



Original article

Interactive effects of exercise and sleep on frailty severity in community-dwelling older adults: a cross-sectional study

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Abstract

Objectives: This study examined the effects of the interaction between exercise and sleep on frailty severity in community-dwelling older adults.

Materials and Methods: This was a cross-sectional study. Data were collected in July 2019. In total, 2021 adults participated who responded to a questionnaire. Among them, 672 participants (317 men and 355 women) with valid responses were included in the analysis. Ordinal logistic regression analysis was performed to examine the association between frailty severity and the interaction between exercise and sleep. The dependent variable represents three different levels of frailty. The independent variables included basic information and interaction between exercise and sleep.

Results: The results of ordinal logistic regression analysis (odds ratio [OR]) showed that the period from the start of exercise (OR=0.96), age (OR=1.00 for participants in their 60 s, OR=1.65 for those in their 70s, and OR=3.13 for those aged >80 years), poor subjective health perception (OR=2.12), poor quality of sleep (OR=1.88), stress (OR=1.62), and exercise–sleep interaction (OR=1.00 based on good-exercise–good-sleep interaction, OR=3.09 poor-exercise–good-sleep interaction, and OR=3.50 poor-exercise–poor-sleep interaction) significantly contributed to the model. The Nagelkerke coefficient of determination adjusted for degrees-of-freedom (R^2), which represents the contribution rate of the regression equation, was 0.334.

Conclusions: Our results suggest that a combination of good exercise and good sleep is needed to prevent frailty progression in community-dwelling older adults.

Key words: community-dwelling older adults, pre-frailty, frailty, severity, exercise–sleep interaction

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Introduction

Frailty leads to adverse outcomes, including restricted mobility, reduced self-reliance and disability, falls, hospitalization, and increased mortality^{1, 2}. Frailty is a public

health problem with a prevalence of approximately 10% in the community-dwelling elderly population on worldwide data³, and pre-frailty is the preliminary stage of frailty. Frailty and pre-frailty are reversible conditions if treated appropriately⁴. There are several factors associated with the prevention or improvement of pre-frailty and frailty, with habitual exercise as one of the most important factors^{5, 6}. Theou *et al.*⁷ examined the impact of exercise on frailty in older participants in the community based on a systematic review and reported a high-quality evidence based on which exercise for 30–45 min per exercise session for prolonged periods (≥ 5 months) are effective in preventing frailty. Thus, habitual exercise as part of the activities of daily living is closely related to the prevention of frailty and is extremely important for maintaining the health of the elderly⁸.

Habitual exercises and adequate sleep are included in the

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prevention and improvement of frailty^{9, 10}. Thus, inadequate sleep has been shown to increase the total number of deaths and other disorders¹¹. In a previous study that included 1,726 community-dwelling older adults, poor quality of sleep and shortened sleep periods (< 6 h) were associated with the severity of pre-frailty and frailty. A high-quality systematic review by Pourmotabbed *et al.*¹⁰ also indicated that shortened sleep periods are associated with an increased risk of frailty. Therefore, adequate sleep (>6 h) periods are extremely important for preventing and improving frailty and maintaining health in community-dwelling older adults.

Several studies have reported the importance of exercise and sleep in the prevention or improvement of frailty in community-dwelling older adults⁵⁻¹¹. There is a relationship between exercise and sleep. For example, habitual exercise leads to better sleep¹². In addition, some reports have indicated that habitual exercise is needed for good sleep¹³. Thus, it is expected that there will be an interaction between exercise and sleep. However, it is not known whether exercise and sleep have an interactive effect on frailty severity. If there is an interaction between exercise and sleep, this will constitute important information for effective frailty prevention.

Therefore, this study examined the interaction between exercise and sleep and its effects on frailty severity in community-dwelling older adults.

Materials and Methods

Study design

This was a cross-sectional study. The study protocol adhered to the Declaration of Helsinki and was reviewed and approved by the ethical committee (approval number: 19-022). Information regarding participant names, date of birth, and address were not collected to maintain the anonymity of the participants. This study was performed in accordance with strengthening the reporting of observational studies in epidemiology statements.

