A systematic review and meta-analysis of the prevalence and correlation of mild cognitive impairment in sarcopenia

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Abstract

Sarcopenia is a progressive skeletal muscle disorder involving the loss of muscle mass and function, associated with an increased risk of disability and frailty. Though its prevalence in dementia has been studied, its occurrence in mild cognitive impairment (MCI) has not been well established. As MCI is often a prelude to dementia, our study aims to investigate the prevalence of MCI among individuals with sarcopenia and to also ascertain whether sarcopenia is independently associated with MCI. The Cochrane Library, PubMed, Ovid, Embase and Web of Science were systematically searched for articles on MCI and/or sarcopenia published from inception to 1 February 2022. We reviewed the available literature on the number of individuals with MCI and/or sarcopenia and calculated odds ratios (ORs) of sarcopenia in MCI and MCI in sarcopenia, respectively. Statistical analyses were performed using the meta package in Stata, Version 12.0. A total of 13 studies and 27 428 patients were included in our analysis. The pooled prevalence of MCI in participants with sarcopenia was 20.5% (95% confidence interval [CI]: 0.140–0.269) in a total sample of 2923 cases with a high level of heterogeneity ($P < 0.001$; $I^2 = 95.4\%$). The overall prevalence of sarcopenia with MCI was 9.1% (95% CI: 0.047–0.134, $P < 0.001$; $I^2 = 93.0\%$). For overall ORs, there were 23 364 subjects with a mean age of 73 years; the overall adjusted OR between MCI and sarcopenia was 1.46 (95% CI: 1.31–1.62). Slight heterogeneity in both adjusted ORs ($P = 0.46$; $I^2 = 0\%$) was noted across the studies. The prevalence of MCI is relatively high in patients with sarcopenia, and sarcopenia may be a risk factor for MCI.

Keywords   elderly; mild cognitive impairment (MCI); risk factor; sarcopenia

Introduction

Mild cognitive impairment (MCI), a common disease in the elderly, is defined as a type of cognitive disorder that can occur as a stage between the expected cognitive decline of normal ageing and dementia. More than 50% of patients with MCI develop Alzheimer's disease (AD) or other forms of dementia within 4 to 6 years.[1] With the progression of global ageing, the number of patients diagnosed with dementia is increasing rapidly. It is estimated that the global prevalence of dementia is doubling every 20 years and the number of patients could reach 131.5 million by 2050.[2] Additionally, individuals with MCI tend to experience more subjective cognitive concerns, functional impairment, self-rated health problems and psychopathology.[3] For instance, those with MCI are approximately twice as likely to have depressive symptoms compared to similarly aged healthy adults, with more severe levels of cognitive impairment predicting more severe depression.[4,5] Therefore, continued research into the early detection and intervention of MCI is of vital importance for the future of our elderly populations.

Sarcopenia is a disease of age-related progressive, generalized loss of skeletal muscle and/or muscle strength resulting from accumulated adverse muscle changes throughout life. It is associated with increased risk of falls, disability, frailty and other adverse outcomes.[6] Results from systematic reviews and meta-analyses confirm that patients with sarcopenia experience an impaired overall quality of life,[7] increased healthcare costs[8] and even increased mortality.[9] Studies determining its incidence are sparse, though emerging evidence suggests that its incidence increases progressively with age. In order to mitigate its adverse health outcomes, reduce the heavy burden on patients and the entire healthcare system, more research in the field of sarcopenia is being pursued to prevent or delay the onset of this disease.[9]

Although there are many causes of disability in the elderly population, sarcopenia and cognitive impairment in particular play an important role.[10] Recently, the association between sarcopenia and cognitive decline has been demonstrated in several studies. Data from China, Ghana, India, Mexico and Russia show a positive association between sarcopenia and MCI.[11] However, not all the studies came to this conclusion. For instance, an observational study from South Africa identified that an inconsistent association may occur between sarcopenia and MCI in countries with more pronounced differences in income levels.[11] In addition, the reported prevalence of MCI in patients with sarcopenia has varied widely, ranging from 7.5% to 69.3%.[12]

Despite strong suggestions from such studies that cognitive impairment may be independently associated with sarcopenia,[13] there is a relative lack of research specifically focusing on the occurrence and relationship of MCI and sarcopenia. Therefore, the purpose of this systematic review and meta-analysis is to investigate the prevalence of MCI in individuals with sarcopenia (MWS) and also the prevalence of sarcopenia in participants with MCI (SWM) based on the available data and to determine whether there is an independent association between sarcopenia and MCI.

