Table 1 Selected variable characteristics of participants at baseline by study group

Variables†	Ex + TC (n = 32)	Ex (n = 32)	TC (n = 32)	HE (n = 32)	ANOVA P-value
Age (years)	81.1 ± 3.7	79.6 ± 4.2	80.0 ± 4.0	80.2 ± 5.6	0.525
Height (cm)	145.0 ± 5.5	145.9 ± 5.8	145.6 ± 4.9	145.9 ± 5.4	0.892
Bodyweight (kg)	43.7 ± 4.1	41.5 ± 4.5	42.4 ± 5.7	42.7 ± 5.0	0.413
Percent body fat (%)	29.0 ± 3.7	28.1 ± 4.2	27.8 ± 4.8	30.3 ± 3.6	0.110
Lean body mass (kg)	30.2 ± 3.2	30.4 ± 3.6	29.9 ± 3.1	30.5 ± 2.8	0.894
Muscle mass (kg)	27.8 ± 3.0	28.0 ± 3.3	27.5 ± 2.9	28.1 ± 2.6	0.917
Legs muscle mass (kg)	10.2 ± 1.2	10.2 ± 1.3	10.2 ± 1.2	10.3 ± 1.0	0.992
Grip strength (kg)	18.5 ± 3.5	18.2 ± 4.9	16.1 ± 3.4	17.2 ± 4.0	0.078
Usual walking speed (m/sec)	1.3 ± 0.2	1.2 ± 0.3	1.2 ± 0.2	1.2 ± 0.2	0.677
Maximal walking speed (m/sec)	1.7 ± 0.3	1.6 ± 0.3	1.7 ± 0.3	1.7 ± 0.3	0.235
Timed up & go	6.61 ± 1.63	7.13 ± 1.68	7.07 ± 1.96	6.82 ± 1.21	0.597
One leg standing time with eyes open	27.1 ± 23.5	24.8 ± 21.8	32.1 ± 24.5	34.5 ± 24.4	0.375
Knee extension strength (Nm)	50.4 ± 10.7	44.5 ± 14.8	46.4 ± 9.7	47.0 ± 10.7	0.242
Exercise habit, yes (%)	48.4	40.7	37.5	19.2	0.144
Urinary incontinence, yes (%)	45.2	40.6	40.6	38.5	0.962
Frequency of outings, >once per day (%)	22.6	31.3	34.4	42.3	0.455
Fear of falling, yes (%)	71.0	84.4	68.8	73.1	0.489
Falls, yes (%)	25.8	31.3	21.9	11.5	0.347
Self-rated health, unhealthy (%)	12.9	34.4	25.0	15.4	0.163

†Data are presented as mean and standard deviation for continuous variables, and percentage for categorical variables. ANOVA (one-way analysis of variance) for continuous variables and χ^2-test for categorical variables. Ex, exercise group; HE, health education group; TC, tea catechin group.

between strength and mass is not linear. Recently, the European Working Group on Sarcopenia in Older People recommended using both low muscle mass and muscle strength or low physical performance as indicators for sarcopenia.[20] In the present study, sarcopenic women were operationally defined based on the declines in muscle strength or walking speed that accompany the loss of skeletal muscle mass or low BMI. The results of the present study showed that the combination of exercise and TC can effectively improve muscle mass and walking speed in sarcopenic elderly women; however, the present results could not confirm the efficacy of the combined intervention on both muscle mass and strength.

The benefits of resistance training in increasing muscle mass and strength for older people have been made quite clear throughout the literature.[6–8] According to a recent review, resistance exercise has been shown to increase muscle protein synthesis, and evidence suggests increases in size of both type 1 and type 2 muscle fibers, leading to overall improvement in muscle power and physical functioning.[5] However, our data did not show beneficial effects of exercise alone on measures of muscle mass or strength. This might be because of the intensity the participants in this intervention exercised at, as some studies showed that higher intensity and volume training were associated with greater strength improvements among older populations, compared with low- and moderate-intensity training.[7,21] Nevertheless, high-intensity exercise for frail elderly people is difficult and might lead to negative or adverse outcomes. Exercise at high intensities might aggravate previously mild discomforts of the lower back or knee, potentially causing mild, moderate or even severe pain. Furthermore, motivating frail elderly people to properly carry out high-intensity exercise is very challenging. Even though exercise of high intensity and volume can increase muscle mass and strength effectively, Taaffe[22] has suggested that training once or twice a week at moderate intensity is sufficient for improvement; therefore, the use of such training on frail elderly people should be reconsidered.

The role of anti-oxidants in aging has recently been a topic of interest. Studies have reported that aging skeletal muscle has been associated with decreased oxidative capacity, which might be linked to mitochondrial dysfunction.[23–25] One previous study suggested that TC might prevent decreases in muscle force production in mice.[26] Another mice study indicated that TC can effectively decrease oxidative stress, which might contribute, to a certain extent, to the maintenance of skeletal muscle mitochondrial function and energy metabolism; therefore, the concomitant intake of TC and regular exercise might suppress age-related declines in physical function.[10]

Table 2 Comparison of muscle mass and functional fitness variables among groups after 3-month interventions

Variables†	Group	Baseline	After 3-month intervention	ANOVA (G × T); *P*-value
Muscle mass (kg)	Ex + TC	28.38 ± 2.46	28.33 ± 2.69	*F* = 0.323 *(0.809)*
	Ex	29.09 ± 2.85	28.92 ± 2.98	
	TC	27.47 ± 3.02	27.28 ± 2.83	
	HE	28.23 ± 2.40	28.35 ± 2.33	
Appendicular skeletal muscle mass (kg)	Ex + TC	14.31 ± 1.30	14.18 ± 1.41	*F* = 1.280 *(0.286)*
	Ex	14.79 ± 1.45	14.45 ± 1.57	
	TC	13.66 ± 1.66	13.58 ± 1.51	
	HE	13.96 ± 1.21	14.11 ± 1.23	
Legs muscle mass (kg)	Ex + TC	10.45 ± 0.98	10.57 ± 1.08	*F* = 0.524 *(0.667)*
	Ex	10.59 ± 1.23	10.73 ± 1.22	
	TC	10.14 ± 1.29	10.12 ± 1.14	
	HE	10.30 ± 0.92	10.50 ± 0.94	
Grip strength (kg)	Ex + TC	18.63 ± 3.39	19.33 ± 4.71	*F* = 0.519 *(0.670)*
	Ex	19.11 ± 4.67	19.26 ± 4.54	
	TC	16.41 ± 3.34	17.11 ± 2.81	
	HE	17.84 ± 4.03	17.74 ± 3.59	
Timed up & go (s)	Ex + TC	8.68 ± 1.99	7.37 ± 1.64	*F* = 15.408 *(<0.001)*
	Ex	8.81 ± 1.60	7.03 ± 1.34	
	TC	8.89 ± 2.20	8.44 ± 2.15	
	HE	8.43 ± 1.70	8.88 ± 2.09	
Usual walking speed (m/s)	Ex + TC	1.25 ± 0.21	1.37 ± 0.24	*F* = 4.327 *(0.007)*
	Ex	1.26 ± 0.22	1.36 ± 0.30	
	TC	1.25 ± 0.24	1.24 ± 0.19	
	HE	1.27 ± 0.18	1.26 ± 0.20	
Maximum walking speed (m/s)	Ex + TC	1.74 ± 0.30	2.01 ± 0.39	*F* = 15.161 *(<0.001)*
	Ex	1.73 ± 0.23	2.06 ± 0.32	
	TC	1.78 ± 0.27	1.71 ± 0.23	
	HE	1.79 ± 0.33	1.71 ± 0.30	
Knee extension strength (Nm)	Ex + TC	52.81 ± 9.39	49.85 ± 8.97	*F* = 2.556 *(0.061)*
	Ex	51.39 ± 13.01	49.73 ± 13.38	
	TC	47.34 ± 9.56	39.42 ± 8.29	
	HE	47.54 ± 11.28	43.13 ± 10.93	

†Data are presented as mean and standard deviation. A post-hoc analysis was carried out using the Scheffe method. ANOVA two-way repeated-measure analysis of variance. Ex, exercise group; G, group; HE, health education group; T, time; TC, tea catechin.

