Title: Daily sleep duration and the risk of incident disability among younger-elderly Japanese in the New Integrated Suburban Seniority Investigation (NISSIN) Project: a prospective study using competing event analysis

Short running title: Sleep duration and incident disability

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LZ contributed to the conception, analysis and interpretation of data, and preparation of manuscript. SU contributed to the analysis and interpretation of data, preparation of manuscript, critical review and feedback. ZW and SO contributed to the critical review and feedback. MA, KW, and TK contributed to the design, acquisition of data, critical review and feedback. AT contributed to the design, acquisition of data, interpretation of data, critical review and feedback.

Abstract

Aim: This study aimed to investigate the association between daily sleep duration and incident disability among younger-elderly individuals in Japan.

Methods: We conducted a prospective cohort study, the New Integrated Suburban Seniority Investigation Project, including 1,895 (962 men and 933 women) Japanese physically and socially independent individuals aged ≥65 years. Information on daily sleep duration, demographic, lifestyle characteristics, and medical status were collected by questionnaire and health check-up in every year from 1996 through 2005. Dates of incident disability were confirmed using the certification for the Long-term care insurance in Japan. We treated censored cases due to death as competing events. Competing risk model was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) for incident disability.

Results: During a median of 12.7 years of follow-up, 256 participants (114 men and 142 women) incident disability. Compared with a sleep duration of 7-7.9 hours/day, sleeping < 6hours/day was increased risk of incident disability (HR 1.64; 95%CI, 1.13-2.38 for total; HR 1.90; 95%CI, 1.19-3.03 for women).

Conclusions: The present findings suggest that shorter sleep duration was associated with a higher risk of incident disability among Japanese elderly people.

Key Words: Disability, Prospective cohort study, Sleep duration.

Introduction

Sleep is considered to be a fundamental lifestyle along with dietary habit and physical activity [1]. Previously, several observational studies for elderly population revealed that short or long sleep duration is associated with the incident stroke [2], ischemic heart disease[3], as well as all-cause mortality[4].

With the population aging, the number of elderly individuals disability is increasing worldwide[5]. Especially, the number of people with disability aged 65 or older is constantly increasing in Japan where facing the super-aging society and reached around 0.63 million people (18.1% of elderly people) [6], and costed approximately 184.1 thousand yen (100 yen = 0.88 dollars) per person on long-term care in 2016[7]. Although, there is one prospective cohort study included 4,756 elderly Japanese participants suggested that long sleep duration was associated with higher rate of incident disability[8], the association between sleep duration and incident disability has not yet been fully elucidated. Thus, additional prospective evidence regarding the association between daily sleep duration and subsequent incident disability is needed.

Because risks of incident disability coincide with a decline in functional status and cognitive decline, risks of incident disability are also linked to mortality risk in the older adult population, and evidences suggest that predictors of incident disability are often those that also predict mortality[2], but the previous study does not recognize death as a censored event related to loss of information[8]. Therefore, the present study aimed to investigate the association between daily sleep duration and incident disability with treating all-cause mortality as a competing event among physically and socially independent elderly people based on a Japanese age-specific cohort.

Methods

Study population

The New Integrated Suburban Seniority Investigation (NISSIN) Project is an age-specific prospective cohort study and has been reported in detail elsewhere[9]. Briefly, 3,073 community-dwelling elderly individuals who were aged 64/65 years and lived in the city of central Japan were enrolled in this study. They completed baseline comprehensive medical examination and asked to complete a self-reported questionnaire every June between 1996 and 2005. We excluded individuals who registered before 2000 (n=1,107) because the Long-term Care Insurance in Japan has started in 2000, those with lower level physical and social functioning (n=39) and missing information on physical and social functioning (n=32). Accordingly, 1,895 (962 men and 933 women) individuals were analyzed in the present study. The physical and social functioning was assessed by using the Tokyo Metropolitan Institute of Gerontology index of competence which measures the functional capacity and has been adapted for and validated in the senior Japanese population[10]. A higher score indicated higher independence of elderly individuals, so a score of 10 or higher was treated as an independent in this paper[10]. This study was approved by the Ethics Committees of Nagoya University Graduate School of Medicine, the National Center for Geriatrics and Gerontology of Japan, Aichi Medical University School of Medicine, and Hokkaido University Graduate School of

Medicine.

