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Cognitive impairment is associated with sarcopenia mainly due to attention and calculation in hospitalized Chinese male elderly

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ABSTRACT

Background and Objectives: Sarcopenia and cognitive impairment are the most prevalent causes of disability in older individuals. The aim of this study was to assess the prevalence of sarcopenia and the association between cognitive impairment and sarcopenia in older patients.

Methods and Study Design: A cross-sectional study was undertaken, comprised 250 male patients aged 65 and over. Sarcopenia was defined using the diagnostic recommended consensus by the Asian Working Group for sarcopenia, and the participants were classified into the sarcopenia and non-sarcopenia groups according to this definition. The cognitive functions of older patients were assessed using the Mini-Mental State Examination (MMSE). After bivariate analyses, a multivariate logistic regression model was constructed to determine the association of study variables with sarcopenia. **Results:** The prevalence of sarcopenia and cognitive impairment was 20.8% and 19.6% respectively. Additionally, we found 10.8% patients had nutritional risk, 19.6% patients had cognitive impairment in this study. Multivariate analysis identified age (OR: 1.105, 95% CI 1.027, 1.188, $p=0.008$), cognitive impairment (OR: 4.005, 95% CI 1.421, 11.569, $p=0.009$) and nutritional risk (OR: 13.692, 95% CI 3.063, 61.214, $p=0.001$) were significantly associated with sarcopenia. The prevalence of sarcopenia significantly increased stepwise with lower MMSE score. Additionally, the score on the attention and calculation (OR:0.684, 95% CI: 0.514, 0.911, $p=0.009$) subsection of the MMSE was associated with the presence of sarcopenia. MMSE score was correlated with the fat free mass, handgrip strength ($p<0.05$). **Conclusions:** Cognitive impairment, especially in the calculation and attention, and nutritional risk, are associated with sarcopenia in hospitalized Chinese male elderly. Adequate nutritional support may be the key to solving these diseases.

Key Words: sarcopenia, cognitive impairment, elderly, risk factors, MMSE

INTRODUCTION

China currently houses the world's largest population of 1.4 billion (19.13% of the world population), and is rapidly transforming into an aging nation.¹ As of 2019, the population of mainland China constitutes 18 % of global total, with 164.5 million Chinese citizens aged 65+, 26 million of whom are 80+. By 2050, it is expected that there will be 365 million aged 65+, a number representing 26.1% of the country's total population.² Besides, aging of population is the most serious challenge and inevitable in course of social development in China. Aging is associated with deterioration of muscle mass which can lead to a considerable increase in

costs due to the muscle weakness and duration of hospitalization as well as a decrease in the life quality and a physical disability.³

Sarcopenia is a progressive and generalized skeletal muscle disorder involving the accelerated loss of muscle mass and function that is associated with increased adverse outcomes including falls, functional decline, frailty and mortality.^{4,5} Sarcopenia was recognized as an independent condition with an International Classification of Diseases-10 code in 2016.⁶ The prevalence of sarcopenia in the elderly varies widely (1%-40%) among Chinese older populations.⁷⁻¹⁰ Efforts should be required to identify the factors associated with sarcopenia and to program interventions for the elderly population. Sarcopenia depends on numbers of endogenous and exogenous factors, such as age, genetic factors, dietary, physical activity, other chronic diseases and sleep quality.^{11,12} Due to these deleterious effects, sarcopenia has become a subject of increased focus in the clinical geriatrics and the ageing policy research.

Cognitive impairment is common among older people which influences daily functioning and independence, and characterized by a decline in cognition involving memory, language, social cognition and planning.¹³ These conditions are common among older people, but the effects range from slight forgetfulness to serious enough impairment to interfere with daily functioning and independence. Mitochondrial dysfunction, oxidative stress, chronic inflammation, and hormonal changes are potential pathogenesis mechanism with sarcopenia, all of which are potential causes of cognitive impairment.^{14,15} So cognitive impairment may be closely related to sarcopenia.

A recent systematic review has indicated that sarcopenia may be associated with poorer cognitive function.¹⁶ However, the population were mixed with individuals with dementia. Nevertheless, Abellan et al reported that no significant association was evidenced between sarcopenia and cognitive impairment.¹⁷ Furthermore, there is a scarcity of information on the relationship between sarcopenia and cognitive impairment in Chinese older population. The key to early prevention is to identify precursors of sarcopenia. Therefore, in the present study, we aimed to explore the relationship between sarcopenia and cognition function. Identification of factors associated with sarcopenia in older patients may be of value in preventing worsened QoL from loss of independence.

MATERIALS AND METHODS

Study participants

In this cross-sectional study, all male patients aged or more (n=320) consecutively admitted to participating wards from August 2018 to June 2020 entered the study protocol. The inclusion criteria were as follows: male, age ≥ 65 years, with the ability to perform tests and sign an informed written consent. Patients with the following conditions were excluded: (1) Severe cognitive impairment (defined as a Mini-Mental Status Examination (MMSE) score of ≤ 10); (2) delirium evaluated using the confusion assessment method tool; (3) speech-lost; (4) severely impaired activities of daily living; (5) some reasons that unable to perform BIA. The final sample was therefore comprised of 394 participants. All patients were assessed within the first 2 days of hospital admission and underwent comprehensive geriatric assessment (CGA). We set up a CGA team consisting of geriatricians, nurses, therapists, pharmacists, psychologists and dietitians. A CGA is an in-depth multidimensional evaluation of a patient's health used to identify changes that are potentially treatable to improve patient outcomes. Our CGA comprises the following domains: functional status, comorbidity, polypharmacy, cognition, psychological status, social support, and nutritional status. This study was approved by the Ethics and Research Committee of Shanghai Ruijin Hospital. Informed written consent was obtained from all participants (KY2021-108) (Figure 1).

