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Original article

Association of locomotive activity with sleep latency and cognitive function of elderly patients with cardiovascular disease in the maintenance phase of cardiac rehabilitation

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A B S T R A C T

Background: Because of the advanced age of patients with cardiovascular disease (CVD), prevention of sleep disorder and dementia is a priority for cardiac rehabilitation (CR) during their long-term care. This study aimed to investigate the association of physical activity with sleep quality and cognitive function in elderly patients with CVD in the CR maintenance phase.

Methods: We conducted a multicenter study through the Clinical Exercise Physiology Association Japan network, which included 102 elderly patients (mean age, 74 ± 7.4 years) with CVD undergoing phase III CR at 6 institutions. Physical activity was assessed using a triaxial accelerometer for 7 consecutive days and was classified as locomotive and household activities. Physical fitness was assessed via 6-min walking distance (6MD), hand grip power, 10-m walking speed, one leg standing time with eyes open, and 10 times sit-to-stand tests. Sleep quality and cognitive function were evaluated using the Pittsburgh sleep quality index (PSQI) and mini-mental state examination (MMSE) scores, respectively.

Results: The patients performed 5506.8 ± 3743.6 steps/day and scored 5.8 ± 3.5 points in the PSQI and 28.4 ± 1.7 points in the MMSE. Sleep latency and MMSE scores correlated with locomotive activity, but not with household activity. Locomotive activity and 6MD were independent predictors of sleep latency and MMSE score, respectively. When patients with heart failure were excluded, the relationship between sleep latency and locomotive activity was preserved, but the relationship between exercise tolerance and cognitive function disappeared.

Conclusion: Locomotive activity and exercise tolerance are associated with sleep latency and cognitive function in elderly patients with CVD continuing phase III CR. However, in this study, the relationship between exercise tolerance and cognitive function was offset by the presence of heart failure.

Introduction

The risk of cardiovascular death reduces with an increase in daily physical activity, irrespective of sex, in the general Japanese population [1]. In a meta-analysis, physical activity was associated with a marked decrease in cardiovascular and all-cause mortality, with the higher physical activity group showing a cardiovascular risk reduction of 30% compared to the lower physical activity group

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[2]. However, progress in medical technology and availability of advanced medical treatment have led to a marked increase in the relapse of cardiovascular disease (CVD). The benefit of cardiac rehabilitation (CR) in the secondary prevention of CVD has been established. CR prevents the progression of mild coronary atherosclerosis in patients with acute coronary syndrome, and each 1-metabolic equivalent (MET) increase in their exercise capacity confers a 12% improvement in their survival [3,4]. Therefore, CR should be continued lifelong; however, there are few phase III CR centers and little evidence available.

Because of the advanced age of patients with CVD, prevention of sleep disorder and dementia is a priority in the maintenance phase of their long-term care. Physical inactivity in elderly patients with CVD leads to frailty and impaired cognitive function and increases the risk of self-management failure and recurrence of CVD [5]. Thus, it is extremely important to increase physical activity by providing continuous support to elderly patients with CVD.

Physical activity can be classified into locomotive (walking) or household activities, such as cleaning and washing [6]. It has been reported that physical activity was closely related to sleep conditions, and that a lack of physical activity is related to a decline in cognitive function [7,8]. Decreased physical activity with aging is associated with sleep inefficiency in the form of difficulty falling asleep and increased waking hours after the onset of sleep. A previous study has reported that daily physical activity is an independent predictor of insomnia in the elderly [9]. Moreover, dementia and impaired cognitive function are not only caused by genetic factors but also by an unhealthy lifestyle [10]. Furthermore, one study has suggested that daily walking activity is correlated with hippocampal volume [11]. These reports suggest that physical activity is closely related to sleep quality and cognitive function; however, most of these studies were conducted in healthy elderly people, and there are no such reports on elderly patients with CVD. In addition, it is unclear which of the two categories of physical activity (walking or daily activities) has a more significant influence on sleep quality and cognitive function.

Recently, the Clinical Exercise Physiology Association (CEPA) Japan was founded to improve the skills and advance the social status of health fitness programmers in clinical practice. CEPA Japan was approved as a subcommittee of the Japanese Association of Exercise Therapy and Prevention in 2014 and has been working through information sharing via mailing lists and case studies.

The present study examined the hypothesis that higher walking and daily activities in elderly patients with CVD during phase III CR were associated with better sleep quality and cognitive function and less requirement for long-term care. Accordingly, we investigated the relationship between physical activity or physical fitness and sleep quality and cognitive function in elderly patients with CVD in the maintenance phase by conducting a multicenter study through the CEPA Japan network.

