International Journal of Gerontology 15 (2021) 39–44
https://doi.org/10.6890/IJGE.202101_15(1).0008

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Association of Mild Cognitive Impairment and Muscle Mass/Strength in Community-Dwelling Older Chinese

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ARTICLE INFO

Accepted 25 August 2020

Keywords:
mild cognitive impairment,
muscle mass,
muscle strength,
community-dwelling,
older Chinese

SUMMARY

Background: This study elucidated the association between mild cognitive impairment (MCI) and muscle mass/strength in community-dwelling older Chinese.
Methods: 267 Chinese participants aged 60 years old or above were recruited. Global cognitive function was assessed using the Mini-Mental State Examination (MMSE), and the cut-off for MCI was ≤ 27. Muscle mass and strength were measured using whole-body dual-energy X-ray absorptiometry (DXA) scan and handgrip strength, respectively. The associations between age and MMSE score, muscle strength, muscle mass and physical performance were evaluated. The participants were firstly divided into MCI and normal groups according to the MMSE score, then the participants were stratified by age (60–69 and ≥ 70 years old, respectively) to analyze muscle strength, muscle mass and physical performance.
Results: After adjusting for body mass index (BMI), education level, medical history, health behavior and depressed mood, the decreases in muscle mass/strength, physical performance, and the MMSE score were associated with advancing age in both genders. In female participants ≥ 70 years old, muscle strength significantly decreased in the MCI group ($p < 0.05$) compared with normal group. Muscle mass of the lower limbs also significantly decreased in the MCI group of females ≥ 70 years old compared with normal group ($p < 0.05$).
Conclusion: Older female Chinese community dwellers with MCI had a decreased muscle strength and lower limb muscle mass. Considering the relationship between cognitive status and muscle mass/strength, our study will provide insight to clinicians for developing a screening program for community-dwelling Chinese older than 70 years old.

1. Introduction

Age-related decreases of muscle strength and/or mass and performance, i.e., sarcopenia, were considered to be associated with several worse health outcomes, including infectious complications, prolonged duration of mechanical ventilation, longer hospitalization, greater need for rehabilitation care after hospital discharge, and higher mortality.[1] Its prevalence in elderly community-dwelling Chinese was reported to be 12.5% for women and 8.2% for men according to the definition of the Asian Working Group for Sarcopenia (AWGS).[2,3] However, the mechanism underlying the development of sarcopenia are still not completely understood and most likely multi-factorial. Other than aging, possible causes of sarcopenia include hormonal dysregulation, chronic inflammatory status, ectopic adipose tissue accumulation and malnutrition.[4] Sarcopenia is also recognized as a systemic condition that is related to comorbidities, such as diabetes mellitus, depression, and cardiovascular events.[1] Decreases in cognitive function are also a core feature of aging and comorbidity with chronic diseases, but its association with sarcopenia is also not clear.

Mild cognitive impairment (MCI) was defined as a cognitive decline that exceeded the expectation for an individual's age and education level, but it did not notably interfere with activities of daily life.[5] The MCI prevalence in adults older than 60 years ranged from 3.2% to 23.2% due to different study designs.[6,7] Some people with MCI remained stable or returned to normal over time, but more than half progressed to dementia within 5 years.[8] MCI was a transitional state between normal aging and dementia.[9] Although MCI and sarcopenia are prevalent features of advanced aging, the relationship of these conditions is still not fully understood because of the use of different tools for evaluating cognitive function and modalities for measuring body composition.

A study of community-dwelling Taiwanese has showed an association between sarcopenia and cognitive impairment.[10] However, there were no previous investigation on the association between MCI and muscle strength and/or mass in community-dwelling older Chinese. Therefore, the present study elucidated the relationship of MCI and muscle strength, muscle mass and physical performances in

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community-dwelling older Chinese.

2. Methods

2.1. Participants

Inclusion criteria required each participant to be 60 years or older at the time of examination and to reside in Nanjing (China) city. Subjects with any of the following conditions were excluded: (1) instability in communication to complete the interview; (2) having any diseases such as hyperthyroidism, hypothyroidism, or chronic heart and renal failure; (3) receiving long-term steroid treatment; (4) suffering from a malignant tumor. The characteristics of subjects, including education level, medical history, and health behavior, were obtained through self-report. The interviews were conducted in Mandarin. Body mass index (BMI) and blood pressure were measured before interviews.