Before the initiation of this study, a pilot study was conducted with 10 participants in preliminary investigation to adjust the scale instruments. All researchers involved in this study were trained together. The samples were described by a structured questionnaire, including sociodemographic data, lifestyle.

Sarcopenia diagnosis

The recommendations of the Asian Working Group for Sarcopenia (2019) in Older People were used to characterize sarcopenia: low appendicular muscle mass index, reduced muscle strength, and poor physical performance.¹⁸ We assessed appendicular muscle mass by a multifrequency bioelectrical impedance analysis (BIA) using InBody 770. We also assessed total fat mass, body fat percentage, total muscle mass, skeletal muscle mass and the muscle/fat ratio. This analyzer processes 30 impedance measurements by using six different frequencies (1, 5, 50, 250, 500, 1000 kHz) at each of five segments of the body (right arm, left arm, trunk, right leg, left leg), and 15 reactance measurements using tetrapolar 8-point tactile electrodes by using three different frequencies (5, 50, 250 kHz) at each of the five a forementioned segments of the body.

Appendicular skeletal muscle mass (ASM) was derived as the sum of the muscle mass of the four limbs, and the ASM index (kg/m^2) was calculated. Loss of skeletal muscle mass was

determined based on the Asian Working Group for Sarcopenia criteria for sarcopenia (2019), ASMI $<7.0 \text{ kg/m}^2$ for men and $<5.7 \text{ kg/m}^2$ for women by electrical bioimpedance measurement.

Measurement was made with the participant being seated on an armless chair, feet supported on the floor, hips and knees flexed at 90° , arms parallel to the body, elbows flexed at 90° , and forearms and wrists in a neutral position. Three measurements were made on the dominant side, with one-minute intervals between them, always using verbal stimulation. Results are presented in Kilogram/force (Kg) using the mean of the three measures. Muscle weakness was determined based on the Asian Working Group for Sarcopenia criteria for sarcopenia; handgrip strength $<26 \text{ kg}$ for men and $<18 \text{ kg}$ for women.

Cognitive function

Mini-Mental State Examination (MMSE) is the most commonly used tool to screen for cognitive impairment worldwide.¹⁹ This questionnaire consists of six subsections: orientation, registration, attention and calculation, recall, language and praxis. The maximum score is 30 points, with higher score indicating better cognitive function. All enrolled patients had a high school education or above in this study. Cognitive function was evaluated by MMSE in this study, which was validated for Chinese elder. Cognitive impairment was defined on the cut-offs of MMSE scores < 27 points. We defined normal, mild, moderate and severe cognitive impairment as MMSE ≥ 27 , 21-26, 10-20 and <10 , respectively.²⁰

Other Covariates

Nutritional Risk Screening

The nutritional risk screening of each participant was evaluated by trained dietician using the Nutritional Risk Screening 2002. Its total score ranges from 0 to 7. The lower the score, the better is the nutrition status. Scores of 0-2 indicate normal nutrition status and 3-7 indicate nutritional risk.

Physical performance testing

Impaired physical performance was assessed by the SPPB using the standing balance task, chair stands, and gait speed. The results of these three tests produced a total combined score of 0-12 points. Higher scores indicate greater ability in performing each test, while lower scores indicate poorer performance on this task. Low physical performance is associated with

a greater risk of falling. Participants with scores ≤ 6 on the SPPB were classified as having impaired physical performance.

Assessment of Activities of Daily Living

Lawton Instrumental Activities of Daily Living (IADL) was used for assessment disabilities, including preparing own meals, using the telephone, going shopping, taking medications, performing light housework, performing severe housework and managing money. Participants with scores < 14 on the IADL were classified as poor ability of independence.

Frailty assessment

Frailty assessment was measured using FRAIL scale which includes five items: fatigue, resistance, illness and loss of weight. The total score is between 0 and 5 on an ordinal scale, “non-frailty” participants were those who did not score positively on any of the five items, while “pre-frailty” were those who scored positively on one or two items. “Frailty” individuals were those who scored positively on three or more criteria.

Sleep quality assessment

The Pittsburgh Sleep Quality Index (PSQI) was employed to evaluate sleep quality. It consists of 19 self-rated questions and 5 more to be answered by bed mates or roommates (these last ones are only employed for clinical purposes). Higher scores indicate worse sleep quality.

Fall risk assessment

The Morse Fall Scale was scored by nursing staff at the time of admission, as per the standard ward practice. This scale consists of six items reflecting risk factors of falling including history of falling, secondary diagnosis, ambulatory aids, intravenous therapy, type of gait, and mental status. The total score ranged between 0 and 125, with a cut-off score of ≥ 45 indicating high risk. In this study, we defined that ≥ 45 indicating high risk of fall, 25-45 indicating moderate risk of fall and < 25 indicating low risk of fall.

Statistical analysis

The data analyses were performed using SPSS version 22.0. $p < 0.05$ indicates statistical significance. The normal distributed continuous data were shown as mean (standard deviation [SD]), and the abnormal distributed continuous data were shown as median (interquartile range). These characteristics were compared between the sarcopenia and non-sarcopenia

using the Pearson's Chi-square or Fisher's Exact test. The relationship between sarcopenia and the potentially associated factors was estimated by deriving odds ratios (ORs) and 95% confidence intervals (CIs) from univariate logistic regression models. In these models, age, SPPB score, PSQI score, frail score, NRS-2002 score, IADL score, MMSE score, hemoglobin, Morse score and body mass index were treated as continuous data (per year for age and per SD for the other covariates), whereas the other covariates were treated as categorical data.

A backward stepwise multivariate logistic regression models was performed to identify the independently associated factors. The covariates of age and gender were included in the initial model, and the covariates with a $p < 0.2$ in the univariate logistic regression models. The probability of stepwise entry and removal of variables were $p < 0.05$ and $p > 0.10$, respectively. In addition, the multicollinearity among the covariates was checked using Spearman correlations.