Table 3 Adjusted odds ratio for changes in leg muscle mass and functional fitness after intervention according to study group

Dependent variable†	Type of intervention						
	HE	TC		Ex		Ex + TC	
	Reference	OR	95% CI	OR	95% CI	OR	95% CI
Leg muscle mass and usual walking speed	1.00	1.32	0.40–4.70	1.99	0.57–7.38	3.61	1.05–13.66
Leg muscle mass and knee extension strength	1.00	0.40	0.07–2.08	0.82	0.16–4.06	2.25	0.58–9.93

†Dependent variable; change of muscle mass and functional fitness: 1 = improve, 0 = no change or decrease. Ex, exercise; HE, health education; OR, adjusted odd ratio; TC, tea catechin.

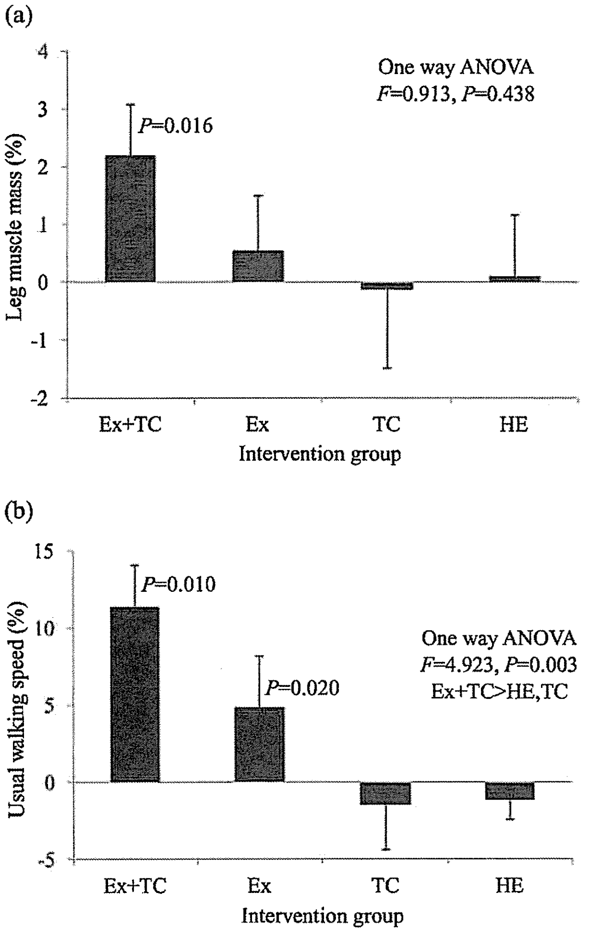

Figure 2 Mean (± SE) changes in (a) leg muscle mass and (b) usual walking speed after exercise (Ex), tea catechin supplementation (TC), usual walking speed after exercise and tea catechin supplementation (Ex + TC), or health education (HE). Bars indicate the average changes from baseline to after the 3-month interventions. A post-hoc analysis was carried out using the Scheffe method.

The data in the present study showed leg muscle mass improvements of 2.21% in the combined exercise and TC group, but the changes in muscle strength were not significant. These results are inconsistent with previous research showing strong associations between increases in muscle mass and increases in strength;[4] hence, further research is necessary.

The improvements observed in walking speed is an important finding, as studies have reported that walking speed is an indicator of vitality and a predictor of functional decline,[27] subsequent disability,[28] survival[29] and other adverse outcomes.[30] A recent statement from the Society on Sarcopenia, Cachexia and Wasting Disease stated that an improvement in gait speed of at least 0.1 m/s can be considered clinically significant.[31] The results of the current study showed that walking speed increased in the Ex group by 0.10 m/s and in the Ex + TC group by 0.12 m/s after the 3-month intervention. Exercise alone or combined exercise and TC supplementation might be effective for improving walking ability in sarcopenic women.

As sarcopenia is a multifactorial condition involving age-related declines in muscle mass, strength or function, effective treatments should target improvements in muscle mass and physical function. In the current study, the OR for muscle mass and usual walking speed improvement was more than threefold as great in the Ex + TC group compared with the HE group. Although investigation into mechanisms of the anti-oxidant capacities of TC together with exercise was beyond the scope of the present study, our results show that the combination of exercise and TC effectively enhanced muscle mass and walking ability.

The present study had several limitations. First, investigation into the mechanisms of the anti-oxidative effects of TC was not explored. Future studies should investigate TC effects on reactive oxygen species and oxidative stress markers in order to provide further understanding and insight into the treatment of sarcopenia. Second, muscle mass was measured using BIA. Other methods of measuring muscle mass, such as magnetic resonance imaging (MRI), computerized tomography and dual-energy X-ray absorptiometry, are typically considered more accurate.[32] Previous studies have reported strong correlations between MRI and BIA measurements for muscle mass in older adults.[12,33,34] Hence, the validity of the BIA measurements has little influence on the interpretation of the results in the present study. Third, 51.9% (138 sarcopenic women) were excluded from the present study based on the exclusion criteria or refused participation, and were not included in this intervention trial. Future research should consider the external validity of the populations included in randomized controlled trials, and perhaps shift the focus to community-dwelling older adults often excluded from intervention studies.

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Disclosure statement

The authors declare no conflict of interest.

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Performance-based assessments and demand for personal care in older Japanese people: a cross-sectional study

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ABSTRACT

Objectives: To identify appropriate clinical tests for determining the demand for personal care in older Japanese people.

Design: Cross-sectional observation study.

Setting: Obu Study of Health Promotion for the Elderly (Obu, Aichi) and Tsukui Ordered Useful Care for Health (241 day-care centres) cohorts in Japan.

Participants: A total of 10 351 individuals aged 65 years or older (6791 with personal care and 3560 without personal care) participated in the study.

Measures: Physical performance tests included grip strength, the chair stand test, walking speed at a comfortable pace, and the timed up-and-go test. Personal care was defined as participants who had been certified in the national social long-term care insurance in Japan.

Results: Individuals who received personal care showed a significantly poorer performance than those without personal care for all physical performance tests ($p<0.001$). Gait speed was the most useful of the physical performance tests to determine the demand for personal care (receiver operating characteristic curve statistics: men, 0.92; women, 0.94; sensitivity: men, 86; women, 90; specificity: men, 85; women, 85). After adjustment for age, sex, cognitive impairment and other physical tests, all physical performance tests were individually associated with the demand for personal care. A slow gait speed (<1 m/s) was more strongly correlated with the demand for personal care than other performance measures (gait speed OR: 5.9; 95% CI: 5.0 to 6.9).

Conclusions: Clinical tests of physical performance are associated with the demand for personal care in older people. Preventive strategies to maintain physical independence may be required in older adults who show a gait speed slower than 1 m/s. Further research is necessary to confirm these preliminary results.

ARTICLE SUMMARY

Article focus

- Measures of physical performance may identify older persons with a preclinical stage of disability.
- However, it is unclear which performance test and cut-point are the most useful to screen for risk of functional dependence in older Japanese people.
- The purpose of this study was to identify appropriate clinical tests for determining the risk of functional dependence in older Japanese people.

Key messages

- Clinical tests of physical performance were associated with a functional decline in older people.
- Preventive strategies to avoid personal care may be required in older adults who show a gait speed slower than 1 m/s.