Materials and methods

Study design

This was a cross-sectional study in elderly patients (aged ≥65 years) with CVD.

Subjects

We studied 102 elderly patients with CVD who were enrolled in phase III of CR at 6 institutions in Japan between September and December 2016. Exclusion criteria were end-stage renal disease, inflammatory diseases, and non-cooperation in the research. All patients were participating in institute-based CR at least once per week. The phase III CR program consisted of a total of 60–90 min of stretching, resistance training, and aerobic exercise at each institution. All participating institutions in this study employed a health fitness programmer who acquired a registered instructor for CR. This study was approved by the ethical committee of the Takeda Hospital Group (approval no. 20160005). Written informed consent was obtained from all patients prior to the study.

Cardiovascular risk factors and cardiac function

Obesity was defined as a body mass index (BMI) >25 kg/m^2; hypertension as systolic blood pressure ≧140 mmHg or diastolic blood pressure ≧90 mmHg; dyslipidemia as low-density lipoprotein (LDL) cholesterol ≧140 mg/dl, high-density lipoprotein (HDL) cholesterol <40 mg/dl, or triglycerides ≧150 mg/dl; and diabetes as fasting plasma glucose ≧126 mg/dl, casual plasma glucose ≧200 mg/dl, or HbA1c ≧6.5%.

Past medical history was collected from medical records. Height and body weight were measured for all patients. Blood pressure was measured from the right arm of the seated participant after at least 15 min of rest. Non-fasting blood samples were collected to determine the serum levels of triglycerides, HDL cholesterol, LDL cholesterol, plasma glucose, HbA1c, estimated glomerular filtration rate, brain natriuretic peptide (BNP), and C-reactive protein.

Cardiac function was measured through the left ventricular end-diastolic dimension and left ventricular ejection fraction (LVEF) via echocardiography.

Physical activity and physical fitness

Physical activity was assessed using a triaxial accelerometer (HJA-750C Active Style Pro; OMRON HEALTHCARE Co., Ltd., Kyoto, Japan). HJA-750C can measure not only the intensity of walking but also the intensity of daily activity with accuracy using a simple algorithm for classification by capturing changes in body movements and postures [12]. The accelerometer was worn on the right waist for at least 10 h and analyzed data that could be measured during waking hours for 7 consecutive days. The accelerometer calculated the average value for 7 consecutive days using the special software version 2.0. Values evaluated were number of steps, MET hours (MET-h), locomotive activity, household activity, and walking time. In addition, the subjects were classified into three groups based on the tertile of total physical activity. Physical fitness was assessed via 6-min walking distance (6MD), hand grip power, 10-m walking speed, one leg standing time with eyes open, and 10 times sit-to-stand tests.

Sleep quality

Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI), a self-reported measure of the perception of habitual sleep quality. The PSQI measures 7 sleep domains (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month) on a scale of 0–3. A global score (0–21 points) is obtained by summing the scale domain scores. A high global score (≥5.5) indicates poor sleep [13]. Internal consistency reliability of the PSQI is typically in the range of 0.77–0.83 [14]. Concurrent and discriminative validity of the PSQI has been demonstrated with comparison to multiple sleep questionnaires, polysomnography, and clinical evaluation.

Long-term care insurance and cognitive function

We obtained information on the Japanese long-term care insurance classification from patient medical records. The long-

Table 1
Clinical characteristics of the study by tertile of total physical activity.