RESULTS

Characteristics of participants

Of the total 250 male participants. The mean age was 79.63 ± 8.59 years old and the mean BMI of 24.71 ± 3.10 kg/m². Table 1 shows the demographic and clinical characteristics of the participants. Among these patients, 52 (20.8%) showed Sarcopenia, 27 (10.8%) patients had nutritional risk, 49 (19.6%) patients had cognitive impairment.

General characteristics of older patients with sarcopenia vs non-sarcopenia

Based on the diagnosis of the Sarcopenia, the participants were divided into two groups: those with Sarcopenia, and those without sarcopenia. Table 2 shows the behavior of age and several anthropometric, body composition, sociodemographic, health, and cognitive status variables, according to Sarcopenia. As for the body composition findings, the group with sarcopenia was older, had lower BMI, ASMI, fat free mass, handgrip strength than the non-sarcopenia group ($p < 0.05$). NRS-2002 score was higher in group of sarcopenia than non-sarcopenia group ($p < 0.05$). 42.3 % patients with cognitive impairment in sarcopenia group, 13.6% in non-sarcopenia group ($p < 0.001$).

Significant factors related to sarcopenia in older patients

Logistic regression analysis was used to develop a model to predict sarcopenia by a list of covariables. All significant variables were introduced into the stepwise regression to generate preliminary models. All continuous variables retained in the model fulfilled the linearity

assumption with the response variable. We eliminated several interaction or collinearity variables. The univariate analysis showed that the following eight variables were significantly associated ($p < 0.05$) with sarcopenia: age, BMI, nutritional risk, Frailty, IADL difficulty, impaired physical performance, cognitive impairment and hemoglobin (Table 3). Four variables, including age (OR: 1.105, 95% CI 1.027, 1.188, $p = 0.008$), cognitive impairment (OR: 4.005, 95% CI 1.421, 11.569, $p = 0.009$) and nutritional risk (OR: 13.692, 95% CI 3.063, 61.214, $p = 0.001$), remained significant and independent on the multivariate analysis (Table 3).

Association between sarcopenia and the MMSE sub-items in multivariate logistic regression models

Logistic analyses focused on the MMSE sub-items indicated that attention and calculation (OR=0.684, 95% CIs: 0.514, 0.911, $p = 0.009$) were significantly associated with sarcopenia (Table 4).

Prevalence of sarcopenia defined according to the classification of MMSE score

Normal cognitive, mild, moderate cognitive impairment were present in 201 (80.4%), 41 (16.4%), 8 (3.2%) respectively of the total older patients (Figure 2A). The prevalence of sarcopenia in normal cognitive, mild and moderate cognitive impairment patients was 30 (14.9%), 16 (39.0%) and 6 (75.0%) respectively, $p < 0.001$ (Figure 2B).

In these male older patients, the variables that were significantly correlated with the MMSE score were fat free mass, handgrip strength and ASMI (Figure 3).

DISCUSSION

The present study used the updated AWGS criteria consensus and found the prevalence of sarcopenia among the elderly inpatients was 23.1%. The prevalence of sarcopenia in the elderly varies widely among countries because of different diagnostic criteria, characteristics of study populations, age, study region and cultural background. A systematic review reported that the prevalence of sarcopenia is 1-29% among elderly people in general public, 10% in hospitalized patients based on diagnostic criteria of the EWGSOP.²¹ Hao et.al revealed that the prevalence of sarcopenia in hospitalized older patients was 31%, higher than our study.⁸

The prevalence of cognitive impairment was 49 (19.6%) in the present study. Multivariate analyses showed that cognitive impairment was associated with increased risk of sarcopenia. Recent meta-analysis reported an independent positive association between sarcopenia and an increased risk of cognitive impairment.^{22,23} Several other studies also showed that sarcopenia

was related to cognitive impairment in different district older patients.²⁴⁻²⁶ Nevertheless, contradictory results have also been reported. In the EPIDOS-Toulouse cohort, decreased muscle mass alone was not associated with cognitive dysfunction after seven years of follow-up.²⁷ Abellan et al showed no significant association between sarcopenia and cognitive impairment in older women.¹⁷ These inconsistent results are probably because of the different criteria and cut-off points used in assessment of sarcopenia and cognitive function. Additionally, a neuroimaging study showed that lean muscle mass decline was related to brain atrophy.²⁸ The exact mechanism relating to sarcopenia and cognitive impairment has not been defined. A system review has shown that muscle could produce myokines, which suggested the existence of muscle-brain cross-talk, and maybe play a role in the involvement in cognitive impairment in sarcopenia.²⁹ The gut microbiota may possibly link sarcopenia and cognitive impairment.³⁰ The concept of the microbiota-gut-brain axis indicated a complex multidirectional cross-talk system among the gastrointestinal tract, the gut microbiota, and the nervous system. Aging is associated with reduced microbiota biodiversity in the gut. Also, age-related excessive chronic inflammation and oxidative stress are capable to alter the balance between synthesis and breakdown of muscle proteins via microbiota-gut-brain axis represented a possible link among sarcopenia and cognitive impairment.^{31,32} However, more high-quality researches are needed to reveal the molecular mechanisms underlying the relationship between cognitive impairment and sarcopenia.

Among the MMSE sub-items, attention and calculation were significantly associated with increase of sarcopenia in older patients. These sub-items test executive function.²⁵ Older adults with normal executive function can plan future behaviour before it is implemented. For instance, older adults are likely to experience calculation and attention before they start going down stairs. On the contrary, older with impaired calculation and attention functions would fail to plan their future behaviour. Kim et al reported sarcopenia-related cognitive impairment was primarily mediated by executive function and processing speed in older adults.²⁵ Boripuntakul et al showed that older adults with cognitive decline have reduced postural control when undertaking a challenging walking task.³³ Therefore, future studies using cognitive assessment that focused on the nature of executive functions may help to explore the relationship between executive function and sarcopenia.