Methods

Study selection and selection criteria

We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement (PRISMA 2020). A systematic search was performed in five electronic databases: the Cochrane Library, PubMed, Ovid, Embase and Web of Science. The search included the keywords, 'sarcopenia' and 'cognitive impairment', from database inception to 1 February 2022, and the particular search strategies for all included databases can be viewed in *Appendix S1*. The inclusion criteria were as follows: (1) cross-sectional or cohort studies and (2) study population involving patients with sarcopenia and/or MCI with clear diagnostic criteria. The exclusion criteria were as follows: (1) The original study did not involve or could not calculate the number of those diagnosed with sarcopenia or MCI; (2) inability to extract data; (3) literature reviews, case reports, animal studies or conference abstracts; and (4) non-English studies.

Data extraction

According to the inclusion and exclusion criteria, two reviewers (YY and MX) assessed the study eligibility independently and made a final decision after consulting with the arbitrator (Yongxue Yang). A standard procedure was performed to extract the data from the studies, including the first author, publication date, country, study design, sample size, mean age, proportion of males, number of MWS and SWM, and methods of evaluating sarcopenia and MCI (techniques for measurement, diagnostic items and cut-off values, and all pertinent covariates modifying the relationship between sarcopenia and MCI). The main outcomes of interest were the prevalence of MWS and the approximate and adjusted association between MCI and sarcopenia, expressed in odds ratios (ORs) and 95% confidence intervals (CIs). Results were adjusted for various confounding factors.

Research quality assessment

The quality of each study was independently scored by two researchers (YY and LL) and assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies and the Agency for Healthcare Research and Quality (AHRQ) for cross-sectional

studies.[14] The highest score for cohort studies was 9 points, and the highest score for cross-sectional studies was 11 points. A higher score indicated a better quality method, and studies with a score >7 in the NOS or 8 in the AHRQ were regarded as moderate-to-high credibility[14,15] (*Appendix S2*). For any disagreements, YY and LL consulted with Yongxue Yang to reach a final resolution.

Statistical analyses

In our meta-analysis, we applied a random-effects model to obtain a relatively conservative finding when the I^2 test detected significant heterogeneity statistically ($I^2 > 50\%$, $P < 0.05$). A fixed-effects model was otherwise applied if no significant heterogeneity was detected.[16,17] To identify potential sources of heterogeneity, we performed meta-regression and subgroup analyses. We further performed sensitivity analyses by evaluating the quality and robustness of the results by deleting one study at a time (*Appendix S3*). In addition, publication bias was evaluated with the Egger test and Begg test

(*Appendix S4*).[17,18] All data analyses were performed using the meta package in Stata, Version 12.0 (StataCorp LLC, TX, USA, http://www.stata.com/).