	All (186.0–905.1 kcal/day) $n = 102$	Low (186.0–405.7 kcal/day) $n = 34$	Moderate (407.7–594.1 kcal/day) $n = 34$	High (601.3–905.1 kcal/day) $n = 34$	*p*-value
Age (years)	74.1 ± 7.4	76.2 ± 8.8	74.2 ± 6.2	71.8 ± 6.5	0.051
Sex (male/female)	64/38	20/14	18/16	26/8	0.113
Height (cm)	160.3 ± 8.4	158.4 ± 9.6	160.2 ± 7.3	162.3 ± 7.8	0.155
Body weight (kg)	58.8 ± 9.9	55.7 ± 10.1	59.3 ± 10.4	61.5 ± 8.4 *	0.045
Body mass index (kg/m^2)	22.8 ± 3.3	22.1 ± 3.1	23.1 ± 4.0	23.3 ± 2.8	0.332
Systolic blood pressure (mmHg)	123.4 ± 13.9	123.9 ± 13.9	121.1 ± 16.2	125.4 ± 11.3	0.435
Diastolic blood pressure (mmHg)	68.7 ± 11.4	68.3 ± 12.5	68.0 ± 12.4	69.8 ± 9.3	0.782
Heart rate (bpm)	74.2 ± 12.4	76.9 ± 11.0	74.7 ± 13.6	70.9 ± 12.2	0.133
LVDd (mm)	48.8 ± 7.3	47.9 ± 6.7	50.0 ± 7.3	48.4 ± 7.9	0.486
LVEF (%)	57.8 ± 13.7	54.7 ± 14.4	56.7 ± 14.3	62.2 ± 11.5	0.069
Alcoholic drinks, *n* (%)	24 (23.5)	2 (5.9)	10 (29.4)	12 (35.3)	0.010
Current Smoker, *n* (%)	3 (2.9)	3 (8.8)	0 (0.0)	0 (0.0)	0.045
Duration of phase III CR (years)	5.3 ± 5.0	4.0 ± 4.0	5.3 ± 5.1	6.6 ± 5.4	0.065
Cardiovascular disease					
Myocardial infarction, *n* (%)	52 (50.9)	14 (41.2)	18 (52.9)	20 (58.8)	0.333
Angina pectoris, *n* (%)	18 (17.6)	7 (20.6)	8 (23.5)	3 (8.8)	0.243
Valvular heart disease, *n* (%)	16 (15.7)	6 (17.6)	4 (11.8)	6 (17.6)	0.743
Aortic disease, *n* (%)	7 (6.9)	4 (11.8)	2 (5.9)	1 (2.9)	0.342
Heart failure, *n* (%)	35 (34.3)	18 (52.9)	9 (26.5)	8 (23.5)	0.019
Intervention					
PCI, *n* (%)	54 (52.9)	16 (47.1)	20 (58.8)	18 (52.9)	0.624
Open heart surgery, *n* (%)	32 (31.4)	11 (32.4)	10 (29.4)	11 (32.4)	0.955
Pacemaker, ICD, *n* (%)	5 (4.9)	3 (8.8)	0 (0.0)	2 (5.9)	0.229
Coronary risk factors					
Obesity, *n* (%)	21 (20.6)	6 (17.6)	9 (26.5)	6 (17.6)	0.583
Hypertension, *n* (%)	78 (76.5)	29 (85.3)	23 (67.6)	26 (76.5)	0.230
Dyslipidemia, *n* (%)	61 (59.8)	19 (55.9)	20 (58.8)	22 (64.7)	0.752
Diabetes Mellitus, *n* (%)	39 (38.2)	15 (44.1)	17 (50.0)	7 (20.6)	0.031
Medication					
ACE, *n* (%)	21 (20.6)	6 (17.6)	8 (23.5)	7 (20.6)	0.835
ARB, *n* (%)	48 (47.1)	16 (47.1)	11 (32.4)	21 (61.8)	0.052
β-blocker, *n* (%)	64 (62.7)	25 (73.5)	20 (58.8)	19 (55.9)	0.272
Calcium-channel blocker, *n* (%)	47 (46.1)	19 (55.9)	15 (44.1)	13 (38.2)	0.331
Diuretic, *n* (%)	32 (31.4)	11 (32.4)	12 (35.3)	9 (26.5)	0.727
Antiplatelet, *n* (%)	67 (65.7)	18 (52.9)	26 (76.5)	23 (67.6)	0.119
Anticoagulant, *n* (%)	30 (29.4)	8 (23.5)	15 (44.1)	7 (20.6)	0.068
Vasodilator, *n* (%)	19 (18.6)	4 (11.8)	4 (11.8)	11 (32.4)	0.042
Statin, *n* (%)	55 (53.9)	18 (52.9)	17 (50.0)	20 (58.8)	0.759
Hypnotics, *n* (%)	18 (17.6)	6 (17.6)	8 (23.5)	4 (11.8)	0.445
Laboratory Examination					
Triglycerides (mg/dl)	131.5 ± 82.7	147.6 ± 105.6	127.4 ± 69.0	120.2 ± 68.8	0.684
HDL Cholesterol (mg/dl)	56.0 ± 14.9	53.7 ± 16.2	57.6 ± 15.4	56.7 ± 13.3	0.547
LDL Cholesterol (mg/dl)	98.4 ± 29.1	102.0 ± 32.5	99.7 ± 25.4	93.5 ± 29.3	0.441
Plasma Glucose (mg/dl)	118.0 ± 35.2	128.1 ± 42.0	118.9 ± 36.4	107.2 ± 21.9	0.188
HbA1c (%)	6.2 ± 0.8	6.6 ± 1.1	6.2 ± 0.5	5.9 ± 0.5 **	0.016
eGFR (ml/min/1.73 m^2)	57.1 ± 15.5	55.5 ± 13.3	57.0 ± 19.7	59.0 ± 12.5	0.655
BNP (pg/ml)	128.9 ± 153.7	185.7 ± 187.7	129.8 ± 163.8	71.0 ± 60.0 *	0.002
CRP (mg/dl)	0.14 ± 0.52	0.24 ± 0.89	0.11 ± 0.19	0.08 ± 0.11	0.711

