Original Article

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(6) 1–11

DOI: 10.1177/0300060520933051
journals.sagepub.com/home/imr

Sex- and age-specific mild cognitive impairment is associated with low hand grip strength in an older Chinese cohort

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Abstract

Background: Few studies have demonstrated the impact of characteristics like age and sex on the association between hand grip strength (HGS) and mild cognitive impairment (MCI). In this cross-sectional study, we aimed to examine the effects of sex and age on the relationship between HGS and MCI.

Methods: We enrolled older adults age $\geq$60 years (n = 1009) and measured HGS and MCI in all participants. We analyzed the differences in MCI prevalence among the different variables. The role of sex and age in the association between MCI and HGS was analyzed using binary logistic regression.

Results: Women had significantly higher prevalence of MCI than men, as did the older group (age $\geq$70 years) compared with the younger group (age 60–70 years). In men, the low and middle HGS tertiles were significantly associated with MCI. In contrast, only the low tertile of HGS was associated with MCI in women. In the older group, the low tertile of HGS was significantly associated with MCI, which was not observed in the younger group.

Conclusions: HGS was associated with MCI in older adults, and this association was stronger in men. HGS may be useful for evaluating MCI in older adults.

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Keywords
Age, sex, hand grip strength, mild cognitive impairment, older adults, tertiles

Date received: 25 November 2019; accepted: 19 May 2020

Introduction

Mild cognitive impairment (MCI) is a neurological condition that falls between the cognitive decline of normal aging and dementia.[1] With the increasing number of older people worldwide, MCI and dementia have become global challenges for health and social care systems. It has been reported that the annual incidence of MCI has increased from 1% to 12.7% and the prevalence has increased from 3% to 22% within the past 10 years.[2] In fact, a recent study showed that in China alone, the prevalence of MCI was around 14.7% in 22 provinces.[3] Additionally, MCI represent an early manifestation of AD.[4] However, no effective treatment for MCI is available;[5] thus, identifying modifiable risk factors to avoid or delay the onset of MCI is a necessary and practical approach that must be emphasized.

Among the various risk factors of MCI, physical frailty has been extensively investigated and implicated in this disease,[6,7] Changes in muscle strength such as hand grip strength (HGS) are thought to represent the level of frailty.[8] Previous studies have indicated that low HGS is associated with a decline in overall cognitive performance and MCI,[9–11] and stronger HGS is correlated with slower cognitive loss and decreased risk of MCI.[12] In one study, the prevalence of MCI was approximately 50% to 60% lower among older people in a high quartile of HGS versus their counterparts in a low quartile.[13] A functional neuromuscular system is essential for stronger HGS, which may boost antioxidative and anti-inflammatory capacity and consequently help to preserve cognitive function.[14,15] HGS can be easily and safely evaluated in older adults and used to measure whole-body muscular strength;[16] therefore, the decline of HGS has been used as a reliable quantitative measure of frailty in older people.[17,18] However, contrasting reports exist on the association between HGS and MCI. For example, decreased HGS failed to predict decline in cognitive function in the Women's Health Initiative Memory Study.[19] Another cross-sectional study did not find a significant association between cognitive impairment and reduced muscle strength among women age 75 years and older.[20] These inconsistent results highlight the need for further studies on underlying factors modifying the relationship between HGS and MCI.

To date, few studies have shown the impact of potential characteristics, such as age and sex, on the association between HGS and MCI. For example, a longitudinal study reported a stronger association between HGS and depression in female than male participants.[21] In an incident hemodialysis cohort, HGS was found to be associated with mortality in a sex-, and age-specific manner.[22] The discrepancies in the association between HGS and MCI may be owing to sex and/or age effects; however, such detailed patient information is not currently available.

In the present study, we aimed to examine the effects of sex and age on the relationship between HGS and MCI in a cross-sectional study. We hypothesized that low-level HGS is associated with a higher prevalence of MCI than higher-level HGS in an older population, in an age-dependent manner.