Strengths and limitations of this study

- Strengths of this study include a large sample size and performance-based assessment, which could determine actual physical capacity and predict subsequent physical disability in older people living in the community.
- We analysed cross-sectional data. Therefore, further investigation of the validity of these tests in predicting the risk of disability in older people using a prospective study design is recommended.

INTRODUCTION

Japan is the fastest ageing society on earth and the first large country in the history to have its population start shrinking rapidly from natural causes. The life expectancy of Japanese people (mean age: men, 79.4 years; women, 85.9 years) is at the highest level in the world. The population of Japan, which currently stands at 127 million, is expected to fall to just under 100 million in the next 40 years. By 2050, 4 of 10 adults in Japan will be older than 65 years of age. Japan implemented the national social long-term care insurance (LTCI) system on 1 April 2000. Every Japanese person aged 65 and older is eligible for benefits based strictly on physical and mental frailty or disability.[1] In June 2006, the Japanese government implemented a major LTCI reform that focused on preventive benefits for the population at high risk of disability (ie, physical and/or cognitive frailty), to contain the skyrocketing costs of the LTCI.[2]

Physical frailty increases with advancing age and is a major risk factor for dependency, institutionalisation, and mortality.[3–5] People with a disability have higher healthcare needs and use compared with those without a disability.[6] Although the biggest risk factor for future frailty is advancing age, other factors that are possibly modifiable through interventions should not be ignored. For the purpose of targeting risk factors for future frailty, adequate assessment of individual people may be required. One of the main characteristics of the elderly population is its heterogeneity, with elderly people in the same age range showing a wide variance with regard to their risk of disability. To prevent frailty or disability, population-based intervention programmes should be targeted at the population at risk. A feasible and valid screening tool available for research and clinical settings is required to identify target populations. The Interventions on the Frailty Working Group developed recommendations to screen, recruit, evaluate and retain frail older persons in clinical trials.[7] They reported that most researchers focus on the following domains for identification of physical frailty: mobility, such as lower extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance; unstable balance and factors related to body composition, such as weight loss, malnutrition and muscle loss.[7]

In an effort to select tailored preventive programmes in the Japanese LTCI system, those at high risk for subsequent disability are identified by a basic functional status questionnaire. Although the questionnaire is relatively quick to administer, a performance-based assessment could determine actual physical capacity and more accurately predict subsequent physical disability in community-living older people. Guralnik *et al*[8] reported that measures of physical performance may identify older persons with a preclinical stage of disability who may benefit from interventions to prevent the development of frank disability. A previous study identified that a rapid gait test was more likely than other mobility performance tests to discriminate older women at high risk of frailty based on the Japanese LTCI system.[9] However, which performance tests including upper and lower limb muscle functions and which cut-points are the most useful to screen for the demand for personal care are not clear. This study investigated the relationships between performance-based physical assessments and demand for personal care in older people using two large sample cohorts in Japan.

METHODS

Participants

We performed a national study of 10 351 individuals aged 65 years and older who had received personal care (n=6791) and those who had not received personal care (n=3560). The study included individuals who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE) and the Tsukui Ordered Useful Care for Health (TOUCH) programme. To enrol in the OSHPE, an individual was recruited from Obu, Japan, which is a residential suburb of Nagoya. Inclusion criteria required that the participant was aged 65 years or older at examination in 2011 or 2012, lived in Obu, and had not participated in another study. Exclusion criteria stipulated that participants be certified as needing support or care by the Japanese public LTCI system, had disability in basic activities of daily living, and could not carry out performance-based assessments. To enrol in the TOUCH programme, an individual had to be 65 years or older and certified as needing support or care from the Japanese public LTCI system. Detailed information was provided in a previous study.[10] In brief, TOUCH sites (241 day-care centres) are located throughout Japan and provide comprehensive, facility-based day-care services (eg, bath, lunch, physical and cognitive recreational activities and physical exercise). Most TOUCH clients have some physical disability and frailty, defined as the presence of weakness, low physical activity and/or slow gait speed, in accordance with the widely accepted definition of frailty.[7]

A total of 10 351 older participants (mean age, 78.8±8.0 years) underwent performance-based assessments. Informed consent was obtained from all participants prior to their inclusion in the study, and the Ethics Committee of the National Centre for Geriatrics and Gerontology approved the study protocol.

Performance-based assessment

The assessment measures were conducted by well-trained staff who had nursing, physiotherapy, occupational therapy or similar qualifications. Prior to start of the study, all staff received training from the authors in the correct protocols for administering all of the assessment measures. The assessment included several physical tests. Upper and lower limb muscle functions were assessed with the grip strength (GS) and the chair stand test (CST), respectively.[11] Gait function was assessed with walking time tests conducted at a comfortable pace (comfortable walking speed, CWS) and with the timed up-and-go (TUG) test.[12]

GS was measured in kilograms in the participant's dominant hand using a Smedley-type handheld dynamometer (GRIP-D; Takei Ltd, Niigata, Japan). The CST involved sitting down and standing up five times, using a chair without an armrest. The score was the time taken to complete the task in seconds. Participants were asked to exert their maximum effort in GS and CST. CWS was measured in seconds with a stopwatch. Participants were asked to walk on a flat and straight surface at their CWS. Two markers were used to indicate the start and end of the path, and a 2 m and over approach was allowed before reaching the start marker so that participants can walk at their comfortable pace within the timed path. They were instructed to continue walking past the end of the path for a further 2 m and over to ensure that the walking pace was consistent throughout the task. The TUG test involved rising from a chair, walking 3 m, turning around, walking back to the chair and sitting down.[12] The TUG test is one of the most frequently used tests of balance and gait, and is often used to assess fall risk in older people.[13] The time to complete the TUG test was measured, in seconds, at each participant's usual pace. Both walking tests were measured once, and if a walking aid was nomally used inside the home, this aid was used during the tests.

Cognitive function

The Mini-Mental State Examination (MMSE)[14] for the OSHPE population and the Mental Status Questionnaire (MSQ) for individuals enrolled in the TOUCH programme were used to measure cognitive functioning, and were used as potential confounders in the association between performance-based physical assessments and functional dependence.[15] Individuals with 23 or fewer points on the MMSE and three or more errors on the MSQ were considered to have cognitive impairment.[15 16]

Statistical analysis

Demographic and clinical variables were compared between the participants with and those without personal care using Student t tests for continuous variables and χ^2 tests for categorical variables. To compare the predictive ability of the study measures, receiver-operated characteristic (ROC) curves were inspected to determine cut-points for each test that best discriminated between the individuals with and those without personal care. Cut-points for maximising the sensitivity and specificity for each test were determined using the Youden index.[17] The area under the curve (AUC), sensitivity and specificity were then calculated for the cut-points. We used multivariate logistic regression analyses to determine ORs and 95% CIs, and to assess independent associations of the cut-points of physical performance measures for demand for personal care. The participants were divided into two groups according to the cut-point of the performance-based physical assessments. Covariates were added sequentially to the logistic model to evaluate the associations at different levels of adjustment. Model 1 included each performance-based physical assessment, and model 2 included the model 1 variables plus age, sex and cognitive impairment as determined by the MMSE or MSQ. Model 3 included all performance-based physical assessments plus age, sex and cognitive impairment. The participants were then divided into five groups as follows: individuals with no risk and those with 1, 2, 3 or 4 risks, according to the number of risks identified by the cut-points of the performance-based physical assessments. The ORs and 95% CIs for the number of risks were calculated adjusted for age, sex and cognitive impairment. All statistical contrasts were made at the 0.05 level of significance, and all data management and statistical computations were performed using the IBM SPSS Statistics V.19.0 software package (SPSS Inc, Chicago, Illinois, USA).

