The Beneficial Effect of Physical Activity on Cognitive Function in Community-Dwelling Older Persons with Locomotive Syndrome: Results of a Pilot Study

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Abstract

Bckground: Cognitive decline is closely related to motor decline. Locomotive syndrome (LS) is defined as a state associated with a high risk of requiring support because of locomotive organ disorders, and can be evaluated using the Locomo 25 questionnaire. This study aimed to clarify the effectiveness of daily physical activity on cognitive function based on the presence or absence of LS.

Methods: Community-dwelling older people who participated in a 3-month health class were divided into two populations based on Locomo 25 scores: < 7 (non-LS) and ³ 7 (LS). Cognitive function was evaluated using the Japanese version of Addenbrooke's Cognitive Examination-Revised (ACE-R). Average daily physical activity (exercise [Ex]) was measured using a portable activity meter.

Results: The Ex threshold for the increase in cognitive function based on receiver operating curve analysis was 2.29 ($p < 0.05$) in the LS population. After 13 weeks, cognitive scores were significantly higher ($p = 0.015$, $h_p^2 = 0.261$) and Locomo 25 scores were lower in the Ex ³ 2.29 than in the Ex < 2.29 group ($p = 0.052$, $h_p^2 = 0.176$) in LS population. Furthermore, a significant increase in the ACE-R memory domain was seen in the Ex ³ 2.29 group (analysis of variance, $p = 0.013$, $h_p^2 = 0.259$).

Conclusions: These results suggest that daily physical activity not only improve Locomo 25 scores, but also increase cognitive function in LS populations. Therefore, locomotor deterioration appears to be a useful evaluation index for deciding when to start exercise for the prevention of dementia.

Trial registration

The trial protocol and the trial were registered at the University Hospital Medical Information

Network Clinical Trials Registry (UMIN000030404) at January 1st, 2018.

Background

In Japan, over 26% of the population was aged ≥ 65 years as of 2015, and by 2040, the proportion of older people (> 75 years) is expected to surpass 20%; therefore, Japan is becoming a super-aging society [1]. Under these circumstances, to realize a society with healthy longevity, it is important to prevent the aged from falling into dysfunction or requiring nursing care. It has been reported that musculoskeletal diseases such as bone fractures and osteoporosis rank first, and dementia ranks third, in terms of causes for requiring long-term care; therefore, the prevention of these diseases is an urgent issue. One such problem associated with exercise disorders for which preventive measures are needed is locomotive syndrome (LS).

LS is defined as a state with a high risk of requiring support or nursing care because of locomotive organ disorders. One of the methods used to evaluate the severity of LS is the Locomo 25 questionnaire, a 25-item LS screening tool that measures the degrees of physical pain, ability to carry out activities of daily living (ADL), sociality, and active living [2]. A Locomo 25 score of ≥ 7 indicates LS [3]. In recent years, we have analyzed cross-sectional studies on factors related to LS in community-dwelling older people, finding that LS is associated with motor function [4], body mass index (BMI) [5], depression [6], and cognitive function [7]. A number of studies on LS and motor function have been conducted [8]. LS has also been found to be closely related to sarcopenia and frailty [9, 10]. In addition, it has reported that cognitive function is closely related to motor function [11]. Therefore, we thought that it would be effective to establish a preventive method that links cognitive function and LS for reducing the need for nursing care.

Adequate exercise and nutrition have been widely suggested as preventive measures for cognitive function decline. In addition, the state at which walking function and cognitive function are reduced at the pre-stage of dementia is called "motor cognitive risk syndrome" [12], and the clinical significance of evaluating motor function in this way is being increasingly recognized. However, it remains unclear to what extent motor therapy is effective to prevent cognitive decline among people with reduced motor function. In addition, many health classes have introduced uniform exercise activities for their participants, but the results are somewhat unclear. We previously identified a strong relationship between Locomo 25 and Mini-Mental State Examination scores, which are used to evaluate cognitive function, in older women living independently in the community: a Locomo 25 scores of 6 points was the cutoff value for normal cognitive function, with scores of ≥ 6 indicating a higher risk for cognitive decline [7].

These findings suggest that cognitive decline would be prevented if musculoskeletal function could be recovered—i.e., a reduction in the severity of LS—by some kind of intervention in the early stage using Locomo 25 as an index. It has been reported that LS-induced back pain improves with exercise [13], and that exercise interventions for osteoarthritis improve ADL [14].