Assessment of Sleep Duration

Information on sleep duration was assessed by asking the following question: “How many hours a day do you sleep over the last year?” The answer was categorized into the following five groups: <6, 6-6.9, 7-7.9, 8-8.9, ≥9 hours/day[11].

Follow-up

Dates of incident disability were confirmed using the certification for the Long-term care insurance (LTCI) by the local government of Nisshin city, which launched in April 2000 in Japan[12]. Dates of death were confirmed using death certificates. We treated relocation out of the city as a censored case. All participants were followed until December 31, 2015, whichever came first.

The LTCI is one of the mandatory national insurance plans for elderly people in Japan, and it was instituted to support the independence of elderly people, rather than simply providing personal care[12]. The certification for LTCI has been reported in detail elsewhere[13]. Briefly, all individuals aged 65 years or older, or those aged 40–64 years who suffer from age-related diseases are eligible for LTCI benefits in Japan. When a person applies to their municipality for LTCI benefits, an authorized care manager examines their physical and mental status using a standardized questionnaire. Then the certification board, which includes medical doctors and nurses, determines the level of long-term care needed based on the estimated time required for care, as well as on comments from the applicant's family physician. The LTCI certifications consist of the following eight levels: independent, support levels 1–2 and care levels 1–5. We defined a person who certified LTCI in the support level 1, described as a person is independent in basic activities of daily living but requires some assistance in instrumental activities of daily living, or higher as a disability.

Statistical Analysis

Baseline characteristics of the participants were expressed as numbers (percentages). The χ^2-test was used to compare categorical variables. Sex-specific multivariable hazard ratios (HRs) and confidence intervals (CIs) for an incident disability were calculated by Cox proportional model. And then, we conducted further analysis using competing risk model[14]. We treated all-cause mortality as a competing event according to previous study[11]. Potential confounders such as year of participation (continuous variable), body mass index (BMI, <18.5, 18.5-24.9, ≥25 Kg/m^2), Educational attainment (lower junior high school, upper high school), working status (employed, unemployed), marital status (married, other), smoking status (never, past, current smokers), drinking status (never, current drinkers), daily walking time (<1, ≥1 hour/day), depressive tendency (presence, absence), physical and social functioning (independent, dependent), a history of cardiovascular disease (yes, no/missing), cancer (yes, no/missing), diabetes mellitus (yes, no/missing), hypertension (yes, no/missing), hyperlipidemia (yes, no/missing) were introduced in the model. BMI was calculated as weight in kilograms divided by height in meter squared. The depressive tendency was assessed by the short-form Geriatric Depression Scale which is a self-rated depression-screening tool for elderly people[15]. The presence of depressive tendency was defined a total score of 6 or higher[16]. Hypertension was defined as individuals with systolic blood pressure ≥140mmHg, or diastolic blood pressure ≥90mmHg, or use of antihypertensive medication. Hyperlipidemia was defined as individuals with self-reported hyperlipidemia, or a total cholesterol level of ≥220 mg/dl or the self-reported use of medications for hyperlipidemia. Hyperglycemia was defined as a fasting plasma glucose ≥126 mg/dl, hemoglobin A1c (HbA1c) ≥6.5%, or the self-reported use of medications for hyperglycemia. The HbA1c levels were converted from the format of the Japan Diabetes Society (JDS) to the National Glycohemoglobin Standardization Program [NGSP: NGSP (%) =1.02 × JDS (%) + 0.25 (%)]. We decided to treat sleep duration of 7-7.9 hours as the reference category because the mortality risk was considered to be the lowest in people who sleep 7-7.9 hours per night in the previous studies[16,17]. An alpha level of 0.05 was considered statistically significant. All statistical analyses were executed using SAS Version 9.4 (SAS Inc, Cary, NC, USA).

Results

During a median of 12.7 years of follow-up, 256 participants (114 men and 142 women) were certain of incident disability, and 133 (95 men and 38 women) died.