RESULTS

Comparison between participants with and those without personal care

Table 1 shows the characteristics of the participants. The participants with personal care were significantly older (p<0.001), included a higher number of women (p<0.001) and a higher number of persons with cognitive impairment (p<0.001) than those without personal care. For the comparison of performance-based assessments, the participants with personal care had significantly lower scores on all physical tests (p<0.001) compared

Table 1 Characteristics of the participants

	Participants with personal care (n=6791)	Participants without personal care (n=3560)
Age (years)*	82.6±6.7	71.8±5.2
Sex, women, n (%)*	4720 (69.5)	1793 (50.4)
Cognitive impairments, n (%)*	2962 (43.6)	562 (15.8) [8]
GS (kg)*	16.3±6.9	27.3±7.8
CST (s)*	13.0±5.6	8.6±2.4
CWS (m/s)*	0.7±0.3	1.2±0.2
TUG (s)*	16.6±7.7	8.9±1.8
Care level in the LTCI, n (%)		
Support need level 1	804 (11.8)	0 (0)
Support need level 2	1112 (16.4)	0 (0)
Care need level 1	2057 (30.3)	0 (0)
Care need level 2	1687 (24.8)	0 (0)
Care need level 3	842 (12.4)	0 (0)
Care need level 4	257 (3.8)	0 (0)
Care need level 5	32 (0.5)	0 (0)
Disability of basic ADLs, n (%)		
Eating	105 (1.5) [136]	0 (0)
Grooming	398 (5.9) [136]	0 (0)
Bathing	1374 (20.2) [136]	0 (0)
Locomotion	745 (11.0) [136]	0 (0)
Stairs	1508 (22.2) [136]	0 (0)

Individuals with 23 or fewer points on the MMSE in the participants without personal care and with three or more errors on the MSQ in the participants with personal care are considered to have cognitive impairment. Beneficiaries of the LTCI can use multiple services for which they are eligible, according to their care plan up to the maximum amount (£382 for Support Level 1; £800 for Support Level 2; £1275 for Care Level 1; £1498 for Care Level 2; £2058 for Care Level 3; £2354 for Care Level 4; £2756 for Care Level 5), in principle, for a 10% copayment and can use more services than covered as long as they pay all the costs for the services beyond the maximum level (calculated at £1=130 yen).
*Comparison between the participants with and without personal care; p<0.001, [ ] missing value.
CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; LTCI, long-term care insurance; MMSE, mini-mental state examination; MSQ, mental status questionnaire; TUG, timed up-and-go test.

Table 2 Cut-points for the risk of demand for personal care and associated sensitivity, specificity, area under the curve (AUC), and OR statistics for all participants

	Criterion	Sensitivity	Specificity	AUC
GS (kg)				
Men	<26	74	89	0.88
Women	<17	80	88	0.90
CST (s)				
Men	≥10	72	74	0.79
Women	≥10	67	77	0.78
CWS (m/s)				
Men	<1.0	86	85	0.92
Women	<1.0	90	85	0.94
TUG (s)				
Men	≥11	76	88	0.88
Women	≥11	79	89	0.90

CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; TUG, timed up-and-go test.

with those in participants without personal care (table 1). The number of participants with and without personal care who used the walking aid during the walking tests were 2593 (38.2%) and 35 (1.0%), respectively.

Cut-points between participants with and those without personal care

ROC curve analysis results, showing the performance cut-points for each test and associated statistics, are shown in table 2. The Youden index determined the cut-points for the demand for personal care as follows: GS in men and women was <26 and <17 kg, respectively; CST was ≥10 s, CWS was <1.0 m/s and TUG was ≥11 s for both sexes. The CWS score had the highest AUC for discriminating the demand for personal care and displayed good sensitivity and specificity (85–90%). High AUCs were also found for GS and TUG, as well as fair to good sensitivity and specificity (74–80%).

Relationships between cut-points and risk of disability

The multiple logistic regression models showed significant relationships between physical performances and the demand for personal care (table 3). The demand for personal care was most closely related to CWS in model 1 (OR=34.7; 95% CI 30.9 to 39.0). These results remained essentially unchanged after controlling for age, sex, cognitive impairment and other physical performance tests. In the final model (model 3), the highest OR of factors related to the demand for personal care was for CWS (OR=5.9; 95% CI 5.0 to 6.9). Figure 1 shows the distribution of CWS for participants with personal care. Participants who walked 1.1 m/s and faster had the lowest amount of personal care (20%). The rate of participants with personal care increased rapidly with a CWS slower than 1.1 m/s, and 90% of participants with a CWS slower than 0.8 m/s had personal care (figure 1A). The rate of functional decline increased rapidly for individuals walking slower than 1 m/s in women (figure 1C) rather than men (figure 1B), and with the rate of functional decline reaching 90% when CWS was slower than 0.8 m/s in both sexes (figure 1B,C).

There was a significant relationship between the number of risks based on the physical performance tests and the demand for personal care. The ORs and 95% CIs for personal care in participants with 1, 2, 3 and 4 risks were 3.1 (2.6 to 3.8), 10.6 (8.7 to 13.1), 35.6 (28.6 to 44.5) and 141.3 (103.6 to 192.7), respectively, compared with participants without risks (p<0.001). Figure 2 shows the distributions of the number of risks for demand for personal care. The rates of participants with personal care who had no risk, 1, 2 and 3 or more risks were 8.7%, 38.5%, 75.6% and 90.0%, respectively (figure 2).

DISCUSSION

Neuromuscular function, including muscle strength, balance and gait, and cognitive function are important risk factors for disability. Performance-based assessment of these factors can be used to identify people at an increased risk of future functional decline. We examined the use of various measures to identify the most useful measure for screening the demand for personal care.

Cut-points of demand for personal care

In the current study, univariate analyses identified all physical tests as being able to discriminate between participants with and those without personal care. When performance was dichotomised for cut-points, GS, CST, CWS and TUG retained statistically significant relationships with personal care. The CWS test (cut-point, 1 m/s) displayed the highest OR in the final model, with good sensitivity and specificity with respect to

Table 3 Relationships between physical performances and the demand for personal care

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
GS (men: <26 vs ≥26 kg, women: <17 vs ≥17 kg)	20.9 (18.6 to 23.5)*	8.5 (7.4 to 9.7)*	4.1 (3.5 to 4.8)*
CST (≥10 vs <10 s)	6.6 (6.1 to 7.3)*	4.1 (3.7 to 4.7)*	1.3 (1.1 to 1.5)*
CWS (<1 vs ≥1 m/s)	34.7 (30.9 to 39.0)*	17.5 (15.3 to 20.0)*	5.9 (5.0 to 6.9)*
TUG (≥11 vs <11 s)	27.1 (24.1 to 30.5)*	15.3 (13.4 to 17.6)*	4.0 (3.4 to 4.8)*

*p<0.01.
Model 1 was crude ORs and Model 2 was adjusted for age, sex and cognitive impairment. Model 3 was adjusted for age, sex, cognitive impairment and physical performances.
CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; TUG, timed up-and-go test.