Results

Search process

The flow diagrams of the literature selection process are shown in *Figure 1*. A total of 13 studies and 27 428 patients were included in our analysis. Seven studies were focused on the prevalence of MWS,[11–13,19–22] four studies included the prevalence of SWM[20,23–25] and only one of them mentioned both the prevalence of MWS and SWM.[20] One study reported whether MCI was a risk factor for sarcopenia,[26] whereas 10 studies analysed whether sarcopenia was a risk factor for MCI.[11–13,21–25,27,28] Except for two studies,[19,20] the rest of them and the study by Beeri et al.,[28] in particular, all raised the question about the association of MCI with
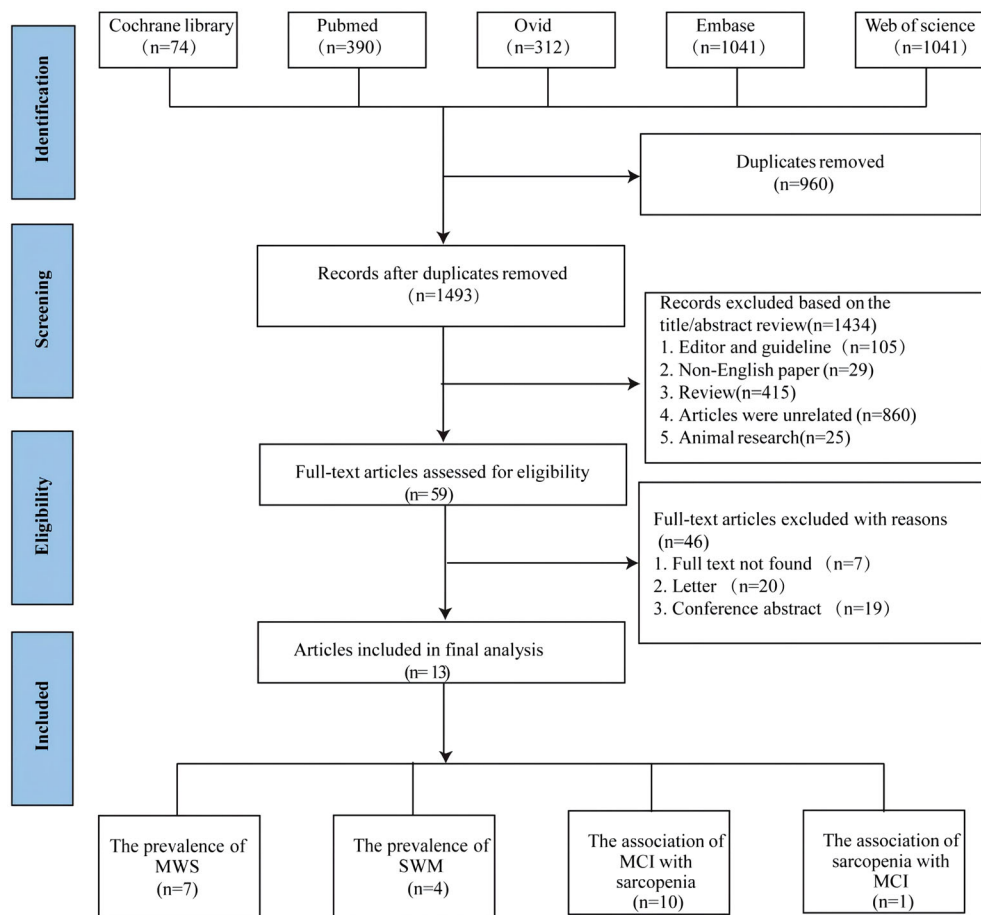
Figure 1 The flowchart of research screening. MCI, mild cognitive impairment; MWS, mild cognitive impairment with sarcopenia; SWM, sarcopenia with mild cognitive impairment.

sarcopenia. The main reasons for excluding articles after reviewing the full text are as follows: (1) We were unable to obtain the required full data, even after contacting the corresponding author of a study, and (2) manuscripts were not formal research investigations (e.g., letter to the editor and conference abstract).

Demographics

The characteristics of the included studies were summarized in *Table 1*. Studies were conducted in various countries, including the United Kingdom, China, Korea, Japan, Ghana, India, Mexico, Russia, South Africa and the United States of

Table 1 Characteristics of studies included in the meta-analysis

Study	Study region	Study design	Sample size	Study population	Age (mean ± SD)	Male (%)	Definition of sarcopenia	Definition of MCI
Louis Jacob 2021[11]	China	Cross-sectional study	4823	Community participants	72.1 ± 10.5	46.3%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Louis Jacob 2021[11]	Ghana	Cross-sectional study	1841	Community participants	73.9 ± 13.8	52.3%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Louis Jacob 2021[11]	India	Cross-sectional study	2149	Community participants	71.2 ± 9.3	52.8%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Louis Jacob 2021[11]	Mexico	Cross-sectional study	1124	Community participants	73.9 ± 14.2	45.6%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Louis Jacob 2021[11]	Russia	Cross-sectional study	1663	Community participants	73.7 ± 9.7	31.7%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Louis Jacob 2021[11]	South Africa	Cross-sectional study	1312	Community participants	72.8 ± 14.8	37.6%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Satoshi Ida 2017[12]	Japan	Cross-sectional study	250	Hospital participants	71.6 ± 5.12	60.0%	SARC-F-J	TYM-J
Xiaolei Liu 2020[13]	China	Cross-sectional study	4500	Community participants	62.4 ± 8.3	36.2%	AWGS	SPMSQ
Fengjuan Hu 2021[19]	China	Cross-sectional study	3810	Community participants	61.94 ± 8.01	36.40%	AWGS	SPMSQ
Taiki Sugimoto 2016[20]	Japan	Cross-sectional study	418	Hospital participants	77.3 ± 7.0	33.30%	EWGSOP	Petersen's definitions
Aarón Salinas-Rodríguez 2021[21]	Mexico	Cohort study	496	Others	65.5 ± 7.3	34.7%	Low SMM, slow gait speed, weak handgrip strength	NIAAA
Anying Bai 2021[22]	China	Cross-sectional study	665	Community participants	86.34 ± 3.57	39.7%	AWGS	MoCA
Efstathios Papachristou 2015[23]	Britain	Cross-sectional study	1570	Hospital participants	78.25 ± 4.55	100.0%	EWGSOP(a) or FNIH(b)	TYM
Xiaoyu Chen 2021[24]	China	Cross-sectional study	1394	Community participants	71.08 ± 5.90	41.2%	AWGS	Modified Petersen's definitions
Noritaka Machii 2020[25]	Japan	Cohort study	438	Hospital participants	67.6 ± 10.4	56.0%	AWGS	MoCA-J
Jwa-Kyung Kim 2013[26]	Korea	Cross-sectional study	95	Hospital participants	63.9 ± 10.0	56.8%	EWGSOP	MMSE
Inhwan Lee 2018[27]	Korea	Cross-sectional study	201	Community participants	74.3 ± 6.6	0.0%	AWGS	MMSE
Michal S. Beeri 2021[28]	America	Cohort study	1175	Community participants	80.9 ± 7.1	22.8%	SMI and weak handgrip strength	MMSE