Values are expressed as the mean ± SD.
p-values are indicated as: * $p < 0.05$, ** $p < 0.01$ vs. low group. Underlines are a characteristic points by residual analysis.
LVDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; CR, cardiac rehabilitation; PCI, percutaneous coronary intervention; ICD, implantable cardioverter defibrillators; ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; CRP, C-reactive protein.

term care insurance system classifies frail older adults into 7 levels (support need levels: 1 and 2 and care need levels: 1 to 5; a larger number indicates a more severe level) using a nationally standardized and validated algorithm. We calculated the certification rate of long-term care need for all 7 levels.

Cognitive function was evaluated using the Mini Mental State Examination (MMSE) score. The MMSE is used to evaluate time, orientation, immediate memory, attention, calculation ability, short-term memory, language repetition, reading and comprehension, presentation skills, operational capabilities, and other cognitive skills. The MMSE cut-off score is 23/24 points for cognitive dysfunction and 27/28 points for mild cognitive impairment [15,16].

Statistical analysis

All data are expressed as mean ± SD. The Shapiro–Wilk test was used to identify the normality of data. The one-way analysis of variance or Kruskal–Walls test followed by post hoc Tukey test was used to evaluate the difference between the three groups by normal or non-normal distributions. Difference for categorical variables was assessed using the Chi square test followed by residual analysis. Correlations between physical activity, sleep quality, cognitive function, and physical fitness were determined using Pearson's coefficient and Spearman's rank order coefficient by normal or non-normal variables. Forward-backward stepwise multiple regression analysis was used to determine independent predictors of sleep latency and MMSE score. All statistical analyses were performed using SPSS 19.0J for Windows (IBM Corp., Armonk, NY, USA). Values of $p < 0.05$ were considered statistically significant.

Results

Clinical characteristics and data measured

Clinical characteristics of the patients are presented in Table 1. The patients had a mean age of 74.1 ± 7.4 years and underwent phase III CR for 5.3 ± 5.0 years. The most common CVD among the patients was myocardial infarction (50.9%) followed by heart failure (34.3%). The high total physical activity group showed significantly higher values for body weight, higher frequency of alcohol drinkers, significantly lower prevalence of diabetes mellitus, and lower levels of HbA1c and BNP compared to the low total physical activity group.

All measured parameters are presented in Table 2. Physical activity consisted of 5506.8 ± 3743.6 steps/day (men: 6078.1 steps/day, women: 4544.2 steps/day), 4.5 ± 2.8 MET-h/day, 158.0 ± 106.5 kcal/day of locomotive activity, 497.0 ± 165.7 kcal/day of household activity, 78.3 ± 40.0 min/day of walking time, 5.8 ± 3.5 points in PSQI global score, 28.4 ± 1.7 points in MMSE, and 10.8% certification rate of long-term care need (support need levels and care need levels). The variables of physical activity and physical fitness showed a significant difference among the three groups. Moreover, the points of sleep latency and habitual sleep efficiency of the high group in PSQI were smaller than those of the low group. The sleep latency time of the high and moderate groups were significantly shorter than those of the low group.

Correlation of sleep latency with physical activity

Correlations of the various components of physical fitness with locomotive and household activities are presented in Table 3. Locomotive activity showed a significant correlation with age, BNP level, 6MD, hand grip power, 10-m normal and maximum walking speeds, one leg standing time with eyes open, and 10 times sit-to-stand, sleep latency, and MMSE score. On the contrary, household activity showed a significant correlation with age, LVEF, 6MD, 10-m normal and maximum walking speeds, one leg standing time with eyes open, and 10 times sit-to-stand. Thus, sleep latency and MMSE score were correlated with locomotive activity, but not with household activity. As these results may be affected by heart failure, we performed a sub-analysis excluding patients with heart failure. As a result, locomotive activity showed a significant correlation with all physical fitness and sleep latency, but not MMSE score. Household activity showed a significant correlation with only one leg standing time with eyes open.

