SLEEP LATENCY IN MEN AND SLEEP DURATION IN WOMEN CAN BE FRAILTY MARKERS IN COMMUNITY-DWELLING OLDER ADULTS: THE KOREAN FRAILTY AND AGING COHORT STUDY (KFACS)

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Abstract: *Objectives:* To test whether sleep disturbances are associated with frailty in older men and women. *Design:* Cross-sectional analysis of cohort study data. The participants were 1168 community-dwelling older adults aged 70 to 84 years who took part in the Korean Frailty and Aging Cohort Study and completed both self-reported sleep parameters and assessment of frailty. Univariate and multivariate survey logistic regression models were used to calculate odds ratios (OR) with 95% confidence intervals (CI) for frailty. Frailty was defined using the Fried's criteria. *Results:* Frailty was associated with sleep latency in men. The odds ratio for this association was 3.39 (95% CI 1.31-8.76) after adjusting for age, body mass index (BMI), physical activity, and select comorbidities, and 2.16 (95% CI 0.75-6.23) after further adjusting for depression. Frailty was associated with long sleep duration of more than 8 hours a night in women. The odds ratio for this association was 3.95 (95% CI, 1.27-12.33) after adjusting for age, BMI, physical activity, select comorbidities, and the number of medications. *Conclusion:* Prolonged sleep latency (≥60 minutes) in men and long sleep duration (>8hr per night) in women were each independently associated with higher odds of frailty. Long sleep latency in elderly men and long sleep duration in elderly women may suggest they have a high chance of frailty.

Key words: Sleep latency, sleep duration, frailty, frailty marker, Korea.

Introduction

Sleep disturbances are common in older adults (1-4) and about half the number of older adults complain of sleep problems (5). Vaz Fragoso CA et al. showed frailty may disrupt sleep cycle and suggested bidirectional association between frailty and sleep disturbance (6).

Other studies have suggested possible relationship between frailty and sleep disorders. One study by Ensrud et al. showed that self-reported poor sleep quality, sleep efficiency <70%, sleep latency ≥60 minutes, and sleep disordered breathing were each independently associated with frailty status in men, but short sleep duration was not associated with frailty in men (7). Higher scores in the Pittsburgh Sleep Quality Index (PSQI) were significantly associated with frailty score (8). Furthermore, Moreno-Tamayo group showed that sleep complaints were associated with frailty in older women, but not in men (9) while poor quality of sleep was associated with poorer physical performance in older women (10). Compared to older adults sleeping 7-7.9 hours at night, those with longer sleeping time (≥ 10 hours in males and ≥ 8 hours in females) had a significantly higher risk of total mortality (11).

Standing on the basis of these studies, subjective sleep disturbances including longer sleep duration and prolonged sleep latency may be important factors that affect or are associated with frailty in older adults. However, to the best of the authors' knowledge, there was no study which showed association between long sleep duration or latency and frailty in women, and little is known about sex differences in terms of association between subjective sleep disturbance and frailty. Therefore, we aimed to evaluate the association between subjective sleep disturbance and frailty in older adults and evaluate the sex differences in this association.

Methods

Participants

This study involved participants aged 70 to 84 years old who took part in the Korean Frailty and Aging Cohort Study (KFACS). The KFACS is a national, multi-center, large-scale cohort study initiated in 2016 with the target number of 3,000 adults aged 70 to 84 years old, stratified by age and gender. It aims to identify risk factors for frailty and measures to prevent it in the community-dwelling older adults. Older adults who did not have serious cognitive impairment and provided informed consent were included. The participants were recruited from 10 participating medical centers (8 hospitals and 2 public health centers) across the country, were interviewed individually, and went through clinical tests. Among 1559 participants of the first year, 1168 people completed all tests and questionnaires required for the Fried frailty index (FFI) and self-reported sleep parameters and were included in this study for analysis.

Sleep parameters

Sleep parameters were self-reported using a questionnaire on the usual sleep pattern for the past 4 weeks. Five questions were extracted from PSQI questionnaire about subjective sleep quality (12): 1) What time did you go to bed? 2) How long did