Setting

Data were collected from July to August 2019 as the City Health Promotion Plan (phase 2), referred to as the “Iki Iki Plan”. Five thousand participants over the age of 20 living in the city were randomly selected as participants. Data from the same participants were analyzed in a previous study by Matsuura *et al.*¹⁴. However, the frailty selection criteria and analyses were different from those in the previous study. Matsuura *et al.*¹⁴ divided the participants into three classes: a) no-frailty, b) cognitive frailty, and c) physical frailty, and multiple logistic regression analysis was then performed. Conversely, in this study, we classified the participants into robust, pre-frailty, and frailty groups and performed ordinal logistic regression analysis to reveal the factors that influ-

enced frailty severity.

Participants

A total of 2,021 participants who responded to a preset questionnaire were included in this study. Of these, only 1,636 participants with valid responses were included. Among them, 672 participants (317 men and 355 women) aged 60 years or older were included in the analysis. These participants were divided into robust, pre-frailty, and frailty groups based on the simple frailty index¹⁵.

Variables

Basic information and information about exercise, sleep, and frailty were extracted from a self-administered questionnaire. Sex was assessed with the following question: “Please specify your sex (male or female)”; age was assessed based the question “Please specify your age (60, 70, or over 80 years old)”; and height and weight were assessed with “Please specify your height and weight (please write a numerical value)”. Body mass index (BMI) was calculated from the height and weight. The nutritional status was assessed using the question, “Do you eat three meals a day? (yes or no)”, and smoking history was determined based on the responses to the question (“smoking, not smoking, or smoked in the past”). Subjective health perception was assessed with “Please specify your health status (very well, fairly well, badly, or very badly)”. Responses of “very well” and “fairly well” were considered to indicate a “healthy” status. Happiness state was assessed using the question “Are you happy? (very well, fairly well, badly, or very badly)”. Responses of “very well” and “fairly well” indicate “happiness”. Stress states were assessed with the question, “Did you have stress (anxiety/trouble) during the past month? (tremendous, average, some, or none)”. Responses of “tremendous” and “average” indicate whether participants “experienced stress (anxiety/trouble) during the month prior to their participation in this study. Their associations with neighbors were assessed with the question, “How do you have connections with neighbors? (very good, fairly good, sometimes, or almost never)”. Responses of “very good” and “fairly good” indicate “connections with neighbors are good”. Trust in others was assessed using the following questions based on a four-point method: “Do you think participants are in general trust worthy?”, “Do you think that a lot of participants try to take advantage of others when they have an opening?”, and “Do you think that in many cases, participants try to be helpful to others? (Do not think at all, do not think much, I think, or I think very well)”. The median of the total score was calculated, and the participants were classified into “good trust in others” (score was higher than the median) and “poor trust in others” (score was lower than the median) groups.

Habitual exercise was assessed with “Do you exercise?”

(yes or no)". If they did not, the exercise time and duration were scored as zero. If they performed exercises, they were considered good exercise and provided the time and duration of the exercise. Time per opportunity and duration were evaluated as follows: "How long do you exercise each time you find an opportunity for exercise? (Please write a numerical value)" and "How long did the exercise last? (please write a numerical value)". The duration since the start of exercise was treated as the duration, and the year was calculated.

The sleep status and quality of sleep were assessed with the question "Were you well-rested after sleep during the past month?" and "Are you satisfied with your overall sleep quality? (very satisfied, fairly satisfied, poorly satisfied, or not satisfied at all)". The responses of "very satisfied" and "fairly satisfied", respectively, indicated that participants felt well-rested from sleep during the month prior to the study and that they received good quality of sleep.

Frailty was determined based on the frailty index¹⁵. The frailty screening index included simple yes/no questions concerning nutrition/shrinking, physical function, physical activity, forgetfulness, and emotions/exhaustion. The index consisted of five items rated as zero or one by the participants. The five items were as follows: (1) "Have you lost 2 kg or more during the past 6 months? Yes=1", (2) "Do you think you walk slower than before? Yes=1", (3) "Do you go for a walk at least once a week to maintain good health status? No=1", (4) "Can you recall what happened 5 min ago? No=1", and (5) "In the past 2 weeks, did you feel tired without a reason? Yes=1". We defined scores of 3 or more as frail, 1 to 2 as prefrail, and 0 as robust according to the Cardiovascular Health Study criteria¹⁶.