Our study also revealed that age and female were associated with sarcopenia. This find is consistent with previous studies conducted in different populations.³⁴ To date, it remains questionable whether gender factor affects the development of sarcopenia. Malnutrition is common among older adults and is associated with adverse outcomes but remains

undiagnosed on healthcare admissions. Nutritional assessment is one of the most important contents in older inpatients. Parenteral and Enteral nutrition society of Chinese Medical Association recommended that older patients should regular implement nutritional assessment, including NRS-2002 or MNA. Our previous study showed that nutritional status was associated with skeletal muscle.³⁵ In this study, nutritional risk was significantly associated with higher risk of sarcopenia (OR=2.341, 1.617, 3.391). In addition, the hemoglobin level in sarcopenia individuals was lower than non-sarcopenia patients. Loss of appetite and reduction of food intake during hospitalization could lead to impaired protein synthesis, and an increased rate of malnutrition and sarcopenia.^{36,37} Although there was no significant associated between NRS-2002 score and sarcopenia by multivariable analyses, we should pay attention to nutrition assessment in older patients. Liu et al demonstrated that nutrition status is a critical mediator of the relationship between cognitive decline and sarcopenia. They suggested that improved nutrition status in older adults with cognitive decline can delay or counteract sarcopenia.³⁸ Besides, we also found that MMSE score was correlated with fat free mass and handgrip strength. Thus, nutrition maybe an essential strategy in the management of cognitively impaired and sarcopenia patients.

The strengths of our study were using a comprehensive assessment of sarcopenia and including a substantial range of covariates in the analysis. However, there are some limitations in our study. Firstly, the data were collected from one hospital in Shanghai, therefore due to sample size limitations, our results might not represent other populations of Chinese older adults. Secondly, this study was limited by its cross-sectional design and did not obtain evidence of a cause-effect relationship between sarcopenia and cognitive impairment. Thirdly, sarcopenia measured with BIA, which could not be performed in patients with pacemakers and other electronic implants. BIA measurements can also be influenced by hydration status. Hence, most of the participants who agreed to participate this investigation on their own were relatively healthy. This may have affected the actual determination of sarcopenia and cognitive impairment prevalence in the study community. However, we analysed the samples that allowed evaluation of regression models after optimally adjusting for multiple confounding factors.

Conclusion

In conclusion, we showed that sarcopenia was independently associated with age, cognitive impairment and nutritional risk. Therefore, nutritional and cognition function assessment, also early therapeutic interventions are imperative, especially for patients with cognitive

impairment. Furthermore, our findings suggest that cognitive impairment domains such as attention and calculation were significantly associated with sarcopenia in male older patients. Additional longitudinal studies are needed to clarify relationships between cognitive function and sarcopenia, and its defining components and cognitive impairment.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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REFERENCES

1. Fang EF, Scheibye-Knudsen M, Jahn HJ, Li J, Ling L, Guo H et al. A research agenda for aging in China in the 21st century. *Ageing Res Rev.* 2015;24:197-205. doi: 10.1016/j.arr.2015.08.003.
2. Fang EF, Xie C, Schenkel JA, Wu C, Long Q, Cui H et al. A research agenda for ageing in China in the 21st century (2nd edition): Focusing on basic and translational research, long-term care, policy and social networks. *Ageing Res Rev.* 2020;64:101174. doi: 10.1016/j.arr.2020.101174.
3. Wang Y, Welc SS, Wehling-Henricks M, Tidball JG. Myeloid cell-derived tumor necrosis factor-alpha promotes sarcopenia and regulates muscle cell fusion with aging muscle fibers. *Aging Cell.* 2018;17:e12828. doi: 10.1111/ace1.12828.
4. Larsson L, Degens H, Li M, Salviati L, Lee YI, Thompson W, Kirkland JL, Sandri M. Sarcopenia: Aging-related loss of muscle mass and function. *Physiol Rev.* 2019;99:427-511. doi: 10.1152/physrev.00061.2017.
5. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet.* 2019;393(10191):2636-46. doi: 10.1016/S0140-6736(19)31138-9.
6. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle.* 2016;7:512-4. doi: 10.1002/jcsm.12147.
7. Fang Q, Zhu G, Huang J, Pan S, Fang M, Li Q, Yin Q, Liu X, Tang Q, Huang D, Liu J. Current status of sarcopenia in the disabled elderly of Chinese communities in Shanghai: Based on the updated EWGSOP consensus for sarcopenia. *Front Med.* 2020;7:552415. doi: 10.3389/fmed.2020.552415.
8. Hao Q, Hu X, Xie L, Chen J, Jiang J, Dong B, Yang M. Prevalence of sarcopenia and associated factors in hospitalised older patients: A cross-sectional study. *Australas J Ageing.* 2018;37:62-7. doi: 10.1111/ajag.12492.
9. Huang J, He F, Gu X, Chen S, Tong Z, Zhong S. Estimation of sarcopenia prevalence in individuals at different ages from Zhejiang province in China. *Aging (Albany NY).* 2021;13:6066-75. doi: 10.18632/aging.202567.