Methods

Study population

Data for this study were acquired from the baseline cohort survey "*Health of Elderly and Controllable Factors of Environment*", which was conducted in Lu'an city, Anhui Province, China, between June and September 2016. The cohort consisted of a rural district (Jin'an District) and an urban district (Yu'an District), which were randomly selected within Lu'an city. This cohort has been described in detail in our previous work.[23] One community in each district was then randomly selected. All people age 60 years or over in the two communities were invited to participate in this study, and a total of approximately 500 people in each community agreed. The questionnaire was completed in a face-to-face interview with every participant, followed by a physical examination at a local community hospital. The whole process lasted about 2 to 3 hours. The interviewers consisted of faculty and students from Anhui Medical University and community hospital physicians. The inclusion criteria for participation were as follows: (1) age ≥60 years, (2) a resident of the community for at least 6 months, (3) no previous history of mental illness, and (4) provided written informed consent. This study abided by the tenets of the Declaration of Helsinki and was approved by the ethics commission of Anhui Medical University.

Protocols of HGS measurement and MCI assessment

HGS measurement. HGS was measured on both hands using a dynamometer (JH-1881; Changzhou Jihao Electronic Co., Ltd, China). The dynamometer was explained and demonstrated to participants before use. Measurements were taken with participants in an upright standing position with feet apart, the elbows flexed at a right angle, and the wrists in a neutral position. Participants were asked to squeeze the dynamometer handle with maximum force for 2 s and HGS was measured three times on each hand. The average value of the three trials was calculated and recorded. The recorded values from the left and right hands were both analyzed in the study. The participants were divided into three groups based on tertiles of HGS, following similar criteria.[24] Briefly, HGS was assigned as low (<20.3 kg), middle (20.3–27.5 kg), and high (>27.5 kg) levels. Then, participants were divided into sex-specific groups (men: low <27.3 kg, middle 27.3–33.4 kg, high >33.4 kg; women: low <17.7 kg, middle 17.7–22.3 kg, high >22.3 kg) and age-specific groups (≤70 years: low <22.2 kg, middle 22.2–29.5 kg, high >29.5 kg; >70 years: low <18.7 kg, middle 18.7–25.4 kg, high >25.4 kg), based on HGS level.

MCI assessment. The Mini-Mental State Examination (MMSE) [25] was used to assess cognitive status among participants. The MMSE consists of a 20-item scale that assesses multiple mental processes including orientation, memory, counting backwards, and language. Participants were asked questions, and they were to respond immediately to the interviewer. MMSE scores ranged from 0 to 30, with lower scores indicating poorer cognitive function. The Cronbach's alpha for participations was 0.79.

The 10-item Activity of Daily Living (ADL) scale[26] was used to assess living independence. The maximum score was 100, with higher scores indicating stronger independence and reduced functional dependence in activities of daily living.

The criteria for diagnosing MCI were based on recommendations of the National Institute on Aging and the Alzheimer's Association,[27] which was validated in our previous publication.[28] In brief, individuals presenting the following conditions were considered to have MCI: (1) a memory problem reported by the patient or family of the patient; (2) cognitive impairment evaluated using the MMSE test (score of <17 for illiterate participants, <20 for participants with 1 to 6 years of education, and <24 for participants with more than 6 years of education); (3) preservation of functional independence evaluated using questions on self-reported difficulties with basic ADL in the previous 30 days (score of <95); (4) no history of dementia or any condition impairing cognition so severely as to prevent the participant from completing the survey.

Covariates. Sociodemographic variables included age, divided into two subgroups (60–70 years, >70 years), sex, marital status (widowed, non-widowed), and education level (illiterate, primary school, middle school and above). Health and vital indices included current smoker (yes or no), current consumption of alcohol (yes or no), physical exercise in the past 3 months (none, ≤1 hour, >1 hour), history of chronic diseases (yes or no), height (m), and body weight (kg). Participants were then grouped based on body mass index (BMI), as follows: underweight (BMI <18.5 kg/m^2), normal weight (BMI = 18.5–23.9 kg/m^2), and overweight (BMI >23.9 kg/m^2).