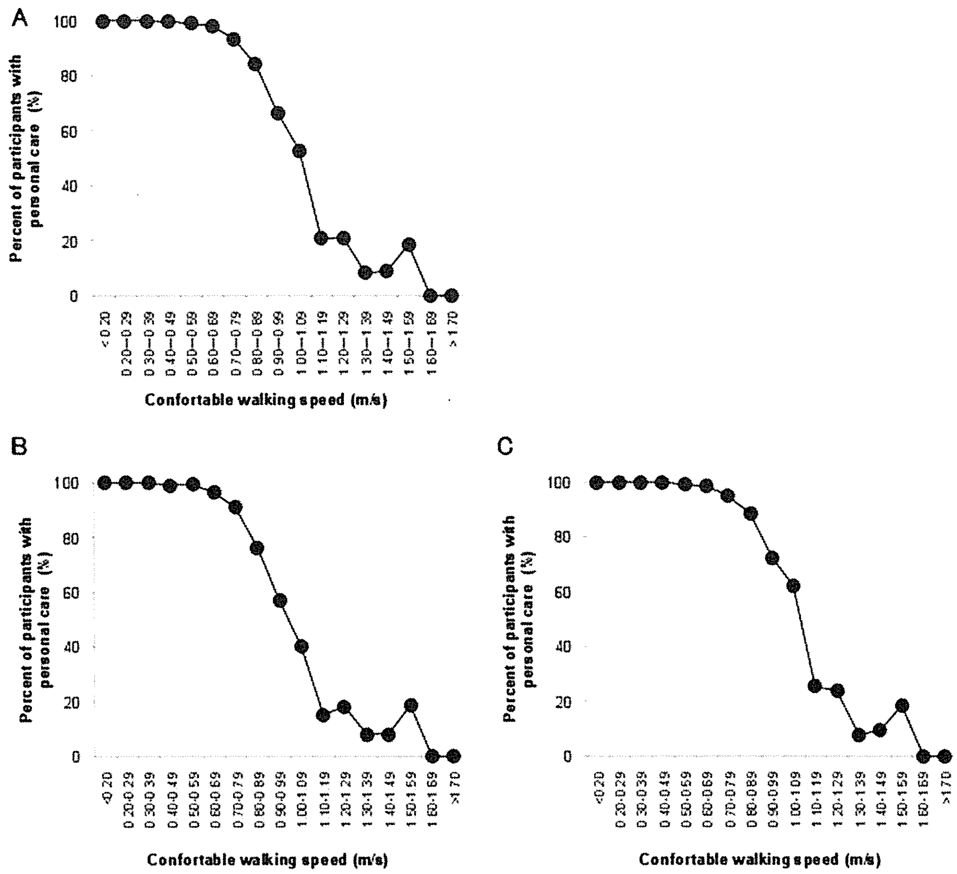

Figure 1 Comfortable walking speed distributions of participants with personal care in all participants (A), men (B) and women (C). The rate of participants with personal care markedly decreased at 1.0 m/s and faster at a comfortable walking speed.

identifying participants with personal care. At identified cut-points, GS (men, 26 kg; women, 17 kg), CST (10 s) and TUG (11 s) could also significantly discriminate participants with personal care with sensitivities and specificities of 67–89%. This result highlights what can occur when dichotomised rather than continuous data are used. There is an associated loss of information and reduced predictive accuracy as a trade-off for ease of scoring and test interpretation. These results, however, are consistent with previous findings that showed associations between measures of muscle strength and mobility and functional decline.[18]

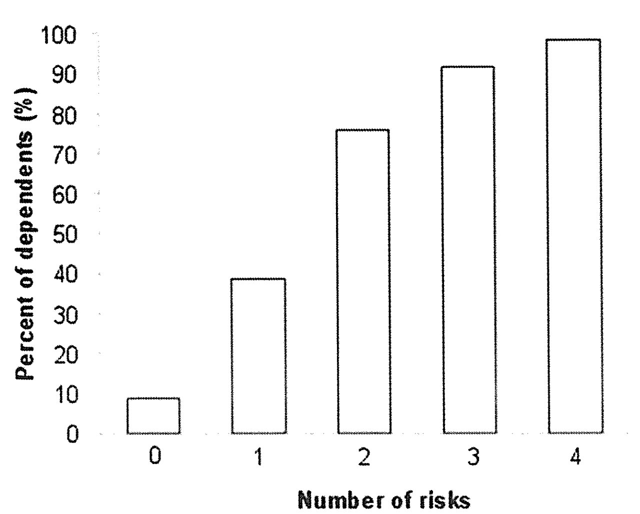

Figure 2 Participants with personal care according to the number of risks identified by cut-points of physical performance tests. Percentages of participants with personal care who had no risk, 1, 2 and 3 or more risks were 8.7%, 38.5%, 75.6% and 90%, respectively.

Gait speed and personal care

Gait velocity, as measured by the CWS test in this study, has been consistently reported to differentiate between participants with and those without personal care, with frail older persons walking significantly slower,[10 19] and has proved to be a strong predictor of adverse events, such as disability,[18 20–25] mortality,[21 22 26 27] hospitalisation[21 22 24 28] and falls.[28 29] Gait slowing, which occurs in the latest stages of life, suggests that mobility is so central to life that energy is shifted away from walking activity only when other vital activities are threatened,[30] which may lead to increased functional independence. In addition, a slower walking speed is an associated factor for subsequent dementia.[31] Dementia is one of the most important factors of health problems for functional decline in the aged population. For our study sample, the cut-point for CWS was 1 m/s, which is the critical point for future functional decline in community-dwelling older people determined by previous studies.[18 21 22 24 25] These results suggest that walking speed may be the most crucial measurement to determine the demand for personal care in older adults. Measurement of walking speed is reliable, valid, sensitive, inexpensive, safe, quick and a simple tool. Therefore, measurement of walking speed is suitable to use in community settings as a screening tool and evaluation for the effect of a care prevention programme.

Muscle strength and mobility and personal care

In the current study, higher ORs were found for GS and TUG, as well as CWS. Hand GS is an estimate of isometric strength in the upper extremity, but also correlates with strength in other muscle groups,[32] and therefore, is considered an estimate of the overall strength. In addition, GS has proved to be a strong predictor of physical functioning and disability,[33 34] morbidity[35] and mortality.[36 37] Our findings support previous evidence and add cut-points of <26 kg in men and <17 kg in women that discriminate those at high-risk for disability in community-living older people. The TUG has been recommended as a screening tool for identifying older people who are at risk for falling.[38 39] Bischoff *et al*[40] proposed a normative cut-point of 12 s for community-dwelling elderly people between 65 and 85 years of age. In daily clinical practice, elderly persons who perform the TUG in >12 s should receive early evaluation and intervention. Our results regarding TUG cut-points are in line with these previous studies.

Strengths and limitations

Strengths of the present study include a large sample size and we used performance-based assessment, which could determine actual physical capacity and predict subsequent physical disability in community-living older people. However, the present study has a number of limitations. One of the limitations is that we analysed cross-sectional data. Therefore, further investigation of the validity of these tests in predicting the risk of disability in older people using a prospective study design is recommended. Another limitation is that many frail older people using healthcare services cannot walk because they have multiple diseases or geriatric syndromes. Non-ambulatory participants were excluded from our study. Therefore, we acknowledge that the study findings may not be generalised to this frailer group.

CONCLUSIONS

This study provides preliminary evidence that clinical tests of physical performances can predict the risk of disability in older people. Logistic regression analysis selected CWS as the best independent correlate of disability, with good sensitivity and specificity. Further investigation is required, and future research should include a prospective measurement of the risk of disability to more accurately determine the validity of screening tests for this population.

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ORIGINAL RESEARCH

Cognitive function affects trainability for physical performance in exercise intervention among older adults with mild cognitive impairment

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Background: Although much evidence supports the hypothesis that cognitive function and physical function are interrelated, it is unclear whether cognitive decline with mild cognitive impairment influences trainability of physical performance in exercise intervention. The purpose of this study was to examine the association between cognitive function at baseline and change in physical performance after exercise intervention in older adults with mild cognitive impairment.
Methods: Forty-four older adults diagnosed with mild cognitive impairment based on the Peterson criteria (mean age 74.8 years) consented to and completed a 6-month twice weekly exercise intervention. The Timed Up and Go (TUG) test was used as a measure of physical performance. The Mini-Mental State Examination (MMSE), Trail Making Test Part B, Geriatric Depression Scale, baseline muscle strength of knee extension, and attendance rate of intervention, were measured as factors for predicting trainability.
Results: In the correlation analysis, the change in TUG showed modest correlations with attendance rate in the exercise program ($r = -0.354$, $P = 0.027$) and MMSE at baseline ($r = -0.321$, $P = 0.034$). A multiple regression analysis revealed that change in TUG was independently associated with attendance rate ($\beta = -0.322$, $P = 0.026$) and MMSE score ($\beta = -0.295$, $P = 0.041$), controlling for age and gender.
Conclusion: General cognitive function was associated with improvements in physical performance after exercise intervention in subjects with mild cognitive impairment. Further research is needed to examine the effects of exercise programs designed to address cognitive obstacles in older adults with mild cognitive impairment.
Keywords: exercise, mobility, rehabilitation, Timed Up and Go test

Introduction

Mild cognitive impairment is widely regarded as a transitional syndrome between normal cognitive ageing and clinical dementia.[1] Deterioration in episodic learning and memory functions constitute the core characteristics of mild cognitive impairment and Alzheimer's disease. Older adults with mild cognitive impairment demonstrate decreased physical performance, which in turn is related to the risk of Alzheimer's disease.[2] Reduced physical function leads to restricted life space mobility,[3] which is associated with increased risk of Alzheimer's disease and cognitive decline among older persons.[4] Improved usual gait speed over a 12-month period predicts a substantial reduction in mortality.[5] Maintaining and improving physical function may be beneficial for preventing conversion to Alzheimer's disease in older adults with mild cognitive impairment.