The Ethics Committee of the First Affiliated Hospital of Nanjing Medical University approved the study, which was performed in accordance with its guidelines for the protection of human subjects. Informed consent was obtained from all participants included in the study.

2.2. Muscle strength measurement

2.1.1. Handgrip strength

Upper limb muscle strength was evaluated via measurement on handgrip strength of the subject's dominant hand. The handgrip strength of the dominant hand was measured in kg using a portable hydraulic dynamometer (Jamar, 5030J1, Jamar Technologies, Horsham, PA, USA). The participants adopted a seated, upright position in a height-adjustable chair with their feet supported, shoulders adducted and neutrally rotated, elbow fixed at 90°, forearm in neutral position, and wrist at an extension between 0° and 30°. The tested arm was positioned on a table to support the weight of the dynamometer. The subjects were instructed and verbally encouraged to squeeze the handgrip as hard as they could. The higher of the two handgrip scores was used for analysis according to previous trials.[11] The measurement was performed by the same skilled staff.

2.3. Chair stand test

The chair stand test, also called the chair rise test, was used as a proxy for leg muscle strength. Participants were asked to stand and sit in a chair five times as quickly as they could with their arms crossed over the chest, and skilled staff measured the time they spent on performing this task using a stopwatch.

2.4. Muscle mass measurement

All subjects underwent whole-body dual-energy X-ray absorptiometry (DXA, Hologic Inc., Bedford, MA, USA) scans to obtain total fat-free mass, including android, gynoid, trunk, upper limb and lower limb. Limb fat-free mass (the sum of lean mass in the arms and legs) was used as a good proxy for appendicular skeletal muscle (ASM) mass. Height-adjusted relative appendicular skeletal muscle (RASM) was calculated (ASM/height^2, kg/m^2).

2.5. Physical performance

2.5.1. Gait speed

Gait speed was evaluated using a 4-meter walk as physical performance. Participants walked straight for 4 meters at his/her usual pace, and skilled staff measured the time they spent on performing this task using the same stopwatch. Each participant was asked to perform twice, and the shorter time was recorded for analysis.

2.6. Short Physical Performance Battery (SPPB)

The SPPB was a composite test that included an assessment of gait speed, a balance test, and a chair stand test.[12] For balance, participants were asked to remain standing with their feet as close together as possible, then move to a semi-tandem position (heel of one foot alongside the big toe of the other foot) and finally to a tandem position (heel of one foot directly in front of the other foot). Each position was held for 10 seconds. Each test was scored from 0 (worst performance) to 4 (best performance), and a total score was obtained for the entire battery, which was the sum of all 3 tests and varied between 0 and 12.[13]

2.7. Cognitive function

The 30-item Mini-Mental State Examination (MMSE) was used to assess cognitive function. MMSE cannot be used to diagnose dementia, but it is practical to use in community surveys as a brief screening test for global cognitive evaluation.[14] When detailed neuropsychological tests are not feasible, MMSE is a promising screening tool, including subtyping for MCI.[15] An MMSE score of 27 or lower is considered as MCI.[9,15] Participants were excluded when the MMSE score was ≤ 17 for illiteracy, ≤ 20 for primary school, ≤ 22 for middle school and ≤ 23 for college.

2.8. Covariates

Demographic characteristics of all participants, including age, gender, height, weight, and body mass index (BMI), were obtained for analysis. Past medical history and health behavior were recorded. Depressive symptoms were measured using the Geriatric Depression Scale (GDS). GDS scores range from 0 to 30, and a GDS score of 11 or greater reflected high depressive symptoms.[16]

2.9. Statistical analysis

Data of continuous variables were expressed as the mean ± standard deviation, and categorical data were expressed as numbers and percentages. All statistical analyses were performed using software SPSS 25.0 (Chicago, IL, USA). Comparisons of continuous variables were performed using Student's *t*-test or Mann-Whiney U-test. Comparisons of categorical variables were performed using the chi-squared test. The associations between age and MMSE scores, muscle strength, muscle mass, and physical performance were evaluated using a partial correlation analysis. A two-tailed p value < 0.05 was considered statistically significant.

3. Results

3.1. Basic characteristics

A total of 267 participants aged 60 years or older living in the community of Nanjing city of China were recruited (Table 1). A total of 37.8% of the 267 elderly participants were male, while 62.2% were female. The mean age was 68.4 ± 6.4 years old. More than half of the participants' education levels were middle school. Self-reported hypertension (59.9%), diabetes (18.0%), coronary artery

Table 1
Characteristics of all participants.