Abbreviations: AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; MoCA-J, Japanese version of the Montreal Cognitive Assessment; MWS, mild cognitive impairment with sarcopenia; NIAAA, National Institute on Aging—Alzheimer's Association; SARC-F-J, Japanese version of the simple 5-item questionnaire; SMI, skeletal muscle mass index; SMM, skeletal muscle mass; SPMSQ, Short Portable Mental Status Questionnaire; SWM, sarcopenia with mild cognitive impairment; TYM, Test Your Memory; TYM-J, Test Your Memory Japanese version.

America. The majority of the study population were recruited from the community or outpatient clinics. One study's data, which came from Mexico, did not clearly indicate whether their sample was from a community or hospital population.[21] Ten studies employed a cross-sectional design, and three studies were cohort based.[21,25,28] Among the included studies, though seven were considered to be of moderate quality, they did not negatively bias the outcome based on our sensitivity analyses.

Sarcopenia was mainly diagnosed based on consensus agreements by the Asian Working Group for Sarcopenia (AWGS), European Working Group on Sarcopenia in Older People (EWGSOP) and Foundation for the National Institutes of Health (FNIH). It was further assessed via methods such as the Japanese version of the simple 5-item questionnaire (SARC-F-J), and skeletal muscle mass index (SMI) or low skeletal muscle mass (SMM). To diagnose MCI, three studies used the Mini Mental State Examination (MMSE), one applied the Montreal Cognitive Assessment (MoCA), one applied the Japanese version of the MoCA (MoCA-J), two were evaluated by the Short Portable Mental Status Questionnaire (SPMSQ), two used guidelines set by the National Institute on Aging— Alzheimer's Association (NIAAA) and, finally, one assessed MCI by administering the Test Your Memory (TYM) test, and one assessed MCI by administering the TYM Japanese version (TYM-J). The details of the diagnostic criteria and cut-off points for sarcopenia and MCI in each study have been listed in *Appendix S5*.
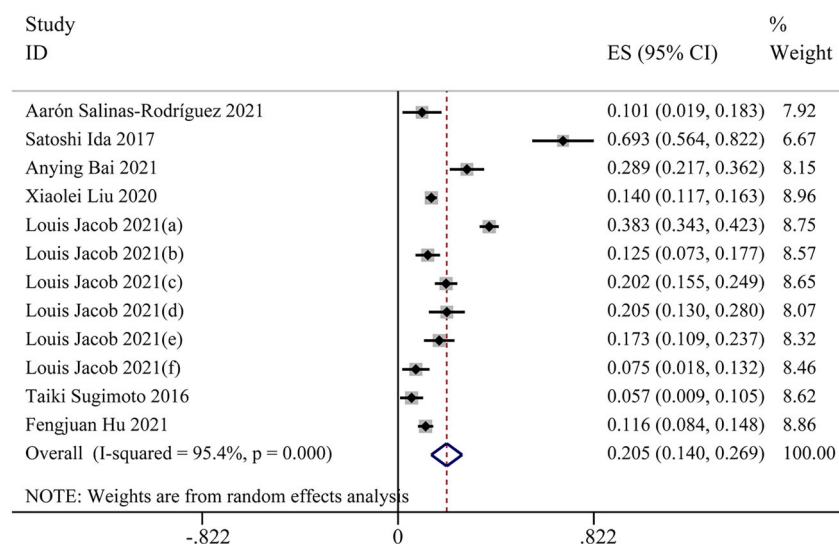
Meta-analysis results

Prevalence of mild cognitive impairment with sarcopenia

Results The pooled MWS prevalence was 20.5% in a total sample of 2923 cases of sarcopenia and 598 of MCI (95% CI: 0.140–0.269) with a high level of heterogeneity ($P < 0.001$; $I^2 = 95.4\%$; *Figure 2*).