Multivariate analysis for sleep latency and MMSE score

We performed a forward-backward stepwise multiple regression analysis to identify independent predictors of sleep latency and MMSE score. We analyzed the factors of single correlation with sleep latency and MMSE before performing multiple regression analysis. From the results, significantly related factors were used as independent variables. The examined independent variables for sleep latency were locomotive activity, mean number of steps, and MET-h from significance of univariate analysis, after adjustment for age, sex, LVEF, and hypnotics. The results revealed that locomotive

Table 2
Results of measurement parameters by tertile of total physical activity.

	All (186.0–905.1 kcal/day) $n = 102$	Low (186.0–405.7 kcal/day) $n = 34$	Moderate (407.7–594.1 kcal/day) $n = 34$	High (601.3–905.1 kcal/day) $n = 34$	p-value
Physical activity					
Steps (steps/day)	5506.8 ± 3743.6	2819.1 ± 2054.2	5178.0 ± 2048.8 **	8523.2 ± 4188.9 ** ††	< 0.001
Metabolic equivalent hours (MET-h/day)	4.5 ± 2.8	2.0 ± 1.2	4.1 ± 1.5 **	7.2 ± 2.5 ** ††	< 0.001
Locomotive activity (kcal/day)	158.0 ± 106.5	73.9 ± 48.2	142.2 ± 65.7 **	257.8 ± 101.4 ** ††	< 0.001
Household activity (kcal/day)	338.9.±105.0	246.8 ± 337.1	337.1 ± 65.1 **	432.6 ± 93.4 ** ††	< 0.001
Walking time (min/day)	78.3 ± 40.0	45.2 ± 20.1	75.2 ± 24.6 **	114.5 ± 37.0 ** ††	< 0.001
Physical fitness					
6-min walking distance (m)	415.9 ± 97.0	367.9 ± 95.8	404.1 ± 68.3	475.7 ± 93.6 ** ††	< 0.001
Hand grip power (kg)	27.2 ± 7.4	24.5 ± 7.7	26.0 ± 6.6	31.0 ± 6.4 ** †	0.001
10 m-normal walking speed (m/s)	1.25 ± 0.27	1.1 ± 0.3	1.3 ± 0.2 **	1.4 ± 0.2 ** †	< 0.001
10 m-max walking speed (m/s)	1.70 ± 0.40	1.5 ± 0.4	1.7 ± 0.3 *	1.9 ± 0.3 ** ††	< 0.001
One leg standing time with eyes open (sec)	41.4 ± 41.0	31.5 ± 36.6	38.4 ± 36.4	54.4 ± 46.9 *	0.042
10 time sit-to-stand (s)	18.0 ± 8.2	20.4 ± 9.8	18.3 ± 6.8	15.3 ± 7.2 *	0.014
PSQI score and sleep status					
C1: Subjective global score (points)	1.0 ± 0.6	1.1 ± 0.6	1.1 ± 0.5	0.9 ± 0.6	0.313
C2: Sleep latency (points)	1.1 ± 1.2	1.5 ± 1.5	1.1 ± 1.0	0.7 ± 0.9 **	0.018
C3: Sleep duration (points)	1.0 ± 0.9	1.0 ± 1.0	1.0 ± 0.9	0.9 ± 0.7	0.998
C4: Habitual sleep efficiency (points)	0.7 ± 1.1	0.9 ± 1.3	0.9 ± 1.3	0.3 ± 0.6 * †	0.036
C5: Sleep disturbances (points)	1.1 ± 0.7	1.0 ± 0.7	1.0 ± 0.6	1.1 ± 0.9	0.980
C6: Use of sleeping medication (points)	0.6 ± 1.1	0.6 ± 1.0	0.5 ± 1.1	0.7 ± 1.2	0.637
C7: Daytime dysfunction (points)	0.5 ± 0.7	0.5 ± 0.6	0.6 ± 0.8	0.3 ± 0.6	0.340
C1-7: PSQI global score (points)	5.8 ± 3.5	6.6 ± 4.1	6.0 ± 3.4	4.9 ± 2.5	0.187
PSQI global score ≧5.5 points, n (%)	50 (49.0)	18 (52.9)	16 (47.1)	16 (47.1)	0.855
Total sleep time (h)	6.7 ± 1.2	6.7 ± 1.6	6.6 ± 1.2	6.7 ± 0.9	0.998
Sleep latency (min)	23.4 ± 27.0	35.7 ± 39.4	18.8 ± 15.5 *	15.9 ± 14.3 **	0.041
Long-term care insurance					
Support need levels, n (%)	10 (9.8)	6 (17.6)	3 (8.8)	1 (2.9)	0.122
Care need levels, n (%)	1 (1.0)	1 (2.9)	0 (0.0)	0 (0.0)	0.364
Cognitive function					
MMSE (points)	28.4 ± 1.7	28.2 ± 1.8	28.6 ± 1.6	28.4 ± 1.5	0.616
MMSE ≦23: Cognitive dysfunction, n (%)	1 (1.0)	1 (2.9)	0 (0.0)	0 (0.0)	0.364
MMSE ≦27: Mild cognitive impairments, n (%)	24 (23.5)	8 (23.5)	7 (20.6)	9 (26.5)	0.849