	Total	Male	Female	*p* value
Number	267	101 (37.8%)	166 (62.2%)	N/A
Age (year)	68.4 ± 6.4	69.8 ± 6.8	67.5 ± 6.0	0.004**
Education level				0.008**
Illiteracy	3 (1.1%)	0 (0.0%)	3 (1.8%)	
Primary school	17 (6.4%)	4 (3.9%)	13 (7.8%)	
Middle school	187 (60.0%)	64 (63.4%)	123 (74.1%)	
College	60 (22.5%)	33 (32.7%)	27 (16.3%)	
Medical history				
Hypertension	160 (59.9%)	68 (67.3%)	92 (55.4%)	0.054
Diabetes mellitus	48 (18.0%)	20 (19.8%)	28 (16.9%)	0.545
Coronary artery disease	37 (13.9%)	12 (11.9%)	25 (15.1%)	0.466
Stroke	41 (15.4%)	15 (14.9%)	26 (15.7%)	0.858
Health behavior				
Cigarette smoking	40 (15.0%)	40 (39.6%)	0 (0.0%)	< 0.001***
Alcohol drinking	30 (11.2%)	30 (29.7%)	0 (0.0%)	< 0.001***
Physical examinations				
Body mass index (BMI, kg/m^2)	24.2 ± 3.0	24.4 ± 2.8	24.0 ± 3.1	0.294
Systolic blood pressure (mmHg)	133.2 ± 17.8	134.3 ± 15.5	132.5 ± 19.1	0.440
Diastolic blood pressure (mmHg)	78.4 ± 9.6	80.8 ± 9.3	77.0 ± 9.6	0.002**
Depressed mood (GDS)				0.480
0~10 points	245 (91.8%)	95 (94.1%)	150 (90.4%)	
11~20 points	21 (7.8%)	6 (5.9%)	15 (9.0%)	
21~30 points	1 (0.4%)	0 (0.0%)	1 (0.6%)	
Cognitive function (MMSE)	27.6 ± 2.1	27.7 ± 1.9	27.7 ± 1.9	0.498
MCI (≤ 27 points)	109 (40.8%)	35 (34.6%)	74 (44.6%)	0.709
Muscle strength				
Handgrip strength (kg)	30.0 ± 9.1	38.9 ± 7.9	24.6 ± 4.3	< 0.001***
Chair stand test (s)	9.4 ± 4.6	9.4 ± 3.2	9.4 ± 5.3	0.907
Muscle mass				
ASM (kg)	16.3 ± 4.0	20.2 ± 2.7	13.5 ± 2.0	< 0.001***
RASM (ASM/height^2)	6.1 ± 1.1	7.1 ± 0.8	5.6 ± 0.7	< 0.001***
Physical performance				
Gait speed (m/s)	1.3 ± 0.3	1.3 ± 0.3	1.3 ± 0.3	0.944
SPPB	11.4 ± 1.2	11.3 ± 1.3	11.5 ± 1.1	0.244

GDS, Geriatric Depression Scale; MMSE, Mini-Mental Status Examination; MCI, mild cognitive impairment; ASM, appendicular skeletal muscle mass; RASM, relative appendicular skeletal muscle mass; SPPB, short physical performance battery.
** *p* value < 0.01, *** *p* value < 0.001.

disease (13.9%) and stroke (15.4%) were the most common medical conditions. Health behavior was recorded, and no females smoke or drank alcohol. The mean value of BMI was 24.2 ± 3.0 kg/m^2. The proportion of participants with mild depression was 7.8%, and 0.4% exhibited moderate to severe depression. The mean MMSE score was 27.6 ± 2.1, and the proportion of participants diagnosed with MCI was 40.8%. The average of handgrip strength was 38.9 ± 7.9 kg for men and 24.6 ± 4.3 kg for women. The mean time in the chair stand test for all participants was 9.4 ± 4.6 sec. The mean RASM of the study participants was 7.1 ± 0.8 kg/m^2 for men and 5.6 ± 0.7 kg/m^2 for women. The mean gait speed was 1.3 ± 0.3 meters/sec, and the mean score of SPPB was 11.4 ± 1.2 for all participants. According to definition of the European Working Group on Sarcopenia in Older People (EWGSOP),[18] 6 males and 7 females of the 267 participants could be diagnosed with sarcopenia, and only 1 female exhibited severe sarcopenia.