10. Chang HK, Lee JY, Gil CR, Kim MK. Prevalence of sarcopenia in community-dwelling older adults according to simplified algorithms for sarcopenia consensus based on Asian Working Group for Sarcopenia. *Clin Interv Aging*. 2020;15:2291-9. doi: 10.2147/CIA.S281131.
11. Rubio-Arias JÁ, Rodríguez-Fernández R, Andreu L, Martínez-Aranda LM, Martínez-Rodríguez A, Ramos-Campo DJ. Effect of sleep quality on the prevalence of sarcopenia in older adults: A systematic review with meta-analysis. *J Clin Med*. 2019;8:2156. doi: 10.3390/jcm8122156.
12. Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A et al. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. *J Cachexia Sarcopenia Muscle*. 2017;8:907-14. doi: 10.1002/jcsm.12224.
13. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7:263-9. doi: 10.1016/j.jalz.2011.03.005.
14. Dhillon RJ, Hasni S. Pathogenesis and management of sarcopenia. *Clin Geriatr Med*. 2017;33:17-26. doi: 10.1016/j.cger.2016.08.002.
15. Morley JE. An overview of cognitive impairment. *Clin Geriatr Med*. 2018;34:505-13. doi: 10.1016/j.cger.2018.06.003.
16. Peng TC, Chen WL, Wu LW, Chang YW, Kao TW. Sarcopenia and cognitive impairment: A systematic review and meta-analysis. *Clin Nutr*. 2020;39:2695-701. doi: 10.1016/j.clnu.2019.12.014.
17. Abellan van Kan G, Cesari M, Gillette-Guyonnet S, Dupuy C, Nourhashémi F, Schott AM, Beauchet O, Annweiler C, Vellas B, Rolland Y. Sarcopenia and cognitive impairment in elderly women: results from the EPIDOS cohort. *Age Ageing*. 2013;42:196-202. doi: 10.1093/ageing/afs173.
18. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21:300-7.e2. doi: 10.1016/j.jamda.2019.12.012.
19. Shulman KI, Herrmann N, Brodaty H, Chiu H, Lawlor B, Ritchie K, Scanlan JM. IPA survey of brief cognitive screening instruments. *Int Psychogeriatr*. 2006;18:281-94. doi: 10.1017/S1041610205002693.
20. Shirooka H, Nishiguchi S, Fukutani N, Tashiro Y, Nozaki Y, Hirata H et al. Cognitive impairment is associated with the absence of fear of falling in community-dwelling frail older adults. *Geriatr Gerontol Int*. 2017;17:232-8. doi: 10.1111/ggi.12702.
21. Cruz-Jentoft AJ, Landi F, Schneider SM, Zúñiga C, Arai H, Boirie Y et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing*. 2014;43:748-59. doi: 10.1093/ageing/afu115.
22. Cabett Cipolli G, Sanches Yassuda M, Aprahamian I. Sarcopenia is associated with cognitive impairment in older adults: A systematic review and meta-analysis. *J Nutr Health Aging*. 2019;23:525-31. doi: 10.1007/s12603-019-1188-8.

23. Chang KV, Hsu TH, Wu WT, Huang KC, Han DS. Association between sarcopenia and cognitive impairment: A systematic review and meta-analysis. *J Am Med Dir Assoc.* 2016;17:1164.e7-1164.e15. doi: 10.1016/j.jamda.2016.09.013.
24. Lee I, Cho J, Hong H, Jin Y, Kim D, Kang H. Sarcopenia is associated with cognitive impairment and depression in elderly Korean women. *Iran J Public Health.* 2018;47:327-34.
25. Kim M, Won CW. Sarcopenia is associated with cognitive impairment mainly due to slow gait speed: Results from the Korean Frailty and Aging Cohort Study (KFACS). *Int J Environ Res Public Health.* 2019;16:1491. doi: 10.3390/ijerph16091491.
26. Kohara K, Okada Y, Ochi M, Ohara M, Nagai T, Tabara Y, Igase M. Muscle mass decline, arterial stiffness, white matter hyperintensity, and cognitive impairment: Japan Shimanami Health Promoting Program study. *J Cachexia Sarcopenia Muscle.* 2017;8:557-66. doi: 10.1002/jcsm.12195.
27. van Kan GA, Cesari M, Gillette-Guyonnet S, Dupuy C, Vellas B, Rolland Y. Association of a 7-year percent change in fat mass and muscle mass with subsequent cognitive dysfunction: the EPIDOS-Toulouse cohort. *J Cachexia Sarcopenia Muscle.* 2013;4:225-9. doi: 10.1007/s13539-013-0112-z.
28. Burns JM, Johnson DK, Watts A, Swerdlow RH, Brooks WM. Reduced lean mass in early Alzheimer disease and its association with brain atrophy. *Arch Neurol.* 2010;67:428-33. doi: 10.1001/archneurol.2010.38.
29. Scisciola L, Fontanella RA, Surina, Cataldo V, Paolisso G, Barbieri M. Sarcopenia and cognitive function: Role of myokines in muscle brain cross-talk. *Life (Basel).* 2021;11:173. doi: 10.3390/life11020173.
30. Gemikonakli G, Mach J, Hilmer SN. Interactions between the aging gut microbiome and common geriatric giants: Polypharmacy, frailty, and dementia. *J Gerontol A Biol Sci Med Sci.* 2021;76:1019-28. doi: 10.1093/gerona/glaa047.
31. Sui SX, Williams LJ, Holloway-Kew KL, Hyde NK, Pasco JA. Skeletal muscle health and cognitive function: A narrative review. *Int J Mol Sci.* 2020;22:255. doi: 10.3390/ijms22010255.
32. Ticinesi A, Nouvenne A, Cerundolo N, Catania P, Prati B, Tana C, Meschi T. Gut microbiota, muscle mass and function in aging: A focus on physical frailty and sarcopenia. *Nutrients.* 2019;11:1633. doi: 10.3390/nu11071633.
33. Albinet CT, Boucard G, Bouquet CA, Audiffren M. Processing speed and executive functions in cognitive aging: how to disentangle their mutual relationship? *Brain Cogn.* 2012;79:1-11. doi: 10.1016/j.bandc.2012.02.001.
34. Kimura A, Sugimoto T, Niida S, Toba K, Sakurai T. Association between appetite and sarcopenia in patients with mild cognitive impairment and early-stage Alzheimer's disease: A case-control study. *Front Nutr.* 2018;5:128. doi: 10.3389/fnut.2018.00128.
35. Bian D, Shi Y, Jiang Y, Zhong J, Sun J, Gu Y. Combined Patient-Generated Subjective Global Assessment and body composition facilitates nutritional support in inflammatory bowel disease: an ambulatory study in Shanghai. *Asia Pac J Clin Nutr.* 2018;27:1230-8. doi: 10.6133/apjcn.201811_27(6).0009.