Baseline characteristics of the participants according to sleep duration are presented in Table 1. Overall, the most frequent sleep duration was 7-7.9 hour, 38.7% of the participants reported sleep 7-7.9 hours, 10.7% of participants reported sleeping less than 6 hours, 29.0%

reported 6-6.9 hours, 18.7% reported 8-8.9 hours, and 2.9% reported more than 9 hours. Compared with participants who sleep in 7-7.9 hours/day among women, shorter sleepers were associated with a significantly less likely to have a history of diabetes mellitus or hyperlipidemia. Whereas, no significant associations were found among men.

The association of average daily of sleep duration with an incident disability was shown in Table2. After adjusting for potential confounders, daily sleeping < 6hours/day was increased risk of incident disability (HR 1.64; 95%CI, 1.13-2.38; for total, HR 1.46; 95%CI, 0.71-3.00 for men; HR 1.90; 95%CI, 1.19-3.03 for women).

Discussion

This age-specific prospective cohort study revealed that shorter sleep duration (<6 hours/day) was increased risk of incident disability, compared with a sleep duration of 7-7.9 hours/day. To our knowledge, this is the first study reported the association between short sleep duration and an incident disability defined a person who certified support level 1 or higher. According to the National Nutrition Survey, the major causes for needing long-term care among Japanese elderly people were stroke (17.2%), dementia (16.4%), bone fracture or falls (12.2%), arthropathy (11%), and cardiovascular diseases (4.7%) in 2013[2].

The mechanisms that the association between shorter sleep duration and incident disability is not fully understood. However, several previous studies showed the association between shorter sleep duration and an increased risk of poor physical function[3], falls[18], low cognitive function such as executive function[19], and incident diseases such as stroke[20], ischemic heart disease[21], osteoporosis[22], and sarcopenia[23] through adverse endocrinologic or metabolic effects such as decreases of testosterone[24] and melatonin secretion[25], through the induction of chronic, low-grade inflammation such as elevated C-reactive protein[26], through increases vascular damage such as coronary artery calcification, or through increases in cortisol secretion[27] or altered growth hormone metabolism[28]. They support our results.

The strength of this study is the design of age-specific cohort. All the participants were enrolled at the age of 64/65 years, and therefore we can get rid of the influence of age on the association between sleep duration and incident disability. Additionally, several meta-analyses reported that shorter sleep duration is a risk factor for all-cause mortality[4]. It could lead to an underestimation of the incident disability because all-cause mortality might be a competing event. Although we found no significant association between sleep duration and all-cause mortality in this study (data not shown), to reduce this bias, we conducted a competing risk analysis.

The limitations of the study also need to be addressed. First, we obtained information on the sleep duration based on self-reported and therefore our results could include some misclassification. Particularly, self-reported long sleepers are more likely to over reported their total sleep time, and their sleep time is almost their time in bed[29]. If we assess objective sleep characteristics using actigraphy[30], our results would be more reliable. Second, although we adjusted potential confounders as far as possible in the statistical model, some residual confounders which could be associated with sleep duration could not be eliminated. For example, this study did not include information on sleep complaint, sleep disorders such as insomnia, sleep apnea, and napping, or history of shift works which may be influenced by normal sleep duration. Third, we only assessed daily sleep duration at baseline. Sleep duration might be changed due to subsequent their health condition. Forth, our results might be included detection bias because not all candidates applied for LTCI certification. Fifth, because we did not consider causes of incident disability, the mechanisms association between sleep duration and incident disability remained unidentified. Sixth, although the results in the subgroup analysis of each confounder may provide them some hints of the biological mechanism underlying the findings observed in this study, we could not obtain sufficient calculations due to a small number of incident disability in each sub-group.

In conclusion, shorter sleep duration was associated with a higher risk of incident disability among Japanese elderly individuals.

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Disclosure statement

The authors declare no conflict of interest.