3.2. The associations between age and MMSE score, muscle strength, muscle mass and physical performance

The present study confirmed that MMSE score was decreased in females with increasing age (Figure 1A, $p = 0.034$), and there was a downtrend in males (Figure 1G, $p = 0.082$). After adjusting for BMI, education level, medical history, health behavior and depressed mood, the decrease of handgrip strength remained strongly associated with increasing age in males and females (Figure 1B and H). Time of the chair stand test was positively correlated with age (Figure 1C and I). As for muscle mass and physical performance, ASM, gait speed and total score of SPPB were all negatively correlated with age (Figure 1D–F and J–L). These results verify the strong association between age and muscle strength, muscle mass, and cognitive function.

3.3. Comparisons between MCI and normal groups

Considering the huge impact of age on cognitive function and sarcopenia, the present study first divided the participants into MCI and normal groups according to the MMSE score, then stratified the participants by age (60–69 and ≥ 70 years old, respectively) to analyze muscle strength, muscle mass and physical performance. We summarized comparisons between MCI and normal groups of male subjects in Table 2. There was no difference of BMI between the MCI and normal groups at either age. Handgrip strength, representing the muscle strength of the upper limbs, time of the chair stand test, representing the muscle strength of the lower limbs, and muscle mass of the upper and lower limbs, gait speed, and SPPB scores were not significant different in male participants ($p > 0.05$). Comparisons between the MCI and normal groups of female subjects were shown in Table 3. There was no significant difference of