36. Sieber CC. Malnutrition and sarcopenia. *Aging Clin Exp Res.* 2019;31:793-8. doi: 10.1007/s40520-019-01170-1.
37. Tsutsumimoto K, Doi T, Nakakubo S, Kim M, Kurita S, Ishii H, Shimada H. Association between anorexia of ageing and sarcopenia among Japanese older adults. *J Cachexia Sarcopenia Muscle.* 2020;11:1250-7. doi: 10.1002/jcsm.12571.
38. Liu X, Xia X, Hu F, Hou L, Jia S, Liu Y et al. Nutrition status mediates the association between cognitive decline and sarcopenia. *Aging (Albany NY).* 2021;13:8599-610. doi: 10.18632/aging.202672.

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Table 1. Characteristics of the study participants

Variable	Total (n=250) mean±SD	N (%)
Age, years	79.63±8.59	
BMI, kg/m ²	24.71±3.10	
Smoking, (%)		11 (3.91%)
Drinking, (%)		62 (22.06%)
Body composition		
Fat free mass, kg/m ²	49.50±6.50	
Appendicular skeletal muscle mass index, kg/m ²	7.19±0.79	
Total body water, kg	36.60±4.89	
Fat mass, kg	20.85±5.93	
Handgrip strength, kg	29.31±9.63	
Sarcopenia, %		52 (20.8%)
Cognitive Function		
MMSE score	27.87±2.82	
Cognitive impairment, (%)		
Sleep quality		
PSQI score	7.29±4.02	
Frailty		
Frail score	1.39±1.06	
Frailty, (%)		34 (13.6%)
Physical performance		
IADL score	0.25±0.56	
IADL difficulty, %		46 (%)
SPPB score	9.44±2.95	
Impaired physical performance, (%)		72 (28.8%)
Nutritional status		
NRS-2002 score	2.01±0.84	
Nutritional risk, (%)		27 (10.8%)
Fall risk		
Morse Fall Scale score	43.98±21.63	
High risk of fall, (%)		94 (37.6%)
Current comorbidities		
Hypertension, (%)		198 (79.2%)
Diabetes, (%)		91 (36.4%)
CKD, (%)		57 (22.8%)
Coronary disease, (%)		194 (77.6%)
GI disease, (%)		58 (23.2%)
Tumor of any type, (%)		59 (23.6%)
Lung disease, (%)		85 (34.0%)
Hemoglobin(g/mL)	131.22±19.09	
1-25(OH)D (ng/mL)	55.02±31.62	
Creatinine, (μmol/L)	93.73±54.34	

BMI: body mass index; PSQI: Pittsburgh Sleep Quality Index; IADL: Lawton Instrumental Activities of Daily Living; SPPB: short physical performance battery; MMSE: Mini-mental State Examination; CKD: chronic kidney disease; GI: gastrointestinal.

Table 2. General characteristics of older patients with sarcopenia vs non-sarcopenia

Variable	Sarcopenia (n=52)	Non-sarcopenia (n=198)	<i>p</i> -value
Age, years	86.33±6.66	77.87±8.17	0.000*
BMI, kg/m ²	23.19±3.24	25.11±2.74	0.000*
Frailty, (%)	12 (23.1%)	21 (11.1%)	0.005*
MMSE score	26.11±4.00	28.34±2.20	0.000*
Cognitive impairment	22 (42.3%)	27 (13.6%)	0.000*
Drinking, (%)	10 (19.2%)	47 (23.7%)	0.359
Smoking, (%)	2 (3.8%)	5 (2.5%)	0.653
PSQI score	6.62±3.41	7.46±4.15	0.346
Nutritional risk, (%)	18 (34.6%)	9 (4.5%)	0.000*
ASMI, kg/m ²	6.36±0.47	7.42±0.70	0.000*
Handgrip strength, kg	20.09±4.86	32.15±8.93	0.000*
IADL difficulty, (%)	23 (44.2%)	23 (11.6%)	0.000*
Impaired physical performance, (%)	27 (51.9%)	45 (22.7%)	0.000*
Hemoglobin, (g/mL)	121.55±19.56	133.74±18.19	0.000*
1-25(OH)D, (ng/mL)	53.86±29.84	55.28±32.14	0.843
Creatinine, (μmol/L)	88.94±22.64	94.96±59.86	0.482
Hypertension, (%)	42 (80.8%)	156 (78.8%)	0.849
Diabetes, (%)	24 (46.2%)	67 (33.8%)	0.108
CKD, (%)	12 (23.1%)	45 (22.7%)	1.000
Coronary disease, (%)	44 (84.6%)	150 (75.8%)	0.195
GI disease	15 (28.8%)	43 (21.7%)	0.274
Tumor of any type, (%)	12 (23.1%)	47 (23.7%)	0.999
Lung disease, (%)	19 (36.5%)	66 (33.3%)	0.742

BMI: body mass index; PSQI: Pittsburgh Sleep Quality Index; ASMI: appendicular skeletal muscle mass index; IADL: Lawton Instrumental Activities of Daily Living; SPPB: short physical performance battery; MMSE: Mini-mental State Examination; CKD: chronic kidney disease; GI: Gastrointestinal.

**p*<0.05 from a t-test for independent samples or a chi-square test, depending on the type of variable and *p*<0.05 from continuous variables (mean ± SD) and categorical variables (percentage).