Statistical analysis

Characteristic data were compared using one-way analysis of variance, Kruskal–Wallis, or χ^2 tests, as appropriate. Variables with significant differences were subjected to post-tests. Ordinal logistic regression analysis was performed to examine the association between frailty severity and the interaction between exercise and sleep. The dependent variable represented the three levels of frailty. The independent variables provided basic information on the interaction between exercise and sleep. Adjusted odds ratios (ORs) for the incidence of disability with 95% confidence intervals were estimated. When the correlation coefficients between independent variables exceeded 0.8, highly correlated factors with the dependent variable were adopted to resolve multicollinearity. To examine the interaction between exercise and sleep, the variables were dichotomous, that is, whether they were performing exercise and whether they felt they had rested well from sleep. The interaction between exercise and sleep was related to three variables derived from the combination of the values from the two

variables: good-exercise–good-sleep, good-exercise–poor-sleep, and poor-exercise–good-sleep with the fourth one, namely, poor-exercise–poor-sleep, as the reference. All statistical analyses were performed using IBM SPSS statistics package (version 23, IBM Corporation, Armonk, NY, USA).

Results

This study included 672 participants (317 men and 355 women) aged 60 years or older. The groups in this study were 139 (20.7%) in the robust group, 418 (62.2%) in the pre-frailty group, and 115 (17.1%) in the frailty group. Participant characteristics are listed in Table 1. The percentages for each of the pre-frailty and frailty factors are listed in Table 2.

Ordinal logistic regression analysis was used to determine the factors that affected frailty severity. The final independent variables included age, sex, BMI, eating three meals a day, presence or absence of feelings of happiness, experience of stress during the month prior to the study, subjective health perception, smoking history, ability to connect with neighbors, trust in others, quality of sleep, and exercise–sleep interactions. The results of ordinal logistic regression analysis revealed that the period from the onset of exercise, age, subjective health perception, quality of sleep, stress, and exercise–sleep interaction were significant predictors of frailty severity (Table 3). The results of ordinal logistic regression analysis showed that the period from the start of exercise, age, poor subjective health perception, poor quality of sleep, stress, and exercise–sleep interaction significantly contributed to the model (Table 4). The Nagelkerke coefficient of determination adjusted for R^2 , which represents the contribution rate of the regression equation, was 0.334.

Discussion

In this study, the percentages of participants who were prefrail or frail were 62.2% and 17.1%, respectively. Several studies^{17, 18} examined the prevalence of pre-frailty and frailty based on the Japan Cardiovascular Health Study or Cardiovascular Health Study criteria and reported that the prevalence of pre-frailty and frailty were in the ranges of 51.9–65.2% and 8.3–11.2% in community-dwelling older adults, respectively. Therefore, the health status of the participants included in our study was similar or slightly lower than those of community-dwelling older adults in previous studies^{17, 18}. In this study, the prevalence values in the cases of no habitual exercise (low activity level), which is one of the factors of frailty, were 56.5% and 92.1% for participants with pre-frailty and frailty, respectively. A systematic review that investigated the prevalence of each frailty item reported that in community-dwelling older adults aged ap-

Table 1 Self-administered questionnaire

Please specify your sex (male or female).
1. Male, 2. female

Please specify your age (60, 70, or over 80 years old).
1. 60s, 2. 70s, 3. Over 80s

Please specify your height and weight (please write a numerical value).

Do you eat three meals a day?
1. Yes, 2. No

Do you smoke?
1. Smoking, 2. Not smoking, 3. Smoking in the past

Please specify your health status.
1. Very well, 2. Fairly well, 3. Badly, 4. Very badly

Are you happy?
1. Very well, 2. Fairly well, 3. Badly, 4. Very badly

Did you have stress (anxiety/trouble) during past month?
1. Tremendous, 2. Average, 3. Some, 4. None

How do you have connections with neighbors?
1. Very good, 2. Fairly good, 3. Sometimes, 4. Almost never