Meta-regression analyses Table 4 showed the results of the meta-regression analysis of the prevalence of MWS. Meta-regression was performed to explore the relationship between MWS and mean age, diagnostic criteria and the diagnostic items of sarcopenia and MCI, population source and study type. The meta-regression found that none of these variables were significant.

Subgroup analyses Table 2 showed the results of the subgroup analysis of the prevalence of MWS. The subgroup analysis showed that the prevalence of MWS was 0.182 (95% CI: 0.090–0.273) in the group diagnosed with sarcopenia according to SMM and functional status; 0.171 (95% CI: 0.106–0.236) in the group diagnosed according to AWGS guidelines; and 0.693 (95% CI: 0.564–0.822) in the group diagnosed according to the SARC-F-J assessment. Similarly, because of different cognitive evaluation methods, various results were obtained. The prevalence of MWS was 0.182 (95% CI: 0.090–0.273) in the group diagnosed with MCI used NIAAA criteria and 0.131 (95% CI: 0.108–0.154) in the group evaluated according to SPMSQ methods. There were six cross-sectional studies describing the prevalence of MWS with a combined prevalence of 0.214 (95% CI: 0.145–0.282). Compared with the community population, the prevalence of MWS in hospitalized patients was not found to be significantly different (0.189 [95% CI: 0.125–0.254] and 0.372 [95% CI: −0.251 to 0.995], respectively). In addition, subgroup analysis showed that the patients with body mass index (BMI) <25 kg/m² had a high prevalence of MWS (0.341 [95% CI: 0.040–0.641]) (meta graph for subgroup analysis can be viewed in *Appendix S6*).

Study ID	ES (95% CI)	% Weight
Aarón Salinas-Rodríguez 2021	0.101 (0.019, 0.183)	7.92
Satoshi Ida 2017	0.693 (0.564, 0.822)	6.67
Anying Bai 2021	0.289 (0.217, 0.362)	8.15
Xiaolei Liu 2020	0.140 (0.117, 0.163)	8.96
Louis Jacob 2021(a)	0.383 (0.343, 0.423)	8.75
Louis Jacob 2021(b)	0.125 (0.073, 0.177)	8.57
Louis Jacob 2021(c)	0.202 (0.155, 0.249)	8.65
Louis Jacob 2021(d)	0.205 (0.130, 0.280)	8.07
Louis Jacob 2021(e)	0.173 (0.109, 0.237)	8.32
Louis Jacob 2021(f)	0.075 (0.018, 0.132)	8.46
Taiki Sugimoto 2016	0.057 (0.009, 0.105)	8.62
Fengjuan Hu 2021	0.116 (0.084, 0.148)	8.86
Overall (I-squared = 95.4%, p = 0.000)	0.205 (0.140, 0.269)	100.00

NOTE: Weights are from random effects analysis

Figure 2 Forest plot of prevalence of mild cognitive impairment with sarcopenia. CI, confidence interval; ES, effect size.