SLEEP LATENCY IN MEN AND SLEEP DURATION IN WOMEN CAN BE FRAILTY MARKERS

Table 1
General characteristics of the study participants

Characteristic	Male (n=549)				Female (n=619)			
	Robust (n=297)	Pre-frail (n=222)	Frail (n=30)	P-value	Robust (n=220)	Pre-frail (n=333)	Frail (n=66)	P-value
Age, year	75.8±3.8	77.3±4.1	78.6±3.2	<0.001	74.7±3.5	76.0±3.9	78.4±4.3	<0.001
BMI, kg/m²	24.0±2.7	24.1±3.1	22.5±3.6	0.013	24.9±2.9	25.1±2.9	24.3±3.6	0.201
Smoking, ever	224 (75.4)	178 (80.2)	24 (80.0)	0.415	5 (2.3)	9 (2.7)	2 (3.0)	0.924
Alcohol drinking[a]	113 (38.0)	65 (29.3)	8 (26.7)	0.078	6 (2.7)	13 (3.9)	6 (9.1)	0.069
Physical activity[b]	66.2±81.1	42.9±65.0	13.2±18.9	<0.001	38.2±34.4	34.3±47.1	13.4±22.6	<0.001
Marital status	27 (9.1)	27 (12.2)	7 (23.3)	0.051	121 (55.0)	187 (56.2)	39 (59.1)	0.840
Sleep duration								
<6 hour	76 (25.6)	68 (30.6)	10 (33.3)	0.488	81 (36.8)	144 (43.2)	32 (48.5)	0.014
6-8 hour	197 (66.3)	136 (61.3)	16 (53.3)		132 (60.0)	176 (52.9)	27 (40.9)	
>8 hour	24 (8.1)	18 (8.1)	4 (13.3)		7 (3.2)	13 (3.9)	7 (10.6)	
Sleep latency, min	18.5±19.3	22.2±26.1	36.0±37.9	<0.001	27.1±35.9	31.2±33.7	36.0±39.3	0.152
>60 min	22 (7.4)	25 (11.3)	9 (30.0)	<0.001	37 (16.8)	79 (23.7)	16 (24.2)	0.126
CVD	18 (6.1)	13 (5.9)	4 (13.3)	0.275	5 (2.3)	12 (3.6)	1 (1.5)	0.512
CHF	3 (1.0)	2 (0.9)	0 (0.0)	0.857	0 (0.0)	1 (0.3)	2 (3.0)	0.006
Angina, MI	25 (8.4)	27 (12.2)	4 (13.3)	0.319	12 (5.5)	30 (9.0)	8 (12.1)	0.144
HTN	140 (47.1)	138 (62.2)	20 (66.7)	0.001	119 (54.1)	204 (61.3)	44 (66.7)	0.106
COPD	10 (3.4)	11 (5.5)	4 (13.3)	0.041	3 (1.4)	6 (1.8)	2 (3.0)	0.667
DM	56 (18.9)	67 (30.2)	11 (36.7)	0.003	34 (15.5)	58 (17.4)	19 (28.8)	0.044
Mental disorder	11 (3.7)	8 (3.6)	3 (10.0)	0.227	12 (5.5)	34 (10.2)	8 (12.1)	0.089
Depression	12 (4.0)	33 (14.9)	14 (46.7)	<0.001	14 (6.4)	78 (23.4)	35 (53.0)	<0.001
Number of med[c]	3.2±2.9	5.5±11.4	8.5±17.3	<0.001	2.8±2.5	4.3±9.4	7.8±16.6	<0.001

Continuous variables are presented as means ± standard deviation or presented as numbers with (percentage). BMI, body mass index; CVD, cerebrovascular Disease; CHF, congestive heart failure; DM, diabetes mellitus; HTN, hypertension; COPD, chronic obstructive pulmonary disease; MI: myocardial infarction; a. Alcohol drinking: ≥ 2times/ week; b. Physical activity in metabolic equivalent for task × hour / week; c. Med: medications

it take to fall asleep after going to bed? 3) What time do you wake up? 4) How long did you actually sleep at night? and 5) How many times do you take a nap per week?

Sleep latency and duration were measured based on the answers provided. Sleep duration of the study participants were categorized as 'short (<6 hours)', 'average (6 to 8 hours)' or 'long (≥8 hours)' (13). Prolongation of sleep latency was defined as taking more than 60 minutes to fall asleep.

Other variables

The medical history of participants was obtained from the checklist of morbidity. Physical activity was assessed using the metabolic equivalent for task (MET) using International Physical Activity Questionnaire (IPAQ). Depressive tendency was evaluated using the Korean version of Short-Form Geriatric Depression Rating Scale (SGDS-K) consisting of 15 questions (14). Score of eight or higher was defined as depression as previously studied. The number of prescribed medications the participants have been taking for 3 months or more was defined

as the number of medications.