On the other hand, physical activity refers to all body movements by the skeletal muscles that expend energy, and includes whole-body endurance, muscular strength, balance ability, and flexibility. Exercise is a planned, intentional, and continuous physical activity aimed at maintaining and improving physical strength. Physical activity is associated with mortality, in that higher levels of physical activity decrease the risk of death [15]. In addition, exercise and physical activity have been shown to be effective in increasing cognitive reserve for the prevention of dementia and reducing brain damage and neuroinflammation [16].

Therefore, the purposes of this study were to categorize community-dwelling older people based on the presence or absence of LS and to clarify the effectiveness of daily physical activity on cognitive function.

Methods

Participants

This study was conducted in Kaizuka city, Osaka Prefecture, from January to April 2019. The study participants had participated in a once-weekly 13-week exercise class co-hosted by Kaizuka city and Osaka Kawasaki Rehabilitation University. The exclusion criteria were: 1) < 60 years of age; 2) previously diagnosed with dementia; 3) having a cardiac pacemaker; and 4) had stopped exercising on the advice of a physician. The measurements described below were performed before participation (baseline) and after 13 weeks. The exercise class was conducted once a week (1 h per session) for 13 weeks by a certified physical therapist. The contents of the class included 15 min of intellectual tasks and 45 min of exercise tasks, such as soft gymnastics and light dancing. At the beginning of the study, a wireless activity meter (AM510N; ACOS Co., Ltd., Nagano, Japan) was handed out to each person. The target values were 6,700 steps per day for men and 5,900 steps per day for women, which are the values proposed by the Ministry of Health, Labour and Welfare of Japan for the prevention of lifestyle-related diseases for people aged ≥ 70 years [17]. A self-administered questionnaire on education history was also implemented.

In total, 98 individuals participated in the baseline measurement. During the 13-week study period, one patient was hospitalized and 15 discontinued. After 13 weeks, 82 participants remained, among whom, four who had lost their activity meter, five who had not answered the questionnaire completely, and three who had a daily activity level ≥ 7.0 metabolic equivalents (METs) × h were excluded. Finally, data from 70 participants (20% men; mean age [standard deviation], 74.7 [5.4] years; age range, 63–91 years) were analyzed. This study was reviewed and approved by the Ethics Committee of Osaka Kawasaki Rehabilitation University (approval No.: OKRU30-A016), and carried out in accordance with the Declaration of Helsinki. Prior to the start of the survey, written informed consent was obtained from all participants. For participants with cognitive decline, the participate was allowed to ask his/her spouse, children or other relatives to answer on his/her behalf.

Measurement Of Variables

BMI was calculated as the weight in kilograms divided by the height in meters squared. Skeletal muscle mass index (SMI) was obtained using a body composition analyzer (InBody 270; InBody Japan Co., Ltd., Tokyo, Japan), which estimates body composition at frequencies of 20 and 1,000 kHz. The participants were instructed to grasp the handles of the analyzer, in which electrodes are embedded, and stand on the electrodes that contact the bottoms of their feet while wearing normal indoor clothing without socks and shoes. Physical activity was measured using a wireless activity meter (AM510N; ACOS Co., Ltd., Nagano, Japan) that the participants attached to their pants for 13 weeks and removed only when taking a bath. After 13 weeks, number of daily steps, number of active steps, activity time, intense activity time, and exercise (Ex) were read by a contactless IC card reader (Ferica RC-S380/S; Sony Co., Tokyo, Japan), and the average value was converted to daily activity level, with ≥ 3 METs · h defined as active.

Evaluation Of Cognitive Function

Cognitive function was evaluated using the Japanese version of Addenbrooke's Cognitive Examination-Revised (ACE-R) [18, 19]. Version A was used at baseline, and version B at after 13 weeks. The classification, which is based on cognitive changes, was calculated by subtracting the baseline ACE-R score from that after 13 weeks. When this difference was > 0, the participant was classified into the group with increased cognitive function, and when the difference was ≤ 0, the participant was classified into the group with non-increased cognitive function.

Assessment Of Ls Status

LS status was evaluated using the Locomo 25 score, which was previously known as the Geriatric Locomotive Function Scale-25 score. The Locomo 25 is a self-administered questionnaire composed of four questions about pain, 16 questions about ADL, three questions about social function, and two questions about mental health status during the last month [20]. All 25 questions are scored from 0 (no impairment) to 4 (severe impairment), with the total score ranging from 0 to 100. Higher scores indicate worse locomotive function, and a pre-specified score of ≥ 7 was considered indicative of LS [20].