A better understanding of the modifiable factors independently associated with improved physical performance is needed.[6] This would ensure effective intervention

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based on a valid theoretical framework for increasing physical performance. Possible modifiable factors include cognitive function, mental status, and physiological function, such as muscular strength. Logsdon et al[7] found that older adults with mild cognitive impairment may benefit significantly from an exercise program specifically designed to address their cognitive needs (ie, memory aids and easy to follow instructions). They suggest that cognitive impairment may prevent successful engagement in exercise. Several studies support the hypothesis that cognitive and physical function are interrelated,[2,8] although it is not clear whether older adults with mild cognitive impairment have decreased trainability for improving physical performance.

The purpose of this study was to examine the association between cognitive function at baseline and trainability of physical performance using a 6-month exercise intervention in older adults with mild cognitive impairment. We used the Timed Up and Go test (TUG) as an assessment of physical performance.[9] This test has frequently been used to assess lower extremity function, mobility, and risk of falls in older adults. Recent research has revealed that TUG is associated with executive function[8] and periventricular leukoaraiosis[10] in older adults with mild cognitive impairment. Changes in TUG before and after intervention were measured as the dependent variable. In the present study, we defined trainability as the ability to be trained and this was expressed by rate of improvement between before and after intervention.[11] By means of correlation and regression analysis, we examined how cognitive function at baseline influenced change in TUG. Other factors including depression, attendance rate, and physiological function (such as muscle strength) were also investigated. Similar to the relationship between physical and cognitive function,[2,8] it is also possible that improvements in physical performance are associated with cognitive function, where cognitive impairment may prevent successful engagement in exercise.

We hypothesized that reduced cognitive functioning affects trainability of physical performance by exercise intervention in older adults with mild cognitive impairment. This investigation is critical for the exploration of the modifiable factors associated with trainability in order to plan future rehabilitation programs that prevent deterioration of physical and cognitive function.

Materials and methods

Subjects

The participants were recruited from two volunteer databases (n = 1543), which included elderly participants aged 65 years and over who either attended a health check in Obu, Japan, or were selected by stratified random sampling. The strata used in our stratified random sampling were age and gender. Criteria for inclusion in this intervention study required that participants were 65 years or older, living independently in the community (ie, no impairment of activities of daily living), and Japanese-speaking, with sufficient hearing and visual acuity to participate in the examinations. In the first eligibility assessment for this study, 528 potential participants who had either a Clinical Dementia Rating of 0.5 or subjective memory complaints were screened. One hundred and thirty-five participants met the criteria for the second eligibility assessment. They also needed to meet the Peterson criteria for a diagnosis of mild cognitive impairment.[1] The final sample consisted of 44 older adults (mean age 74.8 years; 20 males; mean years of education, 11.1 years). These participants were exposed to an exercise intervention and they completed a randomized controlled trial that aimed to examine the effect of multicomponent exercise on cognitive function. The design and the primary results of the study have been reported elsewhere.[12]

Exclusion criteria included a history of major psychiatric illness (eg, schizophrenia or bipolar disorder) and other serious neurological or musculoskeletal diagnoses. This study was approved by the ethics committee of National Center for Geriatrics and Gerontology, Japan. Appropriate written informed consent was obtained for all participants.

Procedures

The 6-month exercise program involved biweekly 90-minute sessions with a combination of aerobic exercise, muscle strength training, and postural balance retraining. In addition, the exercise program focused on promoting exercise and behavior change. Two trained physiotherapists involved in geriatric rehabilitation conducted the interventions. Each supervised session began with a 10-minute warmup period and stretching exercise, followed by 20 minutes of muscle strength exercise. The participants then practiced aerobic exercise, postural balance retraining, and a combination of both activities over a period of 60 minutes.

Before and after each session of the program, physiotherapists conducted a health check of each participant. The physiotherapists and a well trained instructor implemented risk management for adverse events during the program. In the aerobic exercise, participants performed stair stepping and endurance walking. The intensity of the aerobic exercise was prescribed at approximately 40% of maximum heart rate during weeks 1–8. The intensity was then increased to 60% of maximum heart rate from week 9. Heart rate was measured before and after exercise at every training session for risk management and estimation of the strength of training. The strength of aerobic exercise was adjusted by the height of the stair in stair stepping, walking speed, or weights put on participants' feet in endurance walking. Eleven of the 40 classes during the 6-month intervention period included approximately 20–30 minutes of consecutive outdoor walking. Muscle strength training was mainly performed using subjects' own weight; training equipment was not used (eg, knee extension, calf raise, squat). Postural balance exercise (such as tandem walking and side walking on balance boards) was also included in the program. There were five different widths of balance boards (4, 6, 8, 10 and 12 cm), which were narrowed progressively. Further, participants performed a combination of exercises (eg, circuit training including stair-stepping, endurance walking, and walking on balance boards). They also performed concurrent cognitive tasks during exercise (eg, walking while inventing a poem) because effects of dual tasks on brain activation have been reported.[13] Between individual training sessions, participants were invited to sit and rest for about 5 minutes. Participants were required to perform daily home-based muscle strength exercises and walking. These were self-monitored using a booklet and pedometer based on the concept of promoting exercise and behavior change.

Physical performance test to assess trainability

The TUG was used to assess physical performance.[9] The TUG involves rising from a chair, walking 3 meters, turning around, walking back to the chair, and sitting down. Participants were instructed to complete the task at their usual walking pace. The score for this test represents the time (in seconds) that the participant needed to complete the assessment. Lower times indicate better physical performance. The recorded TUG score was the lesser of the times measured in the two trials in order to exclude immediate change by learning effects from the measured value.[14] Licensed and well-trained physical therapists assessed the physical performance tests. Interrater reliability of TUG is very high in community-dwelling older adults (intraclass coefficient of 0.98).[15] Changes in TUG were calculated as trainability using the following formula:

$$(\text{Post score} - \text{pre score})/\text{pre score}.$$ [11]

Thus, a higher negative value represents greater improvement by exercise intervention.