Active smoking was defined for individuals who smoked three or more cigarettes per week during the previous 6 months, alcohol consumption for those who drank at least one alcoholic beverage during the past 30 days, and physical exercise for those who participated in routine physical activities such as jogging or hiking. The history of chronic diseases was self-reported and included the diagnosis of at least one major condition such as hypertension, diabetes, chronic obstructive pulmonary disease, coronary heart disease, cancer/malignant tumor, and stroke.

Statistical analysis

We used SPSS 16.0 software to perform statistical analysis (SPSS Inc., Chicago, IL, USA). Continuous variables are showed as mean ± standard deviation whereas categorical variables are given as frequency and percentage. Chi-square tests or *t*-tests were used to identify the differences in MCI prevalence according to sex, age, marital status, education level, smoking, drinking, physical exercise, BMI, and history of chronic diseases.

We analyzed the association between HGS and MCI in binary logistic regression. First, we used binary logistic regression models with or without adjustment for significant confounders to examine the association of different tertiles of HGS with MCI in the total population. Then, two interaction terms (HGS and sex, HGS and age) were included in the multivariate model. Adjusted models were used to assess the sex- and age-specific associations of MCI with HGS in cases where the interaction terms were significant. *P*-values <0.05 were considered statistically significant.

Results

Baseline demographic characteristics

In total, 1080 participants were initially recruited; after the interviews were completed, those with missing data regarding HGS (n = 71) were excluded and classified as non-participants. Thus, 1009 participants with a mean age of 71.7 years (SD = 6.3) were included in the current study. No significant differences were found for age (mean age 74.6 and 71.7 years, respectively) and proportions of female sex (49.2% and 54.7%, respectively) between participants and non-participants ($P > 0.05$). Of the included participants, 45.3% (n = 457) were men and 25.9% (n = 261) were widowed. Approximately 46.6% (n = 470), 23.6% (n = 238), and 29.8% (n = 301) of participants were classified as being illiterate or having an elementary school or middle school education, respectively.

As shown in Table 1, the prevalence of MCI was 19.4% (n = 196) and was significantly higher among participants in the low tertile of HGS than among those in the high tertile ($P < 0.001$). Significant differences in MCI prevalence were observed between men and women, between older and younger subgroups, between widowed and non-widowed participants, among different educational levels and physical exercise levels, between alcohol drinkers and non-drinkers, between those with and

Table 1. Comparison of the prevalence of mild cognitive impairment among different demographic subgroups.

Variables	N	MCI, n (%)	χ^2	*P*- value
	1009	19.4 (196)		
Sex				
Male	457	16.2 (74)	5.58	0.011
Female	552	22.1 (122)		
Age (years)				
60–70	483	11.8 (57)	34.40	<0.001
>70	526	26.4 (139)		
Marital status				
Widowed	261	26.8 (70)	12.30	<0.001
Non-widowed	748	16.8 (126)		
Education level				
Illiterate	470	28.9 (136)	54.32	<0.001
Primary school	238	7.6 (18)		
≥Middle school	301	14.0 (42)		
Smoker				
No	816	18.6 (152)	0.50	0.269
Yes	193	21.2 (41)		
Drinking				
No	629	21.1 (133)	6.39	0.012
Yes	380	14.7 (56)		
Physical exercise				
No	738	22.0 (162)	19.17	<0.001
≤1 hour	149	11.4 (17)		
>1 hour	122	8.2 (10)		
BMI				
Underweight	53	9.4 (18)	11.35	0.003
Normal	444	48.4 (93)		
Overweight	502	42.2 (81)		
Chronic diseases				
No	395	22.5 (89)	4.18	0.019
Yes	614	17.3 (106)		
HGS				
Low	340	28.5 (97)	30.55	<0.001
Middle	335	17.6 (59)		
High	334	12.0 (40)		

MCI, mild cognitive impairment; HGS, hand grip strength; BMI, body mass index.

without a history of chronic diseases, and among different BMIs (Table 1).