Trust in others
1) Do you think participants are in general trust worthy?
2) Do you think that a lot of participants try to take advantage of others when they have an opening?
3) Do you think that in many cases, participants try to be helpful to others?
1. Do not think at all, 2. Do not think much, 3. I think, 4. I think very well

Do you exercise?
1. Yes, 2. No

How long do you exercise each time you find an opportunity for exercise? (please write a numerical value)

How long did the exercise last? (please write a numerical value)

Were you well-rested after sleep during the past month?
1. Very satisfied, 2. Fairly satisfied, 3. Poorly satisfied, 4. Not satisfied at all

Are you satisfied with your overall sleep quality?
1. Very satisfied, 2. Fairly satisfied, 3. Poorly satisfied, 4. Not satisfied at all

proximately 75 years, the prevalence of no habitual exercise ranged from 12.7% to 67.0%¹⁷⁾. Comparing the findings of these previous studies with the community-dwelling older adults in this study demonstrated that the lack of habitual exercise constitutes a major contributory factor for the onset of frailty.

The results of ordinal logistic regression analysis revealed that the period from the onset of exercise, age, subjective health perception, quality of sleep, stress, and exercise–sleep interaction were significant predictors of frailty severity. Previous studies^{5, 7, 9, 19–28)} also reported that the period from the onset of exercise, age, subjective health perception, quality of sleep, and stress were associated with frailty. Therefore, our results support those of previous studies. Age is known to positively correlate with frailty severity¹⁹⁾. Kojima *et al.*¹⁹⁾ investigated the prevalence of frailty based on age and reported an increased frailty rate for those in their

late 70s. In our study, the prevalence of frailty increased with age. Compared with participants in their 60s, the prevalence of frailty in participants in the 70s and 80s was 1.65 and 3.13 times higher, respectively. BMI is also related to frailty, as demonstrated in previous reports^{20, 21)}. A long-term observational study^{20, 21)} of men from 1970 to 2007 examined the relationship between long-term changes in BMI in four groups: 1) no change in normal range, 2) consistent overweight, 3) weight gain, and 4) weight loss and the appearance of frailty. The results showed that weight loss presents a risk of developing frailty²⁰⁾. Conversely, there have been reports on the association between obesity (high BMI) and frailty, and many reports have shown that the association between BMI and frailty is U-shaped²¹⁾. In the present study, there was an effect on frailty severity at high BMI levels. Regarding subjective health perception, it is known that high subjective health perceptions are associated with high

Table 2 Patient characteristics

Variable	Category	ALL (n=672)	Robust group (n=139)	Pre-frailty group (n=418)	Frailty group (n=115)	P value	Post-test
Age (years)	60s/70s/over 80s	278/293/101	67/56 /16	170/192 /56	41/45/29	0.01	b), c)
Sex	Male/Female	317/355	76/63	192/226	49/66	0.72	
BMI (kg/m ²)		22.9 ± 3.2	23.9 ± 20.8	23.0 ± 3.2	23.5 ± 3.5	0.01	a), b)
Eat three meals a day	Yes/No	616/56	132/7	384/34	100/15	0.07	
History of smoking	Smoking/Smoking in the past/Not smoking	49/145/478	11/29/99	31/93/294	7/23/85	0.48	
Subjective health perception	Very well and fairly well/badly and very badly	532/140	129/10	338/80	65/50	<0.01	a), b), c)
Happiness	Very well and fairly well/badly and very badly	610/62	134/5	382/36	94/21	<0.01	b), c)
Stress during past 1 month	Tremendous and average/some and none	380/292	63/76	232/186	85/30	<0.01	b), c)
Connect with neighbor	Very goodl and fairly good/sometimes and almost never	626/46	136/3	392/26	98/17	<0.01	b)
Trust in others	Do not think at all and do not think much/I do think and I think very well	237/435	39/100	146/272	52/63	0.02	b)
Habitual exercise	Yes/No	377/295	123/16	217/201	37/78	<0.01	a), b), c)
Time per opportunity for exercise (hours)		0.7 ± 1.1	1.2 ± 1.5	0.6 ± 0.9	0.3 ± 0.6	<0.01	a), b), c)
Period from exercise start (years)		6.5 ± 10.7	14.1 ± 14.5	5.1 ± 8.8	2.2 ± 5.6	<0.01	a), b), c)
Rest from sleep during past 1 month	Very satisfied and fairly satisfied/poorly satisfied and not satisfied at all	544/128	124/15	344/74	76/39	<0.01	b), c)
Quality of sleep	Very satisfied and fairly satisfied/poorly satisfied and not satisfied at all	278/394	78/61	175/243	25/90	<0.01	a), b), c)
Good exercise - good sleep interaction		312	111	177	24	<0.01	a), b), c)
Good exercise - poor sleep interaction		65	12	40	13		
Poor exercise - good sleep interaction		232	13	167	52		
Poor exercise - poor sleep interaction		63	3	34	26		