Table 2 The results of subgroup analysis in prevalence of MWS and SWM

Variable	Numbers of studies	Meta-analysis results	Heterogeneity
The prevalence of MWS[a]			
Study design			
Cross-sectional study	11	0.214 (0.145, 0.282)	$I^2 = 95.8\%, P < 0.001$
Cohort study	1	0.101 (0.019, 0.183)	—
Study population			
Community-dwelling participants	9	0.189 (0.125, 0.254)	$I^2 = 94.7\%, P < 0.001$
Hospital participants	2	0.372 (−0.251, 0.995)	$I^2 = 98.8\%, P < 0.001$
Others	1	0.101 (0.019, 0.183)	—
Sarcopenia assessment			
Low SMM, slow gait speed, weak handgrip strength	7	0.182 (0.090, 0.273)	$I^2 = 94.6\%, P < 0.001$
AWGS	3	0.171 (0.106, 0.236)	$I^2 = 89.3\%, P < 0.001$
SARC-F-J	1	0.693 (0.564, 0.822)	—
EWGSOP	1	0.057 (0.009, 0.105)	—
Mild cognitive impairment assessment			
NIAAA	7	0.182 (0.090, 0.273)	$I^2 = 94.6\%, P < 0.001$
SPMSQ	2	0.131 (0.108, 0.154)	$I^2 = 29.9\%, P = 0.232$
TYM-J	1	0.693 (0.564, 0.822)	—
MoCA	1	0.289 (0.217, 0.362)	—
Petersen's definitions	1	0.057 (0.009, 0.105)	—
BMI			
≥ 25 kg/m^2	2	0.114 (0.084, 0.144)	$I^2 = 0.0\%, P = 0.738$
< 25 kg/m^2	3	0.341 (0.040, 0.641)	$I^2 = 97.9\%, P < 0.001$
Unclear	7	0.187 (0.107, 0.266)	$I^2 = 95.3\%, P < 0.001$
The prevalence of SWM[b]			
Study design			
Cross-sectional study	4	0.078 (0.034, 0.123)	$I^2 = 92.7\%, P < 0.001$
Cohort study	1	0.130 (0.085, 0.175)	—
Study population			
Hospital participants	4	0.059 (0.027, 0.092)	$I^2 = 86.1\%, P < 0.001$
Community-dwelling participants	1	0.187 (0.138, 0.236)	—
Sarcopenia assessment			
AWGS	2	0.158 (0.102, 0.213)	$I^2 = 64.5\%, P = 0.093$
EWGSOP	2	0.063 (−0.028, 0.154)	$I^2 = 70.5\%, P = 0.066$
FNIH	1	0.032 (0.018, 0.046)	—
Mild cognitive impairment assessment			
Petersen's definitions	1	0.125 (0.023, 0.227)	—
TYM	2	0.030 (0.021, 0.039)	$I^2 = 0.0\%, P = 0.676$
MoCA-J	1	0.130 (0.085, 0.175)	—
Modified Petersen's definitions	1	0.187 (0.138, 0.236)	—
BMI			
≥ 25 kg/m^2	1	0.130 (0.085, 0.175)	—
< 25 kg/m^2	2	0.173 (0.122, 0.224)	$I^2 = 12.5\%, P = 0.285$
Unclear	2	0.030 (0.021, 0.039)	$I^2 = 0.0\%, P = 0.676$
Gender			
Mix	3	0.152 (0.110, 0.195)	$I^2 = 36.2\%, P = 0.209$
Male	2	0.030 (0.021, 0.039)	$I^2 = 0.0\%, P = 0.676$

Abbreviations: AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health; MoCA, Montreal Cognitive Assessment; MoCA-J, Japanese version of the Montreal Cognitive Assessment; MWS, mild cognitive impairment with sarcopenia; NIAAA, National Institute on Aging—Alzheimer's Association; SARC-F-J, Japanese version of the simple 5-item questionnaire; SMM, skeletal muscle mass; SPMSQ, Short Portable Mental Status Questionnaire; SWM, sarcopenia with mild cognitive impairment; TYM, Test Your Memory; TYM-J, Test Your Memory Japanese version.
[a]As mentioned in the flowchart, a total of seven studies involved the prevalence of MWS, but one of them[11] mentioned relevant data from six countries, so a total of 12 groups of data were analysed in *Table 2*.
[b]As mentioned in the flowchart, a total of four studies dealt with the prevalence of SWM, but one study[23] used two different ways to assess sarcopenia, so there are a total of five sets of data analysis in the subgroup analysis.

Prevalence of sarcopenia with mild cognitive impairment

Results There were 1770 cases of MCI and 116 of sarcopenia in the included studies. The overall prevalence of SWM was 0.091 (95% CI: 0.047–0.134, $P < 0.001$; $I^2 = 93.0\%$) (*Figure 3*).