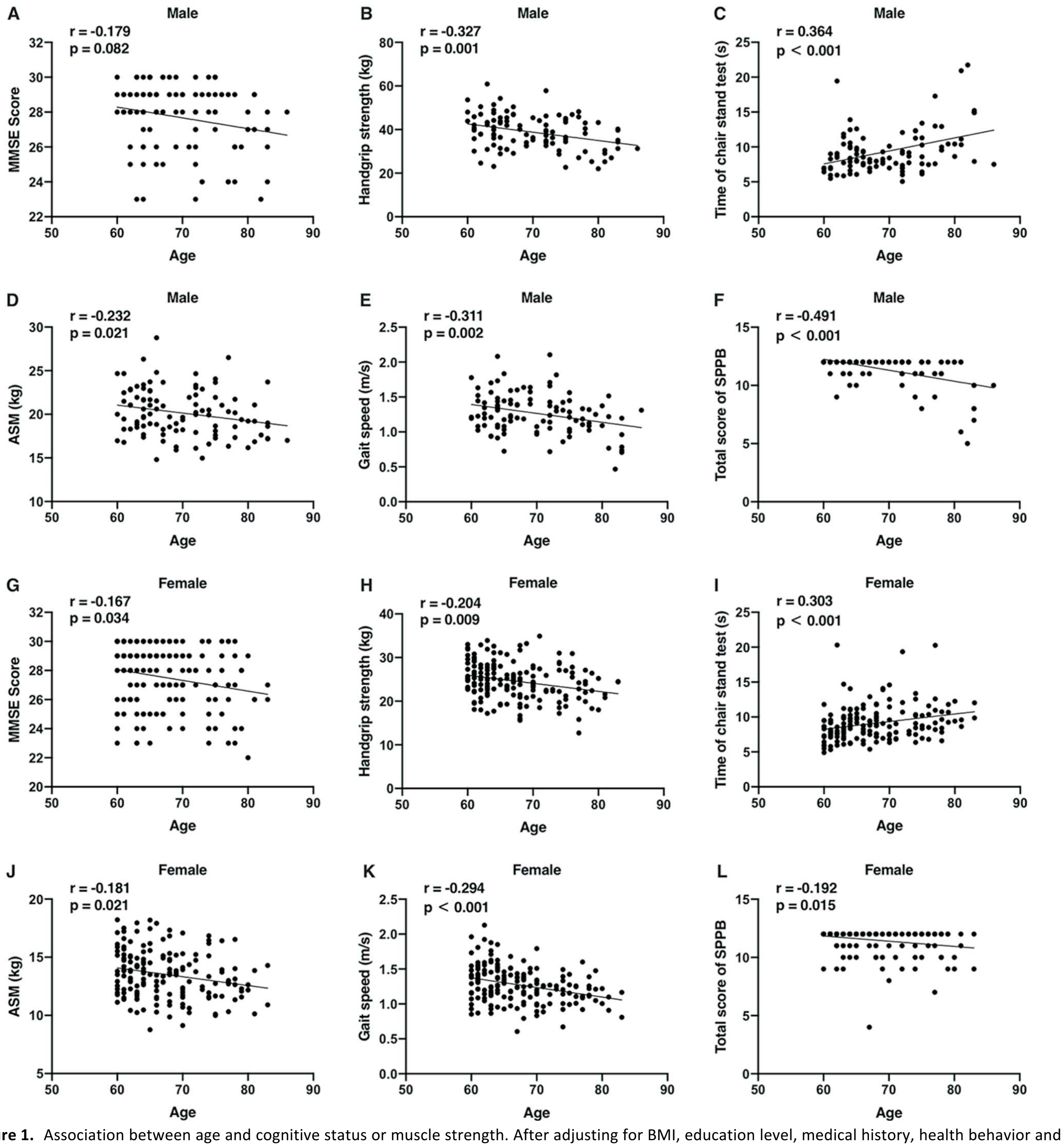

Figure 1. Association between age and cognitive status or muscle strength. After adjusting for BMI, education level, medical history, health behavior and depressed mood, the results from males (n = 101) were shown in A–F and from females (n = 166) in G–L. (A & G**)** Age and MMSE score. (B & H**)** Age and handgrip strength. (C & I) Age and time of the chair stand test. (D & J) Age and appendicular skeletal muscle mass. (E & K) Age and gait speed. (F & L) Age and score of SPPB. r is the partial correlation coefficient.

Table 2
Comparisons of muscle strength, muscle mass and physical performance between normal and MCI male participants by age stratification.

	60–69 years old		*p* value	≥ 70 years old		*p* value
	Normal	MCI		Normal	MCI	
Number	41	13	N/A	25	22	N/A
BMI (kg/m^2)	24.4 ± 2.9	23.6 ± 2.5	0.38	24.4 ± 2.2	24.9 ± 3.2	0.592
Handgrip strength (kg)	40.9 ± 7.6	39.4 ± 8.8	0.565	36.3 ± 7.6	37.6 ± 7.6	0.555
Chair stand test (s)	8.7 ± 2.6	8.2 ± 1.6	0.739	9.4 ± 3.6	10.8 ± 4.4	0.312
ASM (upper limb, kg)	5.8 ± 0.9	5.3 ± 0.8	0.128	5.2 ± 0.7	5.5 ± 0.8	0.138
ASM (lower limb, kg)	14.5 ± 2.3	14.9 ± 2.3	0.532	14.9 ± 1.9	14.5 ± 2.3	0.277
Gait speed (m/s)	1.3 ± 0.3	1.3 ± 0.3	0.751	1.2 ± 0.2	1.2 ± 0.4	0.629
SPPB	11.7 ± 0.7	11.8 ± 0.4	0.815	11.1 ± 1.3	10.5 ± 2.1	0.350

Table 3
Comparisons of muscle strength, muscle mass and physical performance between normal and MCI female participants by age stratification.

	60–69 years old		*p* value	≥ 70 years old		*p* value
	Normal	MCI		Normal	MCI	
Number	67	43	N/A	25	31	N/A
BMI (kg/m^2)	24.1 ± 2.9	24.6 ± 2.9	0.443	23.7 ± 3.2	23.3 ± 3.3	0.647
Handgrip strength (kg)	25.4 ± 4.4	24.6 ± 4.1	0.364	25.1 ± 4.1	22.2 ± 3.5	0.007**
Chair stand test (s)	8.6 ± 2.3	9.0 ± 2.2	0.350	8.9 ± 2.0	10.5 ± 3.2	0.039*
ASM (upper limb, kg)	3.5 ± 0.6	3.4 ± 0.6	0.579	3.2 ± 0.7	3.1 ± 0.5	0.327
ASM (lower limb, kg)	10.4 ± 1.6	10.4 ± 1.4	0.941	10.1 ± 1.5	9.3 ± 1.4	0.044*
Gait speed (m/s)	1.3 ± 0.2	1.3 ± 0.3	0.744	1.2 ± 0.2	1.1 ± 0.2	0.074
SPPB	11.8 ± 0.7	11.4 ± 1.4	0.105	11.5 ± 0.9	11.0 ± 1.5	0.223

* p value < 0.05, ** p value < 0.01.

the above indicators in female participants of 60–69 years old ($p > 0.05$). Notably, muscle strength, including handgrip strength and time of the chair stand test, was significantly decreased in female participants ≥ 70 years old in the MCI group compared with that in normal group ($p < 0.05$). Muscle mass of the lower limbs was also decreased in the MCI group, but physical performance did not change, even in this older age group.