Values are expressed as the mean ± SD.
p-values are indicated as: * $p < 0.05$, ** $p < 0.01$ vs. low group, † $p < 0.05$, †† $p < 0.01$ vs. moderate group.
PSQI, Pittsburgh sleep quality index; MMSE, mini mental state examination.

Table 3
Correlations of the various components with locomotive and household activities.

	Locomotive activity		Household activity	
	r	*p*-value	*r*	*p*-value
Age	−0.355	<0.001	−0.264	0.007
Body mass index	−0.023	0.816	0.148	0.137
LVEF	0.107	0.290	0.310	0.002
eGFR	0.129	0.202	0.161	0.112
BNP	−0.266	0.014	−0.217	0.046
6-min walking distance	0.540	<0.001	0.235	0.018
Hand grip power	0.560	<0.001	0.136	0.173
10 m-normal walking speed	0.529	<0.001	0.343	<0.001
10 m-max walking speed	0.617	<0.001	0.270	0.006
One leg standing time with eyes open	0.335	0.001	0.341	<0.001
10 time sit-to-stand	−0.320	0.001	−0.195	0.049
PSQI global score (points)	−0.193	0.051	−0.148	0.138
Total sleep time (h)	0.108	0.280	−0.056	0.575
Sleep latency (min)	−0.222	0.025	−0.098	0.326
MMSE	0.209	0.036	0.045	0.652

Values are expressed as correlation coefficients.
LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; PSQI, Pittsburgh sleep quality index; MMSE, mini mental state examination

Table 4
Stepwise regression analysis for sleep latency and MMSE.

a. Independent predictors of sleep latency	*β*	*p*-value
Age	−0.046	0.661
Sex	−0.044	0.683
LVEF	−0.019	0.852
Hypnotics	0.011	0.913
Steps	0.004	0.981
Metabolic equivalent hours	0.052	0.796
Locomotive activity	−0.213	0.034
b. Independent predictors of MMSE	***β***	***p*-value**
Age	−0.139	0.225
Sex	0.133	0.193
LVEF	0.091	0.358
Steps	0.047	0.708
Locomotive activity	0.009	0.939
6-min walking distance	0.293	0.003
10 m-max walking speed	0.013	0.939
One leg standing time with eyes open	0.088	0.443

β standardized partial regression coefficient.
LVEF, left ventricular ejection fraction; MMSE, mini mental state examination.

activity was an independent predictor of sleep latency (Table 4). This result remained the same even when patients with heart failure were excluded. The examined independent variables for MMSE score were mean number of steps, 6MD, 10-m maximum walking speed, and one leg standing time with eyes open, after adjustment for age, sex, and LVEF. The results revealed that 6MD was an independent predictor of MMSE score. However, age was only an independent predictor of MMSE score when patients with heart failure were excluded.

Discussion

In this study, elderly patients with CVD during phase III CR performed 5506.8 ± 3743.6 steps/day (men: 6078.1 steps/day, women: 4544.2 steps/day). In contrast, the final report of the National Health Promotion Movement in the 21st century mentioned 5628 and 4584 steps/day in >65-year-old Japanese men and women, respectively [17]. Thus, the patients in this study performed a number of daily steps that was equal to or higher than that of the general elderly population in Japan. In addition, their certification rate of long-term care need was 10.8%, which was lower than the 17.9% as mentioned in the Annual Report on the Aging Society of Japan [18]. The continuation of phase III CR in patients with CVD may contribute not only to the maintenance of physical activity but also to prevention of long-term care needs.