Post-test: a) robust group vs. pre-frailty group, b) robust group vs. frailty group, c) pre frailty group vs. frailty group. BMI: body mass index.

levels of activity²²⁾ and decreased loneliness²³⁾. Therefore, it is presumed that high subjective health perceptions are associated with increased activity and prevention of frailty. Stress has generally been shown to increase vulnerability with advancing age. Frailty is defined as “a state of reduced resilience to stress due to the decline in reserve capacity associated with aging²¹⁾”. Stress is known to affect the severity of frailty. In fact, the results of this study also show that the proportion of participants with stress increases with frailty severity. Sleep quality has also been reported to be related to frailty⁹⁾. Several possible underlying mechanisms may help explain the association between sleep disturbances and frailty. (1) Sleep symptoms may be markers of comorbidities and poor health status that increase the likelihood of frailty²⁴⁾. Although we adjusted for multiple disease covariates in the present study, we could not exclude this possibility. (2) Disrupted circadian rhythms induced by sleep disorders may contribute to the dysregulation of the immune system with increased systemic inflammatory factors that contribute to the development of frailty²⁵⁾. (3) Sleep disorders may contribute to increased oxidative stress levels and alterations in metabolic pathways favoring catabolism, which could serve as a combined risk for the development of frailty²⁶⁾. (4) Dis-

turbed sleep patterns may reduce growth hormone, insulin-like growth factor-1, and sex hormones (such as testosterone secretion) levels, which in turn enhance muscle proteolysis, thus leading to sarcopenia and frailty²⁷⁾. Regarding the exercise period, longer periods from the onset of exercise were associated with lower frailty severity⁷⁾. Accordingly, the period from the onset of exercise decreased with frailty severity in this study. In addition to the duration of exercise, other factors, such as frequency and content, are involved in preventing frailty severity. For example, high frequency of exercise⁵⁾ and exercise, including resistance training²⁸⁾, are associated with the exacerbation of frailty severity.

In the present study, poor-exercise–poor-sleep interaction yielded a 3.5-fold higher OR in frailty compared with OR values attributed to good-exercise–good-sleep interactions. In other words, participants with good-exercise–good-sleep patterns had a lower risk of frailty than those with poor-exercise–poor-sleep patterns. The odds ratio of poor exercise to good sleep interaction was 3.09, indicating that exercise had a strong influence on the severity of frailty. The reason for this may be related to the fact that this study used the frailty index, which reflects physical frailty, and we did not assess sleep in detail. As noted in the Introduction,

Table 3 Percentage of each factor of frailty in pre-frailty and frailty participants

	Pre-frailty group (n=418)	Frailty group (n=115)	P value
Weight loss (%)	8.1	41.7	<0.01
Exhaustion (%)	17.5	78.3	<0.01
Low memory (%)	5.7	27.8	<0.01
Slow gait speed (%)	57.2	93.9	<0.01
Low activity level (%)	56.5	92.1	<0.01