Potential correlates

All measurements were performed before the intervention commenced. Demographic data were recorded, including age, gender, number of medications, and educational history. Depressive symptoms were measured using the 15-item Geriatric Depression Scale (GDS).[16]

All neuropsychological testing was conducted by well trained speech therapists. Each score was rechecked by one therapist who was blinded to all other participant data. General cognitive function was assessed with the Japanese version of 30-item Mini-Mental State Examination (MMSE),[17] the most frequently used cognitive screening measure in cognitive aging research, with good test-retest reliability (intraclass coefficient = 0.827).[18,19] Executive function was assessed using the Trail Making Test Part B (TMT-B).[20] For this task, participants were required to navigate a series of alternating numbers and letters, and connect them in alternating sequential order. In the Japanese version of the TMT-B, letters from the Roman alphabet are exchanged for Kana characters.[21] The time required to complete each task was recorded, where a higher time indicates a poorer performance. The TMT-B has demonstrated adequate test-retest reliability for use in longitudinal studies.[21]

The participants' muscle strength of knee extension was measured twice using a dynamometer (MDKKS, Molten Co, Ltd, Tokyo, Japan). The recorded strength score was the higher of the strength measurements (Nm/kg) in the two trials.[22]

Statistical analysis

The data were analyzed using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc, Chicago, IL). A probability level of $P < 0.05$ was considered to be statistically significant. Data were expressed as mean values and standard deviations. TUG scores were compared before and after intervention using the paired Student's *t*-test. The relationships between change in TUG score and potential correlates (measurements at baseline and attendance rate for exercise intervention) were investigated using Pearson's correlation. A stepwise multivariate linear regression model was used to examine whether potential predictors were independently associated with the change in TUG. Age, gender, and other variables that were significantly correlated with change in TUG were entered as independent variables.

Results

Table 1 shows the demographic and baseline clinical characteristics and attendance rate of the study participants. Mean adherence to the exercise program was 88.2%. TUG showed significant ($P < 0.001$) improvement between before

Table 1 Demographic and clinical characteristics of study participants

Age (years)	74.8 ± 7.3 (65–93)
Education (years)	11.1 ± 2.9
Gender (males)	20 (48)
Medications (n)	2.6 ± 2.3
MMSE (points)	26.9 ± 2.3
GDS (points)	3.7 ± 2.9
TMT-B (seconds)	174.9 ± 75.3
Muscle strength of knee extension (Nm/kg)	1.19 ± 0.4
TUG (seconds)	8.6 ± 1.9
Attendance rate (%)	88.2 ± 19.2

Note: values presented are the mean ± standard deviation or n (%).
Abbreviations: MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; TMT-B, Trail Making Test Part B; TUG, Timed Up and Go test.

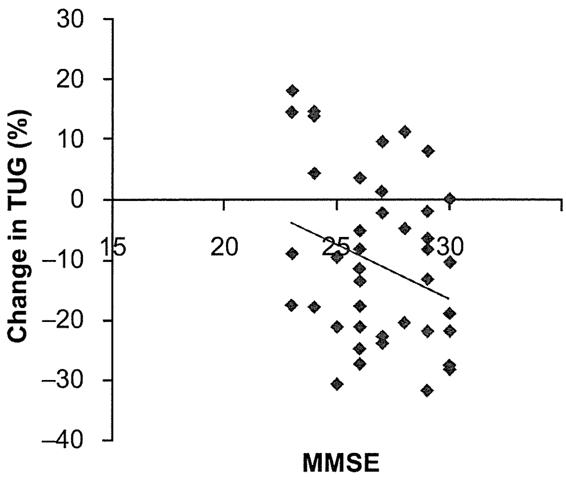

Figure 1 Scatter graph showing the relationship between change in Timed Up and Go test and Mini-Mental State Examination scores.
Abbreviations: MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test.

and after intervention (8.6 ± 1.9 versus 7.6 ± 2.1 seconds, respectively). In the correlation analyses (Table 2), the change in TUG had significant negative correlations with attendance rate (r = −0.354, P = 0.027) and MMSE (r = −0.321, P = 0.034; Figure 1). The change in TUG was not correlated with age (r = 0.146, P = 0.35), TMT-B (r = 0.202, P = 0.19), GDS (r = 0.03, P = 0.85), or muscle strength of knee extension (r = −0.236, P = 0.12).

Table 3 shows the factors that were significantly related to change in TUG in the stepwise multiple regression. The regression model explained 24% of the change in variance of TUG. The factors retained in the final model were attendance rate (β = −0.322, P = 0.026) and MMSE (β = −0.295, P = 0.041). Age and gender did not show a significant relationship with change in TUG.

Discussion

Exercise intervention was considered beneficial for older adults with mild cognitive impairment in the present study, and we showed a significant improvement in physical performance between before and after intervention. However, investigation of the association between physical performance and other variables revealed that improvement in physical performance after exercise intervention depended on general cognitive function, as assessed by the MMSE, in addition to attendance rate. Generally, it has been reported that exercise intervention in older adults improves physical performance, such as gait speed,[23] dynamic balance,[24] and cardiovascular fitness.[25] Previous studies targeting older adults with Alzheimer's disease or dementia have reported larger improvements in TUG (approximately 41%)[26–28] than those reported in the present study (8.6%); however, we targeted relatively healthy older adults with better physical function at baseline. This is the first study to focus on baseline cognitive function and the trainability of physical performance in older adults with mild cognitive impairment.

The results of the present study indicate that general cognitive function may be important for persons with mild cognitive impairment to gain benefit from an exercise intervention. Previous studies support the relationship between cognitive and physical function.[2,8] Therefore, general cognitive function may provide an important basis for improvement in physical performance, particularly in older adults with mild cognitive impairment. It is possible

Table 2 Correlation coefficients for potential correlates and change in TUG

Potential correlates	Change ratio in TUG Correlation coefficient	
	R	*P* value
Age	0.146	0.35
MMSE	−0.321	0.034
GDS	0.03	0.85
TMT-B	0.202	0.19
Muscle strength of knee extension	−0.236	0.12
Attendance rate	−0.354	0.027

Abbreviations: MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test; GDS, Geriatric Depression Scale; TMT-B, Trail Making Test Part B.

Table 3 Factors associated with improved TUG in stepwise multiple regression

	Factors	β	*P* value	R^2
Change ratio in TUG	Attendance rate	−0.322	0.026	0.24
	MMSE	−0.295	0.041	

Abbreviations: TUG, Timed Up and Go test; MMSE, Mini-Mental State Examination.

that persons with mild cognitive impairment may experience several cognitive obstacles, such as difficulties in learning new exercises and remembering how to perform them correctly, even if they have previously participated in the same programs with similar adherence.

Our findings suggest that it is important for therapists and health care practitioners to assess general cognitive function in order to estimate training ability at baseline and adjust their approach to exercise. Logsdon et al[7] reported that older adults with mild cognitive impairment show significant benefit from an exercise program specifically designed to address their cognitive needs. The findings of the present study confirm that physical benefits vary based on the degree of general cognitive functioning. This indicates the necessity for older adults with mild cognitive impairment to engage in an exercise program specifically designed to address cognitive needs (ie, one that provides memory aids and easy to follow instructions). In addition, individually prescribed exercise is a more effective intervention strategy for the improvement of balance, gait performance, and reduction in risk of falling than group exercise in older adults.[29]

When an exercise program is prescribed for older adults in clinical practice, individual physical function is usually considered an important factor, by which strength and contents of exercise are regulated by therapists or practitioners. Our findings suggest that it is also important for therapists or practitioners to assess general cognitive function in order to estimate training ability at baseline and adjust their approach to exercise. Exercise programs designed to address cognitive obstacles should be developed and prescribed according to the level of cognitive functioning in older adults with mild cognitive impairment. For example, we recommend that complex exercise behaviors are broken into small steps and practiced repeatedly in class, and simple written materials are provided along with memory aids to support exercise outside of class.[7] These programs, tailor-made for level of cognitive function, would be effective and efficient for improving physical function in older adults.

Improvement in some aspects of cognitive function has been related to adherence to an exercise program in older adults with mild cognitive impairment.[30] This finding is in line with the present study which shows that attendance rate was associated with improvement in physical performance. Williams et al[31] reported that reduced muscle strength, slow reaction time, and psychoactive drug use explained most of the variance in adherence during an exercise trial. For interventions to be effective it may be important to maintain attendance rates by addressing associated factors.