Table 3. Significant factors related to sarcopenia in older patients

Variable	Univariate		Multivariate	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age	1.149(1.096, 1.205)	0.000*	1.105(1.027, 1.188)	0.008*
BMI	20.667(2.346, 181.291)	0.000*	0.961(0.357, 2.583)	0.936
Nutritional risk	11.118(4.614, 26.791)	0.000*	13.692(3.063, 61.214)	0.001*
Frailty	2.403 (1.092, 5.288)	0.029*	0.385(0.105, 1.416)	0.151
IADL difficulty	6.308(3.099, 12.840)	0.000*	3.344(0.993, 11.253)	0.051
Impaired physical performance	4.232(2.150, 8.329)	0.000*	1.270(0.394, 4.089)	0.689
Cognitive impairment	4.692(2.360, 9.330)	0.000*	4.055(1.421, 11.569)	0.009*
Diabetes	1.676(0.902, 3.114)	0.200	2.235(0.852, 5.860)	0.102
Hemoglobin	3.125 (1.560, 6.261)	0.001*	1.577(0.570, 4.361)	0.380
Fall risk	0.952(0.667, 1.359)	0.787		

Age (continuous vale); BMI: body mass index (in kg/m²:<18.5, 18.5-23.9, ≥24.0); Nutritional risk (NRS-2002≥3, < 14); Frailty (0, 1-2, ≥3); IADL: Lawton Instrumental Activities of Daily Living (< 14, ≥24.0); Impaired physical performance (SPPB≤6, >6); MMSE: Mini-mental State Examination (≤26, ≥27); fall risk (Morse < 25, 25-45, >45); CI: confidence interval; OR: odds ratio.

**p*<0.05.

Table 4. Association between sarcopenia and the MMSE sub-items in multivariate logistic regression models

Variable	OR (95% CI)	<i>p</i> -value
Orientation	0.802 (0.585, 1.099)	0.169
Registration	0.583 (0.235, 1.448)	0.245
Attention and calculation	0.684 (0.514, 0.911)	0.009*
Recall	0.987 (0.624, 1.562)	0.955
Language	0.651 (0.252, 1.684)	0.376
Praxis	0.651 (0.252, 1.684)	0.376

Adjusted for gender, age, BMI, IADL, body mass index, NRS-2002, SPPB, diabetes, alcohol, and haemoglobin. CI: confidence interval; OR: odds ratio.

* $p < 0.05$.

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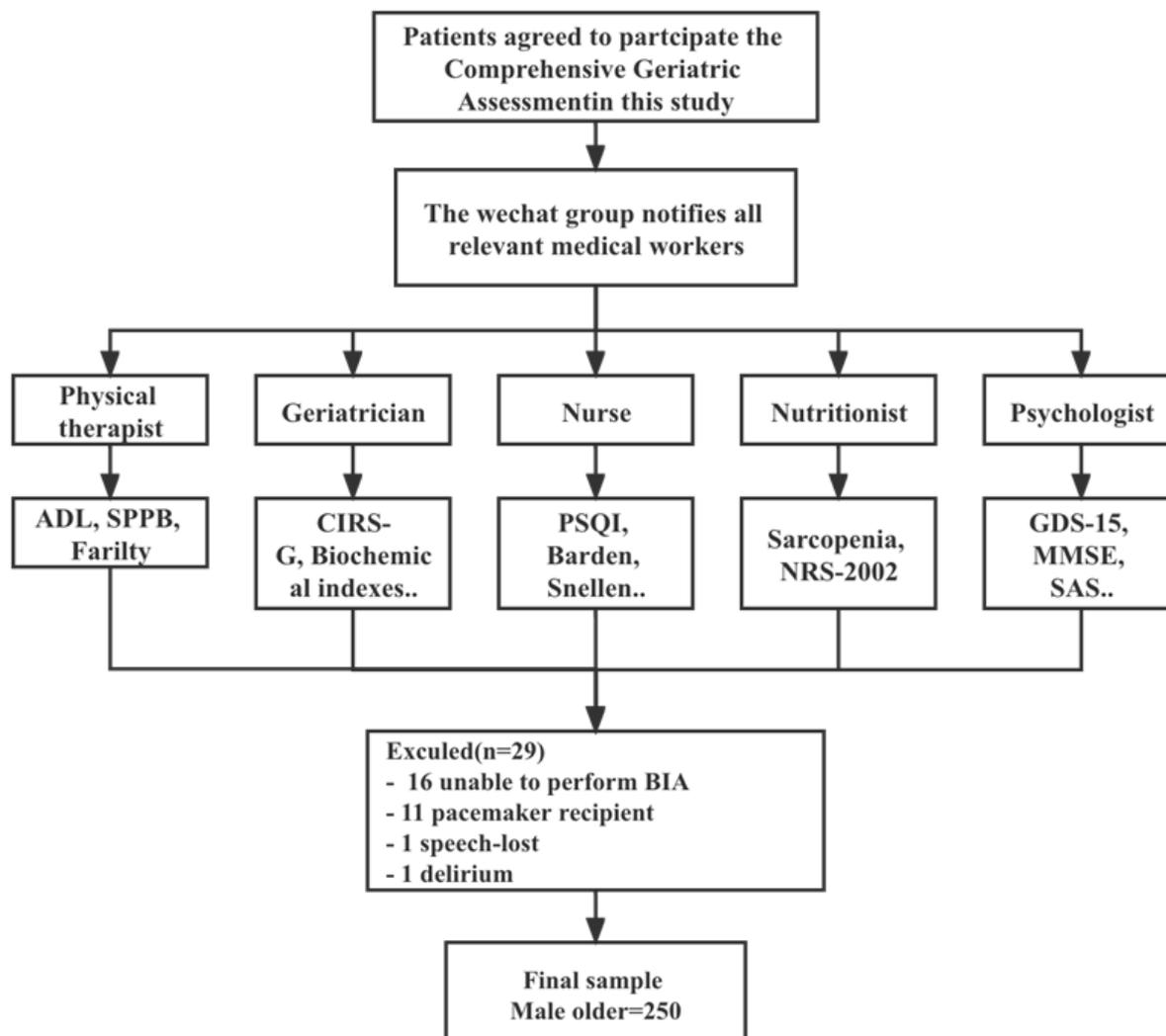


Figure 1. Flow chart of the study population.