Subgroup analyses *Table 2* also displayed the results of the subgroup analysis of the prevalence of SWM. The subgroup analysis showed that the prevalence of SWM was 0.158

(95% CI: 0.102–0.213) in the group diagnosed with sarcopenia according to AWGS guidelines; 0.063 (95% CI: −0.028 to 0.154) in the group diagnosed with sarcopenia according to EWGSOP methods; and 0.032 (95% CI: 0.018–0.046) in the group diagnosed according to FNIH criteria. Analogously, different cognitive assessment methods also have some impact on the prevalence of SWM; the prevalence of SWM fluctuated from 0.030 to 0.187 by using different cognitive
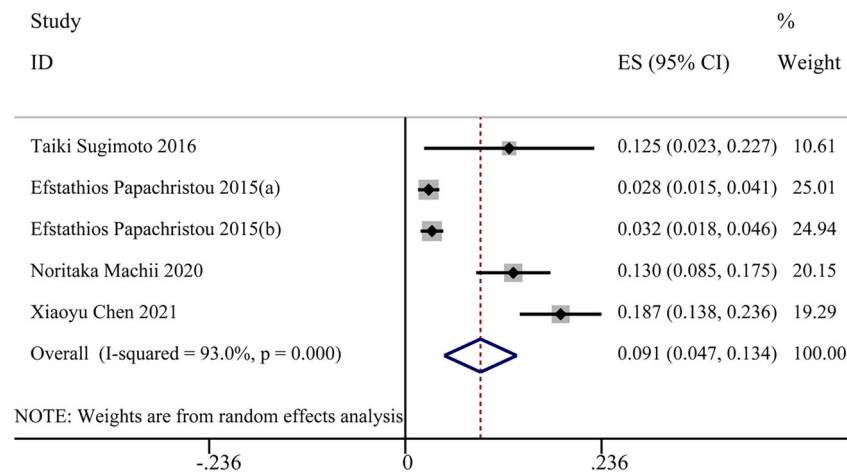
Figure 3 Forest plot of prevalence of sarcopenia with mild cognitive impairment. CI, confidence interval; ES, effect size.

assessment tools. Different study designs also have a certain impact on the results, and the combined prevalence of three cross-sectional studies was 0.078 (95% CI: 0.034–0.123). There was no significant difference in the prevalence of SWM in hospitals and in the community (0.059 [95% CI: 0.027–0.092] and 0.187 [95% CI: 0.138–0.236], respectively). In addition, subgroup analysis showed that patients with BMI < 25 kg/m^2 had a high prevalence of SWM (0.173 [95% CI: 0.122–0.224]). The prevalence of SWM in male was 0.030 (95% CI: 0.021–0.039) (meta graph for this subgroup analysis was shown in *Appendix S6*).

Odds ratio results

Ten studies with 23 364 subjects (mean age of 73 years) were able to be included for calculation of the overall OR (*Table 3*). The overall adjusted OR between MCI and sarcopenia was 1.46 (95% CI: 1.31–1.62). Mild heterogeneity in both adjusted ORs ($P = 0.46$; $I^2 = 0\%$) was noted across the studies (*Figure 4*). Only one study specifically suggested that MCI was also a risk factor for sarcopenia, and the adjusted OR between them was 6.35 (95% CI: 1.62–34.96).[26]

Meta-regression analyses Meta-regression analysis suggested that study type was associated with heterogeneity between studies ($\beta = 0.236$, SE = 0.110, $P = 0.049$). The relevant results of meta-regression were shown in *Table 4*.

Subgroup analyses Results of the subgroup analyses showed that the adjusted OR between MCI and sarcopenia was 1.55 (95% CI: 1.27–1.89) in the group diagnosed with sarcopenia according to AWGS guidelines and 1.62 (95% CI: 1.35–1.93) in those diagnosed according to SMM and functional status assessments. Among the included studies, there were eight methods of assessing MCI. The adjusted OR were as follows: 1.55 (95% CI: 0.80–2.99) in the group diagnosed using TYM test, 2.02 (95% CI: 0.57–7.08) in the group diagnosed using MMSE and 1.62 (95% CI: 1.35–1.93) in the group diagnosed

using the NIAAA criteria. Sarcopenia was found to be one of the risk factors for MCI, regardless of community-dwelling status or hospital admission (OR 1.47 [95% CI: 1.28–1.68], $I^2 = 16.1\%$; OR 1.73 [95% CI: 1.09–2.74], $I^2 = 0\%$; respectively). Different study types were found to have similar results. The adjusted OR was 1.60 (95% CI: 1.40–1.83) in cross-sectional studies and 1.26 (95% CI: 1.07–1.49) in cohort studies. In addition, the OR between MCI and sarcopenia was 1.63 (95% CI: 1.04–2.57) in patients with BMI ≥ 25 kg/m^2 and 1.98 (95% CI: 1.42–2.76) in those with BMI < 25 kg/m^2. Last but not least, in the gender subgroup, the adjusted OR was 1.55 (95% CI: 0.80–2.99) in male. The relevant results were shown in *Appendix S8*.