Several limitations in this study need to be mentioned, such as the small sample size and lack of a control group. Additionally, there may be other compounding factors, such as motivation and self-efficacy, which should be included in future analysis. Only 24% of the change in TUG variance could be explained in the present study. Future research should include a broader range of cognitive impairment levels, more detailed neuropsychological testing, and more extensive physical assessments, particularly those that may have more or less of a cognitive demand than TUG. These areas should be addressed to evaluate the association between various cognitive functions and trainability of physical performance in detail and to determine the cutoff points for predicting improvement in physical performance. Further research is needed to clarify whether specific exercise programs designed to address cognitive obstacles could improve physical function effectively and lead to a potentially preventive effect for conversion to Alzheimer's disease. Our findings concerning the relationship between trainability and cognitive function are specific to older adults with mild cognitive impairment, and cannot be applied to persons with severe dementia.

In summary, despite some limitations, the present study examined the association between cognitive function at baseline and the effect of intervention on physical performance in older adults with mild cognitive impairment. Our results reveal that MMSE and attendance rate were independently associated with improvement in physical performance. A major implication of this study is that general cognitive function may be important for persons with mild cognitive impairment to gain benefit from an exercise intervention.

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Disclosure

The authors report no conflicts of interest in this work.

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RESEARCH ARTICLE | Open Access

Poor balance and lower gray matter volume predict falls in older adults with mild cognitive impairment

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Abstract

Background: The risk of falling is associated with cognitive dysfunction. Older adults with mild cognitive impairment (MCI) exhibit an accelerated reduction of brain volume, and face an increased risk of falling. The current study examined the relationship between baseline physical performance, baseline gray matter volume and falls during a 12-month follow-up period among community-dwelling older adults with MCI.

Methods: Forty-two older adults with MCI (75.6 years, 43% women) underwent structural magnetic resonance imaging and baseline physical performance assessment, including knee-extension strength, one-legged standing time, and walking speed with normal pace. 'Fallers' were defined as people who had one or more falls during the 12-month follow-up period.

Results: Of the 42 participants, 26.2% (n = 11) experienced at least one fall during the 12-month follow-up period. Fallers exhibited slower walking speed and shorter one-legged standing time compared with non-fallers (both *p* < .01). One-legged standing time (sec) (standardized odds ratio [95% confidence interval]: 0.89 [0.81, 0.98], *p* = .02) was associated with a significantly lower rate of falls during the 12-month follow-up after adjusting for age, sex, body mass index, and history of falling in the past year at baseline. Voxel-based morphometry was used to examine differences in baseline gray matter volume between fallers and non-fallers, revealing that fallers exhibited a significantly greater reduction in the bilateral middle frontal gyrus and superior frontal gyrus.

Conclusions: Poor balance predicts falls over 12 months, and baseline lower gray matter densities in the middle frontal gyrus and superior frontal gyrus were associated with falls in older adults with MCI. Maintaining physical function, especially balance, and brain structural changes through many sorts of prevention strategies in the early stage of cognitive decline may contribute to decreasing the risk of falls in older adults with MCI.

Background

Falls and fall-related injuries are a common healthcare problem, and represent important causes of morbidity and mortality in older populations. One-third of all community-dwelling adults age 65 years and older experience at least one fall annually [1]. Many distinct causes for falls in older people have been reported by a large number of studies [1-4]. Impaired physical function, particularly muscle weakness and problems with gait and balance, are the most important contributors to the risk of falling [5]. The ageing of the worldwide population in recent decades has resulted in an increasing number of older adults with cognitive decline [6], and cognitive impairment has also been found to increase the risk of falling [7-10]. As such, correctly identifying the risk factors for falling among older adults with cognitive impairment is an important research question. In addition, people with cognitive impairment recover less well after a fall than those without cognitive impairment [11]. Therefore, the falling may have negative impact on health in older people with cognitive

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impairment compare with those without cognitive impairment. In older individuals with mild cognitive impairment (MCI) in particular, consideration of a broad range of causes of falls could play a role in reducing the fall risk and providing strategies to prevent falls among the high-risk population.

Several studies have examined falling in older adults with dementia, such as Alzheimer's disease [11,12]. However, little research has focused on falling among people with MCI, even though mild declines in cognitive function have been reported to be an important factor associated with falling [13]. Liu-Ambrose et al. demonstrated that older community-dwelling people with MCI but not dementia were at greater risk of falling than those without MCI [14]. Brain structural changes represent one of the key clinical features associated with MCI, including gray matter volume loss [15] and white matter hyperintensities (WMH) [16]. A recent prospective study indicated that greater WMH burden predicts falls over 12 months in non-demented community-dwelling older adults [17].

Although prospective evidence suggests that WMH are an important risk factor for falls in community-based older populations [17,18], it remains unclear whether gray matter volume predicts falls and which regions are related to a greater risk of falls in older adults with MCI. Structural changes in the brain have been linked to motor performance deficits [19]. WMH was reported to exhibit a negative correlation with postural stability involved balance, stepping and gait [20], while reduced gray matter density is associated with impaired gait performance [21-23] and postural instability [24]. Kido et al. [24] suggested that postural instability is associated with gray matter volume loss, and is related to pathological cognitive decline, such as MCI and AD. Lower gray matter volume has been found to be related not only to cognitive decline, but also to decreased physical function. Thus, gray matter volume loss may increase the risk of falls in older adults with MCI. In particular, a smaller volume of the prefrontal area might be associated with poor physical performance [22,23], such as slower gait and poor balance, but no evidence has been reported that smaller brain volume of specific regions is related to the occurrence of subsequent falls in older adults with MCI. In the current study, we sought to examine whether physical performance and gray matter volume were related to falls during a 12-month follow-up period among community-dwelling older adults with MCI.

Methods

Participants

The sample for this longitudinal study consisted of 42 community-dwelling older adults with MCI who completed a randomized controlled trial (RCT) (trial registration: UMIN-CTR UMIN000003662) evaluating the effects of multicomponent exercise on cognitive function. The Ethics Committee of the National Center for Geriatrics and Gerontology approved the study protocol. The study design and the primary results of the RCT have been described previously [25]. All participants gave written informed consent prior to taking part in the study. Briefly, participants enrolled in the RCT were: aged 65 years and over, community dwelling, and did not suffer from dementia. All participants met the Petersen criteria for MCI [26]. Participants who had a Clinical Dementia Rating (CDR) = 0, or a CDR of 1–3, a history of neurological, psychiatric, or cardiac disorders or other severe health issues, use of donepezil, impairment in basic activities of daily living (ADL), and participation in other research projects were excluded from the RCT study. A total of 100 participants took part in the RCT and completed neuropsychological assessments including language, memory, attention, and executive function tests. All subjects in this study had objective impairments at least 1.5 standard deviations below the age-adjusted mean for at least one of the neuropsychological tests. The participants were classified to an amnestic MCI (aMCI) group (n = 50) with neuroimaging measures, and other MCI group (n = 50) before the randomization. The subjects in each group were then randomly assigned to either a multicomponent exercise group or an education control group using a ratio of 1:1. The sample for this longitudinal study involved participants in a control group. Of the 50 participants in the control group, 42 completed fall follow-up assessments during the 12-month follow-up period.

Physical performance measures

At baseline, all participants underwent an extensive assessment of measures by licensed and well-trained physical therapists.

Knee-extension strength

Isometric knee extension strength was tested twice using a dynamometer (Model MDKKS, Molten Co Ltd, Hiroshima, Japan) from the dominant leg (self-reported side they would use to kick a ball as far as possible). Knee extension was measured while the participant was sitting on a chair with a backrest and the knee flexed to 90°. A testing pad was attached to the front lower leg of the participant and strapped to the leg of the chair. The participant was instructed to push the pad with maximal strength. Licensed and well-trained physical therapists confirmed compensatory movement and assessed muscle strength. Participants practiced several times before data collection. Two trials were conducted,