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Table1. Baseline characteristics according to sleep duration(n=1,895)

Variables	Average daily sleep duration (h/day)											
	Men (n=962)						Women (n=933)					
	<6 (n=69)	6-6.9 (n=254)	7-7.9 (n=381)	8-8.9 (n=215)	≥9 (n=43)	p-value	<6 (n=133)	6-6.9 (n=295)	7-7.9 (n=353)	8-8.9 (n=139)	≥9 (n=13)	p-value
BMI (Kg/m^2)												
<18.5	3 (4.3)	7(2.8)	14 (3.7)	10 (4.7)	3 (7.0)	0.68	5 (3.8)	18 (6.1)	15 (4.2)	8 (5.8)	1 (7.7)	0.96
18.5-24.9	43 (62.3)	185 (72.8)	264 (69.3)	145 (67.4)	31 (72.1)		103 (77.4)	217 (73.6)	268 (75.9)	101 (72.7)	9 (69.2)	
≥25	23 (33.3)	62 (24.4)	103 (27.0)	60 (27.9)	9 (20.9)		25 (18.8)	60 (20.3)	70 (19.8)	30 (21.6)	3 (23.1)	
Educational attainment												
Lower junior school	21 (30.4)	49 (19.3)	102 (26.8)	53 (24.7)	15 (34.9)	0.08	45 (33.8)	86 (29.2)	122 (34.6)	54 (38.8)	4 (30.8)	0.34
Upper high school	48 (69.6)	205 (80.7)	279 (73.2)	162 (75.3)	28 (65.1)		88 (66.2)	209 (70.8)	231 (65.4)	85 (61.2)	9 (69.2)	
Working status												
Employed	29 (42.0)	108 (42.5)	164 (43.0)	106 (49.3)	20 (46.5)	0.66	93 (69.9)	215 (72.9)	250 (70.8)	111 (79.9)	10 (76.9)	0.41
Unemployed	38 (55.1)	142 (55.9)	214 (56.2)	107 (49.8)	22 (52.1)		40 (30.1)	76 (25.8)	100 (28.3)	28(20.1)	3 (23.1)	
Marital status												
Married	65 (94.2)	243 (95.7)	365 (95.8)	207 (96.3)	42 (97.7)	0.92	99 (74.4)	255 (86.4)	306 (86.7)	116 (83.5)	10 (76.9)	0.07
Other	4 (5.8)	11 (4.3)	16 (4.2)	8 (3.7)	1 (2.3)		33 (24.8)	40(13.6)	46 (13.0)	22 (15.8)	3 (23.1)	
Smoking status												
Never	14 (20.3)	56 (22.0)	73 (19.2)	35 (16.3)	5 (11.6)	0.21	120 (90.2)	267 (90.5)	325 (92.1)	124 (89.2)	13 (100)	0.72
Past	31 (44.9)	138 (54.3)	201 (52.8)	110 (51.2)	18 (41.9)		7 (5.3)	18 (6.1)	14 (4.0)	11 (7.9)	0.0	
Current	24 (34.8)	60(23.6)	106 (27.8)	70(32.6)	20 (46.5)		6 (4.5)	10 (3.4)	14 (4.0)	4 (2.9)	0.0	
Drinking status												
Never/past	20 (29.0)	89 (35.0)	122 (32.0)	61 (28.4)	11 (25.6)	0.61	106 (79.7)	223 (75.6)	289 (81.9)	111 (79.9)	12 (92.3)	0.26
Current	49 (71.0)	164 (64.6)	259 (68.0)	154 (71.6)	32 (74.4)		27 (20.3)	72(24.4)	64 (18.1)	28(20.1)	1 (7.7)	
Walking status (h/day)												
<1	37 (53.6)	143 (56.3)	186 (48.8)	99 (46.0)	27 (62.8)	0.07	52 (39.1)	98 (34.4)	103 (29.2)	43 (30.9)	7 (53.8)	0.31
≥1	31 (44.9)	111 (43.7)	194 (50.9)	116 (54.0)	16 (37.2)		81 (60.9)	185 (64.9)	247 (70.0)	96 (69.1)	6 (46.2)	
Depressive tendency												
Absence	50 (72.5)	193 (76.0)	306 (80.3)	175 (81.4)	32 (74.4)	0.37	90 (67.7)	216 (73.2)	267 (75.6)	99 (71.2)	11 (84.6)	0.11
Presence	17 (24.6)	53(20.9)	60(15.7)	36 (16.7)	8 (18.6)		41 (30.8)	66 (22.4)	69 (19.5)	30 (21.6)	1 (7.7)	
History of disease												
Cardiovascular disease	2 (2.9)	18 (7.1)	29 (7.6)	19 (8.8)	5 (11.6)	0.44	8 (6.0)	16 (5.4)	15 (4.2)	6 (4.3)	1 (7.7)	0.88
Cancer	1 (1.4)	7 (2.8)	9 (2.4)	11 (5.1)	1 (2.3)	0.34	8 (3.0)	16 (5.4)	18 (5.1)	6 (4.3)	1 (7.7)	0.96
Diabetes mellitus	5 (7.2)	29 (11.4)	55 (14.4)	34 (15.8)	5 (11.6)	0.32	5 (3.8)	18 (6.1)	22 (6.2)	19 (13.7)	2 (15.4)	0.01
Hypertension	33 (47.8)	127 (50.0)	169 (44.4)	123 (57.2)	21 (48.8)	0.06	48 (36.1)	105 (35.6)	146 (41.4)	61 (43.9)	6 (46.2)	0.36
Hyperlipidemia	35 (50.7)	136 (53.5)	205 (53.8)	113 (52.6)	24 (55.8)	0.98	82 (61.7)	186 (63.1)	245 (69.4)	108 (77.7)	8 (61.5)	0.02