Definition of frailty

The definition of frailty was based on the Fried frailty index (FFI) which has five components: unintended weight loss, poor grip strength, exhaustion (self-assessed), reduced walking velocity, and low physical activity (15). First, one point was given for unintended weight loss of 4.5 kg or more in the last year. Second, grip strength of the dominant hand was measured using a hand dynamometer (TTK-5401, Takei Ltd, Tokyo, Japan). The grip strength was measured twice with arms stretched down while not touching the trunk, and the greater value of the two measurements was used. One point was given for grip strength less than 26 kg for men and less than 18 kg for women (16). Third, one point was given for exhaustion when the subject's response to either one of the questions from the Center for Epidemiological Studies-Depression (CES-D) scale, "I felt that everything I did was an effort" or "I could not get going", was yes for three days or more a week (16,

17). Fourth, one point was given for walking speed below 1 meter per second while walking 4 meters at a normal pace (16). Fifth, Metabolic Equivalent Task in minutes per week (MET-min/week) was calculated to determine physical activity. One point was given for values below 494.65 kcal for men and below 283.50 kcal for women, which was the lowest 20% of the gender-specific total energy consumed from a general population-based survey of older adults (18).

Participants with a total score of 3 or more were classified as frail, a total score of 1 or 2 were classified as pre-frail, and participants without any of the criteria were classified as robust (15). In our study, we combined the robust and pre-frail groups into non-frail group for comparison with the frail group.

Statistical analysis

The difference in mean sleep latency between depression and non-depression groups was examined using independent two-sample test. The differences in characteristics according to frailty category (robust, pre-frail, and frail) were compared using analysis of variance for continuous data, and chi-square tests for categorical data. The association between frailty and sleep latency or sleep duration was analyzed with multiple logistic regression analysis. Statistical analysis was performed using IBM SPSS Statistics Version 23.0 (Armonk, NY: IBM Corp.) and significance was defined as P value less than 0.05.

Results

General characteristics of the study population

Among 1168 participants, 517 participants were classified as robust, 555 as pre-frail, and 96 as frail according to the Fried's phenotype (Table 1). The median ages of the robust, pre-frail, and frail participants were 75.8, 77.3, and 78.6 years in men, and 74.7, 76.0, and 78.4 in women, respectively. The proportion of women was higher in the frail group, whereas the proportion of men was higher in the robust group.

The median duration of sleep was 6.49, 6.41, and 6.15 hours in robust, pre-frail, and frail men, respectively, and the median duration of sleep was 6.01, 5.85, and 5.88 hours in robust, pre-frail, and frail women, respectively. Notably, the differences in sleep duration were statistically significant in only women (p = 0.014). The median latency of sleep was 18.45, 22.16, and 36.00 minutes in robust, pre-frail, and frail men, respectively, and the median latency of sleep was 27.09, 31.15, and 36.00 minutes in robust, pre-frail, and frail women, respectively. The differences in sleep latency were statistically significant in only men (p<0.001).

The rates of hypertension, chronic obstructive pulmonary disease, and diabetes mellitus were higher in the frail group than in other groups in both men and women. The rates of depression in men were 4.04% in the robust group, 14.86% in the pre-frail group, and 46.67% in the frail group (p<0.05). The number of prescribed medications was also higher in the frail group in both genders. The level of physical activities was significantly lower in frail men and women (Table 1).

Frailty and sleep pattern in men

Prolonged sleep latency (sleep latency ≥60 minutes) was associated with greater odds of frailty in men with logistic regression after adjusting for age, body mass index (BMI), physical activity, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and hypertension (HTN) (odds ratio [OR] 3.39, 95% confidence interval [CI] 1.31-8.76), but the association became non-significant after further adjusting for depression (OR 2.16, 95% CI 0.75-6.23) (Table 2). The mean sleep latency (mean ± standard deviation [SD]) was 18.92 ± 21.19 in the non-depression group, and 34.38 ± 36.58 in the depression group (p<0.05)

Table 2
Odds ratio of sleep latency for frailty in men

	OR	95% CI	P*
Model1	4.30	1.87 – 9.93	0.001
Model2	4.55	1.86 – 11.18	0.001
Model3	3.39	1.31 – 8.76	0.012
Model4	2.16	0.75 – 6.23	0.155

Model1: unadjusted; Model2: adjusted for age, BMI, COPD, DM, and HTN; Model3: adjusted for age, BMI, COPD, DM, HTN, and physical activity; Model4: adjusted for age, BMI, COPD, DM, HTN, physical activity, and depression; * P-value was obtained by multiple logistic regression analysis; OR, odds ratio; CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension

Frailty and sleep pattern in women

Long sleep duration (total sleep time >8 hours per night) was associated with greater odds of frailty in women compared to the reference sleep duration group of 6-8 hours per night. After adjusting for multiple correlates of frailty and long sleep duration including age, marital status, physical activity, BMI, COPD, DM, HTN, depression, cerebrovascular disease (CVD), congestive heart failure (CHF), and the number of medications, the association between long sleep duration and frailty remained significant (OR 3.95, 95% CI 1.27-12.33) (Table3).

In comparison, short sleep duration of less than 6 hours was not associated with frailty in unadjusted analyses (OR 1.62, 95% CI 0.95-2.79), or after adjustment (OR 1.16, 95% CI 0.62-2.17).