4. Discussion

According to 2018 definition, the EWGSOP2 used low muscle strength as primary parameter of sarcopenia, and muscle strength was considered as the most reliable measure of muscle function.[17] Sarcopenia is probable when low muscle strength is detected, and strength is better than mass in predicting adverse outcomes.[18,19] It was found that muscle strength of the upper and lower limbs decreased in females with MCI who were older than 70 years in current study. However, muscle mass only decreased in the lower extremities. This result also suggested that the decrease of muscle strength might precede the decrease of muscle mass and further confirmed the importance of muscle strength.

Detection of low physical performance predicts adverse outcome, therefore, these measures are used to identify the severity of sarcopenia.[20] Physical performance was not associated with cognitive status in the current study. Physical performance may be related to high physical activities of the study participants, including shopping, housework, and child pick up, in their daily lives. The participants in our study had complete self-care ability, which was also the reason for the low prevalence of severe sarcopenia in this study.

The decrease in muscle strength and MCI were the initial stages of the diseases, but it was not clear that how impaired cognition was associated with lower muscle strength. One theoretical explanation is the existence of shared factors that may lead to a reduction of muscle strength and cognitive function. For example, elevated serum levels of inflammation markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), showed a potential role of chronic inflammation in muscle function decline and cognitive impairment.[21] Previous studies found that higher levels of serum testosterone were associated with higher MMSE scores[22] and greater muscle strength and muscle protein synthesis.[23] Growth hormone–releasing hormone (GHRH) administration exerted favorable effects on cognition in adults with MCI and sarcopenia.[24] These data suggested that similar pathoetiologies accounted for cognitive impairment and muscle function.

A cross-sectional study in Japan revealed that lower-extremity functioning, rather than skeletal muscle mass, was significantly associated with cognitive impairment in multiple dimensions and global cognitive functioning in more than 4000 community-dwelling Japanese older adults, which suggests that the maintenance of lower-extremity functioning may contribute to detecting and preventing cognitive impairment.[25] These results were similar with our study, which might be due to that our study objects were all east Asians. It was also found an association between skeletal muscle mass and cognitive functioning at later stages of global cognitive impairment.[26]

There are also several limitations in current study. Firstly, the sample size of this study was small, and the study participants were relatively young and active, which may lead to a low prevalence of sarcopenia and limit the results of statistical analysis. There was difference in number between male and female participants (37.8% vs. 62.2%). Secondly, the criteria and scales for the diagnosis of MCI are controversial. The present study used MMSE, and the cut-off was ≤ 27. Montreal Cognitive Assessment (MoCA) is another common scale for assessing MCI,[27] and it may be used spontaneously to screen MCI more accurately. Finally, the study was a cross-sectional study to elucidate a causal relationship between MCI and muscle strength, and longitudinal studies are needed.

In conclusion, to our knowledge, this study is the first to evaluate the association of MCI and muscle strength in community-dwelling older Chinese adults. Despite the existence of this difference only in females older than 70 years old, our results emphasize the significance of elucidating the link between muscle function and cognitive status. Decreases in muscle mass/strength, physical performance, and the MMSE score were associated with advancing age in both genders. Mild Cognitive Impairment is prevalent among community-dwelling older Chinese and is associated with declined muscle mass/strength. Older female Chinese community dwellers with MCI had a significant decrease in muscle strength and lower limb muscle mass. More attention should be paid to women older than 70 years old.

Ethics approval and consent to participate

The Ethics Committee of the First Affiliated Hospital of Nanjing Medical University approved the study, which was performed in accordance with its guidelines for the protection of human subjects. Informed consent was obtained from all participants included in the study.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Funding

This study was funded by the grants from Cadre Health Research Project of Jiangsu Province to Bin Lai (BJ18018) and the National Natural Science Youth Foundation of China to Jing Yu (81600688).

Competing interests

There are no potential conflicts of interest to disclose.

Acknowledgements

Not applicable.

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