All values shown are as n (%). The proportion of each variable does not always add up to 100% owing to missing data.

p-values were calculated by χ^2-test.

Table2. Association of average daily sleep duration with incident disability

	Average daily sleep duration (h/day)				
	<6	**6-6.9**	**7-7.9**	**8-8.9**	**≥9**
Total					
Person-years	2,418	6,556	9042	4,312	685
No. of case	36	70	95	54	10
No. of death	8	32	56	31	6
Sex adjusted HR (95% CI)[a]	1.63 (1.11-2.39)	1.11 (0.81-1.52)	1.00	1.19 (0.85-1.67)	1.30 (0.68-2.51)
Adjusted HR (95% CI)[a]	1.61 (1.09-2.40)	1.09 (0.79-1.50)	1.00	1.14 (0.81-1.61)	1.31 (0.68-2.54)
Adjusted HR (95% CI)[b]	1.64 (1.13-2.38)	1.09 (0.80-1.48)	1.00	1.16 (0.82-1.62)	1.27 (0.66-2.42)
Men					
Person-years	800	2,973	4,655	2,612	513
No. of case	9	29	48	28	9
No. of death	4	20	41	24	6
Clude HR (95% CI)[a]	1.27 (0.62-2.59)	1.06 (0.67-1.69)	1.00	1.01 (0.63-1.61)	1.82 (0.89-3.74)
Adjusted HR (95% CI)[a]	1.42 (0.68-3.00)	1.15 (0.70-1.87)	1.00	1.01 (0.63-1.65)	1.74 (0.83-3.62)
Adjusted HR (95% CI)[b]	1.46 (0.71-3.00)	1.14 (0.70-1.85)	1.00	1.01 (0.63-1.62)	1.66 (0.82-3.37)
Women					
Person-years	1,618	3,583	4,387	1,700	172
No. of case	27	41	47	26	1
No. of death	4	12	15	7	0
Clude HR (95% CI)[a]	1.86 (1.15-3.00)	1.17 (0.77-1.80)	1.00	1.49 (0.92-2.42)	0.38 (0.05-2.73)
Adjusted HR (95% CI)[a]	1.91 (1.16-3.15)	1.17 (0.76-1.81)	1.00	1.39 (0.84-2.29)	0.42 (0.06-3.07)
Adjusted HR (95% CI)[b]	1.90 (1.19-3.03)	1.16 (0.77-1.75)	1.00	1.36 (0.84-2.22)	0.43 (0.06-3.11)

HR, Hazard Ratio; CI, Confidence Interval.

[a]Cox proportional model, [b]competing risk model

Adjusted for year of participation, body mass index, education, working status, marital status, smoking, drinking, daily walking, depressive tendency, and history of cardio vascular disease, cancer, hypertension, hyperlipidemia, and diabetes mellitus.