Discussion

In this cohort of community-dwelling older adults, subjective long sleep duration of more than 8 hours a night was associated with frailty in women. Sleep disorders reduce growth hormone secretion and promote cortisol secretion, decreasing muscular mass, and leading to frailty (9). Inversely, frailty may cause sleep disturbances by enhanced inflammation and chronic glucocorticoid secretions, as it is sometimes associated with

depression (19, 20).

Table 3
Odds ratio of sleep duration for frailty in women

	Sleep duration(h)	OR	95% CI	P*
Model1	6-8	1	Ref	Ref
	<6	1.62	0.95 – 2.79	0.079
	>8	3.99	1.55 – 10.29	0.004
Model2	6-8	1	Ref	Ref
	<6	1.50	0.85 – 2.67	0.164
	>8	4.48	1.55 – 12.92	0.006
Model3	6-8	1	Ref	Ref
	<6	1.16	0.62 – 2.17	0.652
	>8	3.95	1.27 – 12.33	0.018

Model 1: unadjusted; Model 2: adjusted for age, marital, and physical activity; Model 3: adjusted for age, marital, physical activity, BMI, COPD, DM, HTN, Depression, CVD, CHF, and number of medications; * P-value was obtained by multiple logistic regression analysis; OR, odds ratio; CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DM, diabetes; HTN, hypertension; CVD, cerebrovascular Disease; CHF, congestive heart failure

Subjective prolonged sleep latency (sleep latency ≥60 minutes) was associated with frailty in men in univariate analysis, but including depression as an explanatory variable eliminated the association in multivariate analysis. Previous studies have shown significant association between prolonged sleep latency and frailty in men even after adjusting for multiple correlates including depression (21). The discrepancy may have risen from high proportion of depressive men in our frailty group, as depression can prolong sleep latency. Therefore, participants with depressive tendency may be prone to longer mean sleep latency as well as high possibility of frailty. Furthermore, subjective depression was significantly associated with weight loss among Korean elderly men in the study of Song et al (22). Weight loss is a component of Fried's frailty criteria, and could provide another explanation for the association between depression and frailty in Korean elderly men.

In this study, long sleep duration (total sleep time >8 hours per night) was associated with greater evidence of frailty in elderly women even after further adjustment for potential confounders (Table 3). Long sleep duration (9 hours or longer) is known to be independently associated with sarcopenia in Korean adults with mean age of 44.1 years (23), and that can explain why long sleep duration is associated with frailty.

To the authors' knowledge, this is the first study to examine the association between sleep duration, sleep latency and frailty in elderly women, although prior studies have suggested association between long sleep duration and mortality (24-31). Although Karla Moreno-Tamayo group showed that sleep complaints were associated with frailty in older women, and not in men, they didn't look into the sleep duration or sleep latency.

In the current study, sex differences were observed in the association between sleep problems and frailty. The explanation of differential association between men and women may be based on the fact that women experience more vulnerability to stress than men according to a systematic review which showed that systemic inflammation provoked by sleep deprivation, insomnia and poor sleep quality varies with sex (32). Women tend to show higher C-reactive protein (CRP) and interleukin-6 levels which act as markers in the pathogenesis of frailty (33).

This study had several limitations. First, the cross-sectional design of this study does not allow inference of causality in the relationship between prolonged sleep latency, long sleep duration and frailty. Since sleep problems and frailty could be associated bidirectionally (21), future research should examine whether prolonged sleep latency and long sleep duration are independently associated with frailty. Second, we did not assess what kind of medications the participants are taking including hypnotics, which may have confounded the results. However, we tried to control to some degree by adjusting for the number of medications taken. Third, the sleep variables were collected by the participants' recall and it may be different from objective sleep measurements. One study reported that self-reported sleep latency was 10 minutes longer than objectively measured sleep latency, and that estimated total sleep duration was significantly shorter than the measured duration (median difference of –18.5 minutes) in adults with mean age of 50 years (34).

However, there are also several noteworthy strengths of this study. We enrolled a large number of community-dwelling older adults aged 70 to 84, and the cohort was gathered from 10 different regions of Korea. Therefore, the cohort can be said to be highly representative of that age group in different regions across the whole country.

Conclusion

Prolonged sleep latency in men and long sleep duration in women were each associated with increased odds of frailty in univariate analysis. The association of prolonged sleep latency and frailty did not remain significant after adjusting for multiple correlates including depression in men. The association of long sleep duration and frailty remained significant after further adjustment for potential confounders in women.

Long sleep latency in elderly men and long sleep duration in elderly women may suggest they are frail. Depression could explain why long sleep latency is associated with frailty in Korean elderly men.

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