Statistical analysis

To compare numerical values between the populations with Locomo 25 scores < 7 (non-LS group) and ≥ 7 (LS group), the normality of distribution and homogeneity of variance were tested prior to comparison across groups. Student's *t*-test was used when assumptions of normal distribution and homogeneity of variance were fulfilled in both groups, and Welch's *t*-test was used when the assumption of normal distribution, but not that of homogeneity of variance, was met. The Wilcoxon signed-rank test was used when data were not normally distributed. Pearson's chi-squared test was used to compare exercise habits between the non-LS and LS populations. The Ex threshold score for discriminating between the increased and non-increased cognitive function groups was evaluated using receiver operating curve (ROC) analysis. The odds ratios (ORs) of measurements for increased cognitive function according to Ex were calculated using multiple logistic regression analyses adjusted for gender and age. Repeated-measures analysis of variance (ANOVA) was carried out to compare changes in Locomo 25, ACE-R, and ACE-R domain scores, and to determine Ex efficacy for outcomes during the 13-week study period. Repeated-measures analysis of covariance (ANCOVA) was also carried out to compare changes in Locomo 25 and ACE-R scores, and to determine Ex efficacy for outcomes during the 13-week study period after adjusting for gender. Eta partial squared (η_p^2) is the value of the sum of squares (SSA) divided by the SSA plus the sum of squared errors of prediction. The η_p^2 values describes an effect size of 0.01 as small, 0.06 as medium, and 0.14 as large [21]. All statistical analyses were conducted using SPSS Statistics software (version 26; IBM Corp., Armonk, NY). All statistical tests were two-tailed, and a significance level of 0.05 was used.

Results

The participants' age, years of education, BMI, SMI, Locomo 25, and ACE-R scores are shown in Table 1. A significant association was found between Locomo 25 and ACE-R scores before the intervention ($r = -0.313$, $p = 0.0082$) (data not shown). Table 2 shows a comparison of changes of measurements from baseline to 13 weeks and physical activity levels between the non-LS and LS populations. No significant differences were observed for all changes in ACE-R and Locomo 25 scores, BMI, SMI, steps, active steps, activity steps, intense activity time, and Ex. Furthermore, exercise habits before the start of the exercise class did not significantly differ between the two populations ($p = 0.9176$) (Table 2).

Table 1
Characteristics of the study participants

	N = 70 (men 14 : women 56)	
Age (y)	74.7	(5.3)
Years of education (y)	12.3	(2.4)
BMI (kg/m^2)	22.9	(2.9)
SMI (kg/m^2)	6.0	(0.9)
Locomo 25 score (points)	7.6	(8.7)
ACE-R score (points)	90.4	(8.2)

Table 2
Comparison of changes of measurements from baseline to 13 weeks and physical activity levels between the non-LS and LS populations

	All	**Non-LS**	**LS**	**P**
N (% men)	70 (20.0%)	47 (23.4%)	23 (13.0%)	
Age (y)	74.71 (5.26)	73.94 (5.12)	76.30 (5.30)	0.0768†
ΔACE-R score (points)	−0.243 (4.54)	−0.191 (4.19)	−0.348 (5.27)	0.8935†
ΔLocomo 25 score (points)	0.986 (6.37)	1.19 (4.88)	0.565 (8.78)	0.7525‡
ΔBMI (kg/m^2)	−0.25 (0.45)	−0.23 (0.40)	−0.33 (0.54)	0.9299§
ΔSMI (kg/m^2)	0.09 (0.14)	0.11 (0.14)	0.06 (0.14)	0.2155§
Steps (steps)	6,100.77 (2,340.18)	6,290.25 (2,325.15)	5,713.59 (2,374.26)	0.3365†
Active steps (steps)	4,667.16 (2,310.48)	4,846.60 (337.36)	4,300.48 (482.25)	0.3567†
Activity time (min)	38.75 (19.27)	224.50 (49.12)	215.72 (57.35)	0.5087†
Intense activity time (min)	221.32 (51.72)	40.11 (19.20)	35.98 (19.56)	0.4029†
Ex (METs · h)	2.56 (1.32)	2.71 (0.19)	2.26 (0.27)	0.1851†
Exercise 7 days/week	17.1%	12.5%	21.3%	0.9176¶
5–6 days/week	14.3%	16.7%	12.8%	
1–4 days/week	58.5%	62.5%	55.3%	
0 days/week	10.0%	8.3%	10.6%	