Low HGS significantly increased the risk of MCI

Compared with the high tertile of HGS, the low and middle tertiles of HGS showed significant associations with MCI in the unadjusted model (Table 2, $P < 0.001$). After adjusting for sex, age, marital status, education level, alcohol consumption, smoking, BMI, physical exercise, and history of chronic diseases, the association with MCI remained for the group in the low tertile of HGS relative to the group in the high tertile of HGS (OR 2.35, 95% CI 1.48–3.73) (Table 2). Furthermore, women and the older subgroup exhibited a stronger relationship with MCI than men (OR 1.54, 95% CI 1.05–2.28) and the younger subgroup (OR 2.44, 95% CI 1.68–3.55).

Effects of sex and age on the relationship between HGS and MCI

Further analysis showed that HGS and sex, and HGS and age had statistically significant interactions ($P = 0.028$ and $P = 0.001$, respectively); therefore, we performed stratification analyses (Table 3). In men, the low (OR 5.83, 95% CI 2.08–16.38) and middle tertile HGS levels (OR 3.84, 95% CI 1.35–10.94) were significantly associated with MCI, as compared with the high tertile. In contrast, women only showed an association with MCI in the low tertile (OR 2.64, 95% CI 1.46–4.7).

In the younger subgroup, the low and middle HGS tertiles were not found to be significantly related to MCI. In the older subgroup, the low tertile HGS was significantly associated with MCI (OR 3.10, 95% CI 1.70–5.65) (Table 3).

Discussion

In the present study, we found that a low HGS level was associated with a significantly increased risk of MCI in both men and women. Furthermore, a higher risk of MCI was found in the population over 70 years of age, before and after adjusting for sex, age, marital status, educational level, physical exercise, drinking, smoking, BMI, and chronic diseases. These results are

Table 2. Multivariable odds ratios for mild cognitive impairment.

	Unadjusted model		Adjusted model*	
	OR (95% CI)	P-value	OR (95% CI)	P-value
HGS				
Low	2.93 (1.96–4.40)	<0.001	2.35 (1.48–3.73)	<0.001
Middle	1.57 (1.02–2.42)	0.041	1.43 (0.89–2.30)	0.137
High	1.00		1.00	
Sex				
Male	1.00		1.00	
Female	1.47 (1.07–2.02)	<0.019	1.54 (1.05–2.28)	0.029
Age (years)				
60–70	1.00		1.00	
71–94	2.68 (1.91–3.76)	<0.001	2.44 (1.68–3.55)	<0.001

*Adjusted variables included marital status, education, physical exercise, smoking, drinking, body mass index, and chronic diseases.
OR, odds ratio; MCI, mild cognitive impairment; CI, confidence interval.

Table 3. Adjusted odd ratios of mild cognitive impairment stratified by sex and age.

	MCI, n (%)	OR	95% CI	*P*-value
Male[1]				
HGS				
Low	39 (25.7)	5.83	2.08–16.38	0.001
Middle	27 (17.5)	3.84	1.35–10.94	0.012
High	8 (5.3)	1.00		
Female[1]				
HGS				
Low	62 (33.7)	2.64	1.46–4.75	0.001
Middle	34 (18.2)	1.07	0.58–1.98	0.826
High	26 (14.4)	1.00		
Age 60–70 years[2]				
HGS				
Low	22 (16.4)	2.47	0.98–6.23	0.055
Middle	16 (11.2)	1.29	0.49–3.43	0.610
High	11 (7.9)	1.00		
Age > 70 years[2]				
HGS				
Low	71 (34.5)	3.10	1.70–5.65	<0.001
Middle	43 (22.6)	1.42	0.76–2.64	0.272
High	33 (16.8)	1.00		

[1]Adjusted for age, marital status, education, physical exercise, smoking, drinking, body mass index, chronic diseases.
[2]Adjusted for sex, marital status, education, physical exercise, smoking, drinking, body mass index, chronic diseases.

consistent with previous study findings regarding the association of reduced HGS with poor cognitive function.[12,13,29]

The prevalence of MCI was approximately 19.4% in the present study, which is similar to the results of a report among community residents age 60 years or older in Shanghai (20.1%),[30] but higher than those of a systematic review (14.1%) among adults age ≥60 years in China.[31] Nevertheless, the present study and others[10,32] all showed a higher prevalence of MCI in women than in men and in older than in younger groups.