Table 4 Ordinal logistic regression analysis

Variable	Odds ratio	95% confidence interval		Regression coefficient	Standard error	P value
		lower limit	upper limit			
60 years old	1.00			Reference		
70 years old	1.65	1.15	2.37	0.50	0.19	0.01
80 years old over	3.13	1.86	5.27	1.14	0.27	<0.01
Female	1.00			Reference		
Male	0.77	0.52	1.15	-0.255	0.20	0.21
BMI	1.08	1.03	1.14	0.08	0.03	<0.01
Eat three meals	1.00			Reference		
Not eat three meals	1.04	0.57	1.91	0.04	0.31	0.89
Not smoking	1.00			Reference		0.55
Current smoking	0.84	0.42	1.67	-0.178	0.35	0.61
Smoking in the past	1.33	0.83	2.13	0.29	0.24	0.23
Good subjective health perception	1.00			Reference		
Poor subjective health perception	2.12	1.36	3.30	0.75	0.23	<0.01
Happiness	1.00			Reference		
Not happiness	1.67	0.92	3.03	0.51	0.30	0.09
Not have stress during past 1 month	1.00			Reference		
Have stress during past 1 month	1.62	1.14	2.32	0.49	0.18	0.01
Connect good neighbor	1.00			Reference		
Connect poor neighbor	1.42	0.70	2.88	0.35	0.36	0.33
Good trust in others	1.00			Reference		
Poor trust in others	1.18	0.83	1.68	0.17	0.18	0.35
Time per opportunity for exercise (hours)	0.92	0.76	1.12	-0.081	0.10	0.42
Period from exercise start (years)	0.96	0.94	0.98	-0.044	0.01	<0.01
Good quality of sleep	1.00			Reference		
Poor quality of sleep	1.88	1.30	2.73	0.63	0.19	<0.01
Good exercise - good sleep interaction	1.00			Reference		
Good exercise - poor sleep interaction	1.86	0.99	3.49	0.62	0.32	0.05
Poor exercise - good sleep interaction	3.09	1.90	5.04	1.13	0.25	<0.01
Poor exercise - poor sleep interaction	3.50	1.75	7.00	1.25	0.35	<0.01

BMI: body mass index. Model: χ^2 $P < 0.05$, Nagelkerke $R^2 = 0.334$.

a relationship exists between exercise and sleep, and good sleep is essential for good exercise¹²). Moreover, the OR value increased if sleep was good (3.09 vs. 3.50). Therefore, we consider that the combination of good exercise and good sleep is more effective than good exercise alone. Several studies have reported the effects of exercise or sleep alone on frailty, but the interaction between exercise and sleep has not been examined. To the best of our knowledge, this is the first study to report an interactive effect of exercise and sleep on frailty severity. Multiple factors, including inflam-

mation, oxidative stress, and decreased levels of anabolic hormones, contribute to the development of frailty²⁹⁻³¹). As mentioned above, sleep disturbances negatively affect inflammation, oxidative stress, and anabolic hormones. Conversely, habitual exercise had a positive effect on these factors. Habitual exercise decreased the markers of inflammation, such as interleukin-6 (IL-6) and C-reactive protein, and increased activity was associated with higher levels of anti-inflammatory mediators, such as adiponectin and IL-10²⁹). Chronic exercise also reduces oxidative stress associ-

ated with aging²⁹). Additionally, prolonged exercise may improve the levels of an anabolic hormone, insulin-like growth factor-1²⁹). Thus, although habitual exercises or good-sleep patterns alone may reduce the risk of frailty, the combination of these two factors will have a synergistic effect and further reduce the risk of frailty.

The three limitations of this study are as follows. First, mental frailty was not considered in this study. There are three aspects of frailty: physical, social, and mental. A previous study³²) reported a worse prognosis for multifaceted frailty, including physical, mental, and social frailty, compared with physical frailty alone. Therefore, future studies are needed to develop models to predict improvements attributed to multifaceted frailty, including mental frailty. Second, the relationship between disease severity and frailty severity was not considered in this study. We were unable to investigate the presence of the disease. These diseases have been found to influence frailty severity³³). Future prospective studies should examine the interactions between the disease and sleep. Thirdly, the assessment of sleep was rough. Sleep can be assessed in several ways, including the Pittsburgh Sleep Quality Index, sleep duration, sleep war-time, and number of mid-wake awakenings. However, this study was conducted using a questionnaire because it was

a large study. Therefore, it is difficult to evaluate sleep in detail. In the future, a detailed evaluation of sleep and its interaction with exercise should be conducted.

Conclusion

Our results suggest that a combination of good exercise and good sleep is needed to prevent the exacerbation of frailty in community-dwelling older adults.

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