ROC analysis was conducted in regard to Ex in the all, non-LS, and LS populations. A threshold for discriminating between the non-increased and increased cognitive function groups was identified as follows. A high area under the ROC curve (AUC) value (0.808, $p < 0.05$) in the LS population, a middle AUC value (0.649, $p < 0.05$) in the all population, and a low AUC value (0.577, $p = 0.43$) in the non-LS population were observed. The threshold was 2.29 METs · h in the LS population, 2.06 METs · h in the all population, and 1.97 METs · h in the non-LS population (Table 3). ORs for the prevalence of increased cognitive function according to the threshold Ex values in the all, non-LS, and LS populations are shown in Table 4. In the all and LS populations, the high Ex group (≥ 2.06, ≥ 2.29) showed increased cognitive function, with an OR of 3.06 or 18.82 ($p < 0.01$) as determined by multiple logistic regression analysis (Table 3).

Table 3
Threshold Ex values for increased cognitive function and odds ratios (ORs) for increased cognitive function according to Ex

Population	**Threshold value†**	**Area under the curve**	**Sensitivity (%)**	**Specificity (%)**	**p**	**Cutoff value of Ex‡**	**OR**	**95% CI**	**p**
All	2.06	0.649	78.79	67.16	**0.0475**	< 2.06	1	1.11–8.43	**0.0265**
						≥ 2.06	3.06		
Non-LS	1.97	0.577	58.33	24.28	0.4268	< 1.97	1	0.75–12.90	0.1058
						≥ 1.97	3.12		
LS	2.29	0.808	80.00	64.62	**0.0468**	< 2.29	1	1.72–205.36	**0.0161**
						≥ 2.29	18.82		

Table 4
Comparison of changes in ACE-R and Locomo 25 scores in the Ex group

				Repeated-measures ANOVA			Repeated-measures ANCOVA†		
				Time · Group			Time · Group		
		Baseline	13 weeks	F	P	η_p^2	F	P	η_p^2
All									
	ACE-R (points)								
	Ex < 2.06 (n = 27)	88.56 (10.29)‡	86.81 (10.88)	5.064	**0.028**	0.069	4.77	**0.033**	0.066
	Ex ≥ 2.06 (n = 43)	91.05 (6.58)	91.74 (6.41)						
	Locomo 25 (points)								
	Ex < 2.06 (n = 27)	9.63 (10.50)	12.85 (13.22)	5.72	**0.020**	0.078	7.70	**0.007**	0.103
	Ex ≥ 2.06 (n = 43)	6.37 (7.16)	5.98 (6.60)						
Non-LS									
	ACE-R (points)								
	Ex < 1.97 (n = 14)	87.29 (9.03)	85.50 (10.78)	3.00	0.090	0.063	2.91	0.095	0.062
	Ex ≥ 1.97 (n = 33)	92.97 (5.77)	93.45 (5.37)						
	Locomo 25 (points)								
	Ex < 1.97 (n = 14)	2.79 (2.08)	5.93 (7.44)	3.28	0.077	0.068	3.681	0.062	0.077
	Ex ≥ 1.97 (n = 33)	2.73 (1.70)	3.09 (2.85)						
LS									
	ACE-R (points)								
	Ex < 2.29 (n = 13)	89.15 (11.31)	86.46 (10.52)	7.689	**0.011**	0.268	7.046	**0.015**	0.261

				Repeated-measures ANOVA			Repeated-measures ANCOVA†		
	Ex ≥ 2.29 (n = 10)	87.70 (7.24)	90.40 (8.17)						
	Locomo 25 (points)								
	Ex < 2.29 (n = 13)	18.15 (9.55)	21.15 (13.25)	2.448	0.133	0.104	4.275	0.052	0.176
	Ex ≥ 2.29 (n = 10)	16.90 (7.71)	14.30 (8.19)						

Table 4 shows a comparison of changes from baseline to 13 weeks between each Ex group among the all, non-LS, and LS populations by ANOVA or ANCOVA after adjusting for gender. Using repeated-measures ANCOVA, the changes in ACE-R scores were significantly higher in the high than in the low Ex groups in the all and LS populations ($p = 0.033$, $\eta_p^2 = 0.066$ in all; $p = 0.015$, $\eta_p^2 = 0.261$ in LS). No significant differences were observed in these scores between the two Ex groups in the non-LS population ($p = 0.095$, $\eta_p^2 = 0.062$) (Table 4). Similar results were observed using repeated-measures ANOVA. Using repeated-measures ANCOVA, the changes in Locomo 25 scores were significantly lower in the high than in the low Ex groups in the all and LS populations ($p = 0.007$, $\eta_p^2 = 0.103$ in all; $p = 0.052$, $\eta_p^2 = 0.176$ in LS). No significant differences were observed in these scores between the two Ex groups in the non-LS population ($p = 0.062$, $\eta_p^2 = 0.077$). From both types of analyses, the LS population showed a larger effect size than the all population for changes in ACE-R and Locomo 25 scores (Table 4).

