but the findings are inconsistent. One possible reason of the disagreement is that these studies only have used single conception of sleep quality or insomnia, and have not discriminated types of sleep disorders. Quality of sleep is supposed to be more complex, requiring detailed classification of sleeping troubles to clarify its characteristics [24, 25]. However, Foley et al. [26] analyzed the association between mortality and sleep complaints with distinction of five major sleep problems including trouble falling asleep, awaking during night, awaking not rested, awaking too early and needing to nap. Against our findings, troubles of falling asleep and awakening were not related with mortality risk, but only "needing to nap" showed a slight elevation of the risk. While Foley et al. dichotomized each sleep complaint in terms of the frequency of complaint (never or rarely vs. sometimes or most of the time), we divided subjects according to awakening state and ease of falling asleep. It should be notified that we have found non-linear associations of total mortality with awakening state: good / normal / bad, and ease of falling asleep: easily / normally / with difficulty.

Our findings regarding sleeping pill use showed similar trends to the literature [6, 13, 27, 28]; females and the elderly were more likely to use sleeping pills than males or the young, and a positive association between use of sleeping pills and mortality risk in females was observed. Lower prevalence of pill users, particularly in males, compared to other studies [6, 8] may be a possible explanation for the lack of a clear positive association with pills in males in our study.

Our research has several limitations. First, various physical disorders such as heart diseases [1, 29], cerebrovascular diseases [30, 31], chronic obstructive pulmonary diseases [32], arthritis [33, 34], and urinary incontinence [35] are known to affect sleep conditions. In our study, 11.3% of the total subjects had one or more physical diseases such as hypertension, cerebrovascular disease, heart disease, renal disease and diabetes at the baseline, and 17.3% of the subjects had some of such disorders in the past. We adjusted for the major present and past medical history in the multivariate analysis and obtained the similar results. However, it still remains possible that other physical disorders at baseline might influence both sleep patterns and mortality. To test this possibility, we repeated the analyses excluding those who died within 2 years after the baseline examination. The results were almost the same as presented above (data not shown). Furthermore, the main findings were not substantially altered even when those with the present and past medical history were excluded (data not shown).

The second limitation is that sleep patterns are known to be associated with psychological factors [13, 25, 26, 28, 36], which are suggested to be related to mortality [26, 37]. Furthermore, psychological factors have been speculated to influence the accuracy of self-reported sleep conditions [38]. Therefore, mental health factors, which we did not deal with in this study, should be considered in further surveys. Finally, we did not analyze cause-specific mortality in this study because the number of deaths separated by cause was too small to analyze. Further investigations may reveal differences in the associations between sleep patterns and mortality across different causes of death.

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