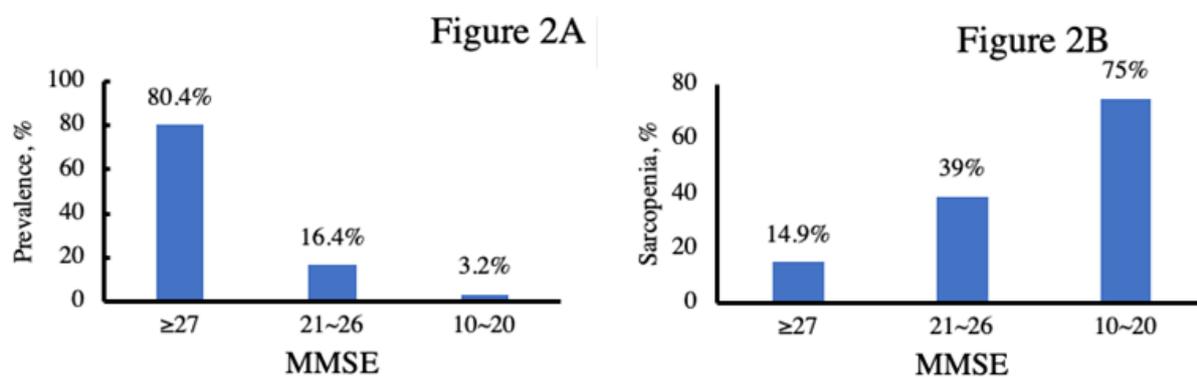


Figure 2. (A) Distribution of the MMSE score in older patients. (B) The prevalence rates of sarcopenia based on the MMSE score in older patients.

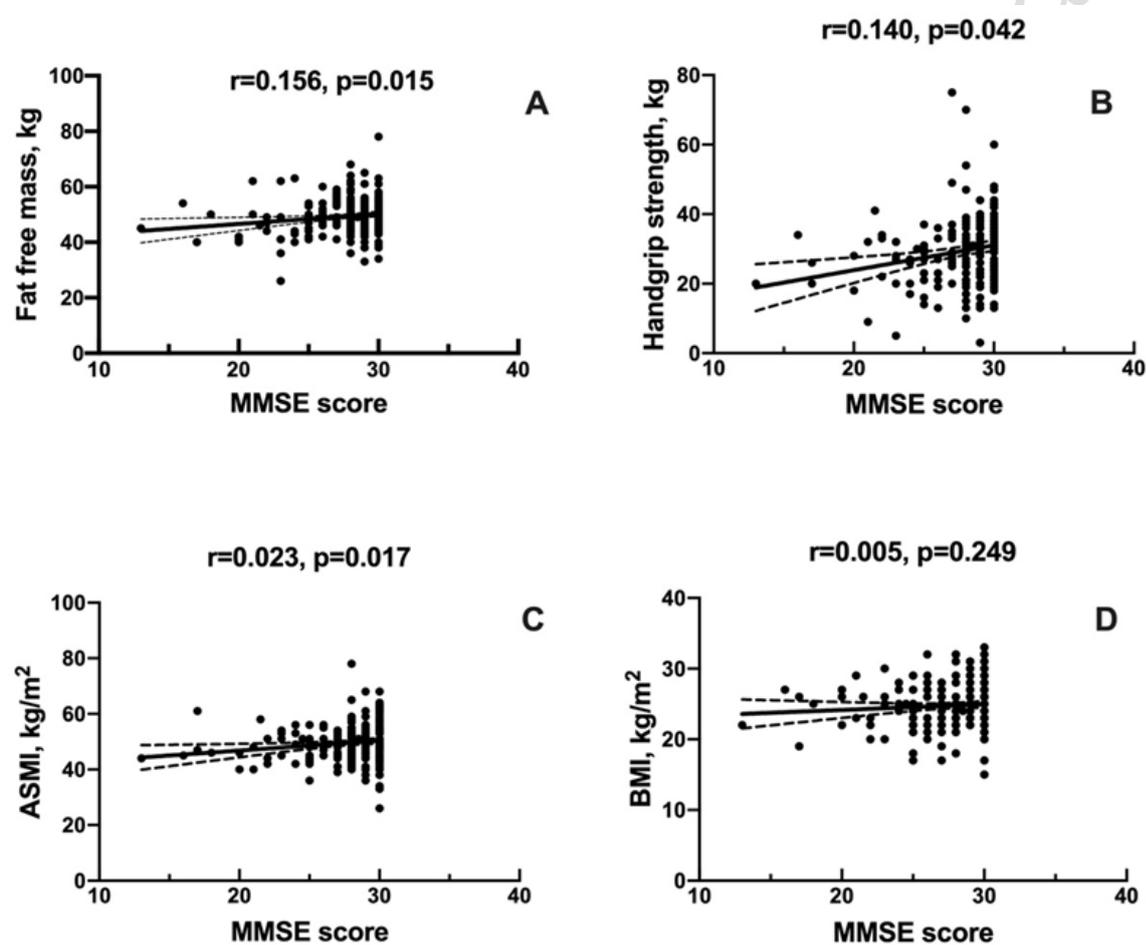


Figure 3. Dispersion graphs depicting correlations between MMSE and body composition (Fat free mass, handgrip strength, ASMI, BMI).