Physical activity was classified into two types, locomotive and household activities, and correlations between each activity type and physical fitness, sleep quality, and cognitive function were examined. Interestingly, sleep latency and MMSE score showed a significant correlation with locomotive activity, but not with household activity. Thus, stepwise multiple regression analysis revealed locomotive activity as an independent predictor of sleep latency after adjustment for age, sex, cardiac function, and hypnotics. Sleep disorder is a risk factor for CVD, and insomnia tends to induce physical and psychiatric symptoms in such patients [19]. Sleep disorders not only impede the recovery of physical fatigue but also increase the risk of recurrence of CVD [20]. The results of our study are supported by those of a previous study reporting that habitual physical activity reduces the occurrence of abnormal sleep latency periods [21]. Moreover, our study classified physical activity into locomotive and household activities, and it is the first study to show the association between locomotive activity and sleep latency in elderly patients with CVD during phase III CR. Although the mechanism for this association is unclear, it is thought to be due to an increase in the parasympathetic nervous activity, improvement in the psychological state after walking, and an increase in thermoregulation and brain serotonin (5-hydroxytryptamine) levels after exercise [22–26]. Moreover, it has been reported that night variations in sleep efficiency influence physical activity levels the following day [27]; that is, the relationship between increased locomotive activity and shortened sleep latency period may be interactive.

Stepwise multiple regression analysis revealed 6MD as an independent predictor of MMSE score. Exercise tolerance is a strong predictor of mortality and morbidity in patients with CVD, and participation in CR is independently associated with decreased mortality [28]. Our results suggest that exercise tolerance is a predictor of cognitive function and not only mortality in elderly patients with CVD. A previous meta-analysis, using the quality-effects model, suggested that participants with higher levels of physical activity are at reduced risk of cognitive decline and dementia than those with lower levels of physical activity [29]. Moreover, it has been reported that cardiorespiratory fitness is associated with the whole brain and white matter volumes after controlling for age in early Alzheimer's disease [30]. For the above reasons, improvement in circulation and metabolism due to physical activity has various benefits, and as a result, it can be expected to reduce risk factors and promote protective factors for dementia.

In this study, we selected patients who were continuing the maintenance phase of CR, because data on maintenance phase CR are lacking in Japan. If elderly CVD patients had high locomotive activity and exercise tolerance, it may benefit them even if they had not participated in CR. However, we believe that it is useful for elderly CVD patients to participate in the maintenance phase of CR and to receive advice from professionals for improving their quality-of-life.

Study limitations

There are several limitations to this study. First, it was a cross-sectional study, and the causal relationship of locomotive activity with sleep latency and cognitive function is unknown. Therefore, a prospective longitudinal study is needed to confirm this relationship. Second, because physical activity was measured using an accelerometer, we could not evaluate the type of physical activity performed, such as cycling or underwater walking. Third, the independent factor of MMSE changed after exclusion of patients with heart failure; it is therefore necessary to analyze MMSE according to classification of CVD in the future. Finally, it is unknown whether elderly patients with CVD who do not continue CR achieve similar results, because the patients in this study were continuing phase III CR. Nevertheless, physical activity is increased or maintained through continuation of phase III CR, and it may contribute to the prevention of sleep disorders and cognitive decline in elderly patients with CVD. Moreover, our study suggests the possibility of reduction in healthcare and long-term care expenditure in elderly patients with CVD, and the clinical impact of this would be high. Phase III CR is not only a program that provides exercise therapy, it is also useful for education and disease management tailored to individuals and pathological conditions, and widespread reach and awareness of this program are recommended.

Conclusion

Locomotive activity but not household activity was associated with sleep latency, and exercise tolerance was associated with cognitive function in elderly patients with CVD who were continuing phase III CR. However, in this study, the relationship between exercise tolerance and cognitive function was offset by the presence of heart failure.

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Conflicts of interest

All authors have reported that they have no relationships relevant to the contents of this study to disclose.