Interestingly, in the present study, we found that the association between HGS and MCI was sex- and age-specific. To the best of our knowledge, this is the first report to show that low-level HGS is strongly associated with higher MCI prevalence in men than women and in older than younger adults. These results are supported by those of a previous study,[24] which found a sex-dependent relationship between HGS and mortality in older people. Compared with those study participants who had high-level HGS, male participants with low-level HGS had a four-fold greater risk of all-cause mortality than their female counterparts.[24] Another longitudinal study found that male participants with low-level HGS were more likely to report depression than female participants with low-level HGS.[33] The sex-dependent associations between low-level HGS and poor health outcomes may be partially owing to sex differences regarding inflammatory load. Some inflammatory factors such as interleukin-6 are higher in male individuals than female individuals of similar age,[34] which could explain this effect. In fact, inflammatory cytokines are risk factors for a decline in muscle strength and cognitive functioning.[35,36] Future studies are needed to explore the role of inflammation in HGS and MCI.

The effect of age on the relationship between HGS and MCI was first reported in the present study. Other studies have shown that low physical activity is correlated with low-level HGS[37] and that low-level HGS is significantly and positively associated with MCI, although only in adults age $\geq$65 years.[28]An age-specific association of HGS with mortality has also been reported in an incident hemodialysis cohort.[22] Thus, our findings support the effects of age on MCI and HGS; however, further studies with long-term follow-ups are needed to confirm the existence of an age-specific association between lower levels of HGS and MCI.

It has been reported that some risk factors can contribute to the increased risk of MCI.[38] Changes in BMI and weight have been found to be associated with increased risk of MCI and dementia; however, these findings are not consistent. Some investigators[39–41] have found an association of lower BMI with higher risk of dementia, although instances where higher BMI can increase the risk of MCI have also been noted.[42,43] In the present study, we found fewer participants with MCI in the lower BMI group than in the normal or high BMI groups. Owing to the limited size of our sample, we were unable to further analyze age- and sex-specific associations between BMI and MCI; however, our results indicated that BMI should also be considered as a risk factor for MCI. Nevertheless, our study findings are consistent with those of the abovementioned studies reporting that BMI may be a risk factor for MCI and might be considered in preventing or slowing the development of MCI and dementia.

Limitations in the present study include the cross-sectional study design and the relatively small sample size, which made it impossible to draw causal conclusions regarding the relationship between HGS and MCI. In addition, no participants had a clinical diagnosis of MCI in the present study. Thus, there is a possibility of MCI misclassification, which could affect our results and conclusions. Nevertheless, the prevalence of MCI in our study was consistent with that of previous studies.[30]

In older people, low-level HGS was found to be significantly associated with a higher prevalence of MCI compared with high-level HGS in a sex- and age-specific manner. A stronger association between low levels of HGS and MCI was observed in men than in women and in participants with older age versus younger participants. These findings strongly suggest the importance of maintaining a high level of HGS later in life. Clinicians should be particularly interested in the findings regarding men with respect to MCI, and in older populations.

Acknowledgment

The authors are grateful to all participants in the study, the research group *Elderly Health and Modified Factors*, the Lu'an Center for Disease Control and Prevention, Chengbei Township Health Center, and Beishi community health service center.

Authors' contributions

XL and JC: Conceptualization; data curation, methodology, validation, visualization; and writing-original draft.

RW, BC, PX and Lin-Sheng Yang: Validation, formal analysis, resources; and writing-review and editing.

RG and KL: Conceptualization, methodology, validation, visualization; writing-review and editing; funding acquisition and supervision.

All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This study was supported by Key Projects on Introduction of Leading Talents and Teams to Anhui for colleges and universities in 2016 (0303011224), the National Natural Science Foundation of China (81202209), and the Key Scientific Research Fund of Anhui Provincial Education Department (grant no. KJ2017A189, KJ2018A0164).

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