Table 5 shows a comparison of changes from baseline to 13 weeks in ACE-R domain scores between the < 2.29 and ≥ 2.29 Ex groups with LS by ANOVA. Memory scores were significantly higher in the ≥ 2.29 than in < 2.29 Ex group with a large effect size ($p = 0.013$, $\eta_p^2 = 0.259$) (Table 5).

Table 5
Comparison of changes in ACE-R domain scores in the Ex group with locomotive syndrome

			Time · Group		
	Baseline	13 weeks	F	P	η_p^2
Orientation/Attention (points)					
Ex < 2.29	17.46 (1.13) †	17.54 (1.39)	0.039	0.846	0.002
Ex ≥ 2.29	17.20 (0.79)	17.40 (0.84)			
Memory (points)					
Ex < 2.29	21.08 (5.55)	18.62 (5.12)	7.348	**0.013**	0.259
Ex ≥ 2.29	18.60 (5.17)	20.70 (5.08)			
Verbal Fluency (points)					
Ex < 2.29	11.85 (2.51)	10.92 (3.64)	1.285	0.270	0.058
Ex ≥ 2.29	12.60 (1.51)	12.80 (1.69)			
Language (points)					
Ex < 2.29	24.69 (2.75)	23.92 (2.46)	0.016	0.902	0.001
Ex ≥ 2.29	25.30 (1.89)	24.60 (2.55)			
Visuospatial (points)					
Ex < 2.29	14.08 (1.19)	15.46 (0.88)	1.521	0.231	0.068
Ex ≥ 2.29	14.00 (1.41)	14.80 (1.62)			

Discussion

As exercise habits before the start of the exercise class did not significantly differ between the non-LS and LS groups ($p = 0.9176$; Table 2), the difference found in the amount of physical activity in this study was considered to be the result of the effort of each participant in aiming to achieve the target number of steps presented at the beginning of the study. In this study, increased cognitive function during the 13-week study period was associated with higher average physical activity in the LS population, and the ROC analysis showed a threshold of 2.29 Ex. On the hand, no significant relationship was found between physical activity and cognitive function in the non-LS population. When the LS population was classified into < 2.29 and ≥ 2.29 Ex groups, a significant decrease in Locomo 25 scores and a significant increase in ACE-R scores were observed in the ≥ 2.29 Ex group. From these results, it is considered that ≥ 2.29 Ex was effective in improving LS and restoring cognitive function in the LS population. As 2.29 Ex is extremely light exercise and a large amount of time spent in sedentary is associated with low cognitive function [22], it is expected that the time spent in sedimentary is strongly involved in cognitive decline in the LS.

Exercise has been shown to be effective for all of three strategies for preventing dementia: 1) increase cognitive reserve; 2) reduce brain damage; and 3) reduce neuroinflammation. There have been many reports on the relationship between exercise/physical activity and events related to cognitive function [16]. Clinical studies have reported a correlation between low levels of motor function and high amyloid β deposition [23]. Cohort studies have reported that a high level of physical activity reduces the risk of cognitive decline and Alzheimer's disease (AD) [24, 25, 26].

Exercise promotes the production of vascular endothelial growth factor and insulin-like growth factor-1 in skeletal muscle, and enhances cerebrovascular plasticity and neuroplasticity [27]. Exercise has also been reported to increase the production of neuroprotective brain-derived neurotrophic factor in skeletal muscle [28] and kynurenine aminotransferase, and to reduce kynurenine-induced neurotoxicity [29]. Thus, myokines secreted from skeletal muscle act on the brain and mediate the enhancement of cognitive reserve through exercise. However, no relationship has been found between physical activity levels and amyloid-β image level or the cerebrospinal fluid biomarker for AD [30, 31]. Thus, there are two aspects of a high level of physical activity: one suppresses or delays the development of AD pathology, and the other increases other cognitive functions independently of AD pathology, i.e., it compensates for impaired cognitive function and promotes high brain plasticity [32]. It is speculated that these mechanisms are involved in the relationship between physical activity and cognitive function identified in this study.