References

[1] Inoue M, Iso H, Yamamoto S, Kurahashi N, Iwasaki M, Sasazuki S, et al. Daily total physical activity level and premature death in men and women: results from a large-scale population-based cohort study in Japan (JPHC study). Ann Epidemiol 2008;18:522–30.
[2] Nocon M, Hiemann T, Müller-Riemenschneider F, Thalau F, Roll S, Willich SN. Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. Eur J Cardiovasc Prev Rehabil 2008;15:239–46.
[3] Kurose S, Iwasaka J, Tsutsumi H, Yamanaka Y, Shinno H, Fukushima Y, et al. Effect of exercise-based cardiac rehabilitation on non-culprit mild coronary plaques in the culprit coronary artery of patients with acute coronary syndrome. Heart Vessels 2016;31:846–54.
[4] Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002;346:793–801.
[5] Harkness K, Heckman GA, Akhtar-Danesh N, Demers C, Gunn E, McKelvie RS. Cognitive function and self-care management in older patients with heart failure. Eur J Cardiovasc Nurs 2014;13:277–84.
[6] Oshima Y, Kawaguchi K, Tanaka S, Ohkawara K, Hikihara Y, Ishikawa-Takata K, et al. Classifying household and locomotive activities using a triaxial accelerometer. Gait Posture 2010;31:370–4.
[7] Passos GS, Poyares DL, Santana MG, Tufik S, Mello MT. Is exercise an alternative treatment for chronic insomnia? Clinics 2012;67:653–60.
[8] Barnes DE, Whitmer RA, Yaffe K. Physical activity and dementia: the need for prevention trials. Exerc Sport Sci Rev 2007;35:24–9.
[9] Morgan K. Daytime activity and risk factors for late-life insomnia. J Sleep Res 2003;12:231–8.
[10] Wang HX, Karp A, Winblad B, Fratiglioni L. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. Am J Epidemiol 2002;155:1081–7.
[11] Varma VR, Chuang YF, Harris GC, Tan EJ, Carlson MC. Low-intensity daily walking activity is associated with hippocampal volume in older adults. Hippocampus 2015;25:605–15.
[12] Ohkawara K, Oshima Y, Hikihara Y, Ishikawa-Takata K, Tabata I, Tanaka S. Real-time estimation of daily physical activity intensity by a triaxial accelerometer and a gravity-removal classification algorithm. Br J Nutr 2011;105:1681–91.
[13] Doi Y, Minowa M, Uchiyama M, Okawa M, Kim K, Shibui K, et al. Psychometric assessment of subjective sleep quality using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) in psychiatric disordered and control subjects. Psychiatry Res 2000;97:165–72.
[14] Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. J Psychosom Res 2002;53:737–40.
[15] Tsoi KK, Chan JY, Hirai HW, Wong SY, Kwok TC. Cognitive tests to detect dementia: a systematic review and meta-analysis. JAMA Intern Med 2015;175:1450–8.
[16] Tariq SH, Tumosa N, Chibnall JT, Perry MH, Morley JE. Comparison of the Saint Louis University mental status examination and the mini-mental state examination for detecting dementia and mild neurocognitive disorder -a pilot study. Am J Geriatr Psychiatry 2006;14:900–10.
[17] Ministry of Health, Labour, Welfare. A basic direction for comprehensive implementation of national health promotion. Ministerial Notification No. 430 ?of the Ministry of Health, Labour and Welfare; 2012. p. 1–25.
[18] Cabinet Office Japan. The Aging Society: Current Situation and Implementation Measures. Annual Report on the Aging Society (Summary); 2017. p. 2–23.
[19] Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378–84.
[20] Taylor DJ, Lichstein KL, Durrence HH. Insomnia as a health risk factor. Behav Sleep Med 2003;1:227–47.
[21] Inoue S, Yorifuji T, Sugiyama M, Ohta T, Ishikawa-Takata K, Doi H. Does habitual physical activity prevent insomnia?. A cross-sectional and longitudinal study of elderly Japanese. J Aging Phys Act 2013;21:119–39.
[22] Sato S, Makita S, Majima M. Additional physical activity during cardiac rehabilitation leads to an improved heart rate recovery in male patients after coronary artery bypass grafting. Circ J 2005;69:69–71.
[23] Sakuragi S, Sugiyama Y. Effects of daily walking on subjective symptoms, mood and autonomic nervous function. J Physiol Anthropol 2006;25:281–9.
[24] Rebar AL, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C. A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. Health Psychol Rev 2015;9:366–78.
[25] Uchida S, Shioda K, Morita Y, Kubota C, Ganeko M, Takeda N. Exercise effects on sleep physiology. Front Neurol 2012;3:48.
[26] Kondo M, Nakamura Y, Ishida Y, Shimada S. The 5-HT3 receptor is essential for exercise-induced hippocampal neurogenesis and antidepressant effects. Mol Psychiatry 2015;20:1428–37.
[27] Lambiase MJ, Gabriel KP, Kuller LH, Matthews KA. Temporal relationships between physical activity and sleep in older women. Med Sci Sports Exerc 2013;45:2362–8.
[28] Witt BJ, Jacobsen SJ, Weston SA, Killian JM, Meverden RA, Allison TG, et al. Cardiac rehabilitation after myocardial infarction in the community. J Am Coll Cardiol 2004;44:988–96.
[29] Blondell SJ, Hammersley-Mather R, Veerman JL. Does physical activity prevent cognitive decline and dementia?.: A systematic review and meta-analysis of longitudinal studies. BMC Public Health 2014;14:510.
[30] Burns JM, Cronk BB, Anderson HS, Donnelly JE, Thomas GP, Harsha A, et al. Cardiorespiratory fitness and brain atrophy in early Alzheimer disease. Neurology 2008;71:210–6.