The effect of Ex on changes in Locomo 25 scores was observed when using repeated-measures ANCOVA adjusted for gender. This result suggested that 2.29 or more physical activity had the effect of reducing the level of LS. Locomo 25 mainly includes questions about the degrees of physical pain and daily activities. According to a recent survey by the Ministry of Health, Labour and Welfare of Japan [33], chronic pain in the locomotive organs is severe, and usually at sites necessary for movement, such as the hip and lower limb joints, so pain is strongly associated with LS. As with various types of exercise-induced analgesia during and after exercise, such as aerobic, resistance, and isometric exercise [34, 35], exercise has also been reported effective for chronic low back pain associated with LS [13]. It has also recently been reported that active middle-aged and older persons are more resistant to pain [36], and that exercise interventions for osteoarthritis improve ADL [14]. Based on the above, it was considered that the decrease in Locomo 25 scores in ≥ 2.29 Ex group with LS was due to an increase in physical activity, a decrease in pain, and an increase in the ability to carry out ADL.

Moderate to severe persistent pain, which reflects chronic pain, has been reported to be associated with accelerated cognitive decline and increased dementia onset in the aged [37]. This report supports the relationship between decreased LS scores and increased cognitive function in the present study.

According to the Ministry of Health, Labour and Welfare's “Physical Activity Standards for Health Promotion 2013” [38], a physical activity level of 10 Ex/week should be maintained regardless of strength. However, the results of the present study suggest that a physical activity level of ≥ 16 Ex/week is needed to improve cognitive function; 10 Ex/week had no effect on improving cognitive function in people with LS.

In the present study, a significant increase was observed in the memory score domain of the ACE-R in the group with 2.29 or more physical activity in the LS population. It has been reported that moderate physical activity is positively correlated with hippocampal capacity, as is physical activity and memory [39]. It has also been reported that smaller hippocampal volume in the healthy aged is associated with severe acute and chronic pain [40]. Furthermore, it has been reported that persistent pain in a longitudinal cohort of older people is associated with decreased memory and an increased likelihood of dementia [37]. The results of the present suggest that the LS population may have increased memory owing to increased physical activity and pain relief.

In this study, no relationship was found between physical activity and cognitive function the non-LS population. In this population, factors other than physical activity may be involved in the recovery of cognitive function. In this study, Locomo 25 scores were therefore used as an index for lifestyle interventions to improve cognitive function.

This study did have several limitations. First, the number of study participants (n = 70) was small. The criteria for LS in terms of Locomo 25 scores have two levels: ≥ 7 points and ≥ 16 points. However, in this study, few people in the target population had a Locomo 25 score of ≥ 16 points, so a score of ≥ 7 was considered to indicate LS. In the future, exercise intervention times can be expected to be identified more accurately by conducting surveys on more participants and categorizing them into more severe and milder groups in the LS population. In addition, since this study involved only Japanese participants, caution should be taken when generalizing the results to other populations.

Conclusion

The results of this study suggest that physical activity improve not only Locomo 25 scores, but also cognitive function in individuals with LS. These findings need to be investigated further in a larger trial.

List Of Abbreviations

LS	Locomotive Syndrome
ACE-R	Addenbrooke's Cognitive Examination-Revised
Ex	Exercise
ADL	Activities of Daily Living
BMI	Body Mass Index
METs	Metabolic Equivalents
SMI	Skeletal Muscle Mass Index
ROC	Receiver Operating Curve
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
AUC	Area Under the ROC Curve
OR	Odds Ratio
AD	Alzheimer's Disease
CI	Confidence Interval

Declarations

Declarations

Ethics approval and consent to participate

The Ethics Committee of Osaka Kawasaki Rehabilitation University approved the study protocol (Reference No. OKRU30-A016). All patients provided written informed consent before the study start. For participants with cognitive decline, the participate was allowed to ask his/her spouse, children or other relatives to answer on his/her behalf.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors had significant roles in designing, conceiving, and conducting the study and drafting the manuscript. MN and MI contributed to designing the study. MN, MI, FT, MH, HN, and TO collected the data, and analyzed by MN and HH. HK and MT were the supervisor of the whole research and checked the data. The final report and article were written by MN. All authors read and approved the final manuscript.

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