Discussion

Our study is the first systematic review and meta-analysis to focus on the prevalence on SWM and MWS and the correlation between them. Based on 13 studies with 27 428 cases, the pooled prevalence of MWS was 20.5%, which corresponded to a 9.1% prevalence of SWM. At the same time, we found that there was a positive correlation between sarcopenia and MCI, and this relationship remained unchanged after adjustment for related covariates.

Risk factors and predictors of dementia remain an intense area of investigation. The annual per capita conversion rate from normal cognition to MCI is 30%.[29] Moreover, the proportion of those with MCI who eventually develop dementia increases progressively with age,[30] with the prevalence of AD almost doubling every 5 years after age 65.[31] As sarcopenia is highly prevalent in those with dementia,[32,33] our study highlighting its early presence in MCI suggests another avenue of research to pursue. However, based on our results, age alone cannot explain the strong correlation between MCI

Table 3 The results of subgroup analysis for ORs between sarcopenia and mild cognitive impairment

Variable	Numbers of studies[a]	Meta-analysis results	Heterogeneity
Study population			
Community-dwelling participants	11	1.47 (1.28, 1.68)	$I^2 = 16.1\%, P = 0.290$
Hospital participants	4	1.73 (1.09, 2.74)	$I^2 = 0\%, P = 0.656$
Others	1	1.74 (1.02, 2.96)	—
Study design			
Cross-sectional study	13	1.60 (1.40, 1.83)	$I^2 = 0\%, P = 0.761$
Cohort study	3	1.26 (1.07, 1.49)	$I^2 = 0\%, P = 0.438$
Sarcopenia assessment			
Low SMM, slow gait speed, weak handgrip strength	7	1.62 (1.35, 1.93)	$I^2 = 0\%, P = 0.836$
AWGS	5	1.55 (1.27, 1.89)	$I^2 = 0\%, P = 0.410$
EWGSOP	1	1.40 (0.56, 3.50)	—
FNIH	1	1.72 (0.67, 4.41)	—
SARC-F-J	1	2.96 (1.11, 7.87)	—
SMI and weak handgrip strength	1	1.21 (1.01, 1.45)	—
Mild cognitive impairment assessment			
National Institute on Aging—Alzheimer's Association	7	1.62 (1.35, 1.93)	$I^2 = 0\%, P = 0.836$
TYM	2	1.55 (0.80, 2.99)	$I^2 = 0\%, P = 0.759$
MMSE	2	2.02 (0.57, 7.08)	$I^2 = 76.8\%, P = 0.038$
Modified Petersen's definitions	1	1.67 (1.04, 2.68)	—
TYM-J	1	2.96 (1.11, 7.87)	—
SPMSQ	1	1.41 (1.10, 1.81)	—
MoCA	1	1.86 (1.04, 3.33)	—
MoCA-J	1	1.39 (0.59, 3.28)	—
BMI			
≥25 kg/m^2	2	1.63 (1.04, 2.57)	$I^2 = 0.0\%, P = 0.66$
<25 kg/m^2	4	1.98 (1.42, 2.76)	$I^2 = 0.0\%, P = 0.405$
Unclear	10	1.39 (1.24, 1.56)	$I^2 = 0.0\%, P = 0.602$
Gender			
Mix	13	1.44 (1.30, 1.60)	$I^2 = 0.0\%, P = 0.512$
Male	2	1.55 (0.80, 2.99)	$I^2 = 0.0\%, P = 0.759$
Female	1	4.50 (1.32, 15.35)	—

Abbreviations: AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; EWGSOP, European Working Group on Sarcopenia in Older People; FNIH, Foundation for the National Institutes of Health; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; MoCA-J, Japanese version of the Montreal Cognitive Assessment; ORs, odds ratios; SARC-F-J, Japanese version of the simple 5-item questionnaire; SMI, skeletal muscle mass index; SMM, skeletal muscle mass; SPMSQ, Short Portable Mental Status Questionnaire; TYM, Test Your Memory; TYM-J, Test Your Memory Japanese version.
[a]Papachristou et al.[23] used two different methods to assess sarcopenia so that there were two unequal OR values, so we divided the study into two groups for analysis; Jacob et al.[11] gave sarcopenia in six different countries and mild cognitive impairment, so we divided the study into six groups for analysis, resulting in a total number of 16 studies in this table.
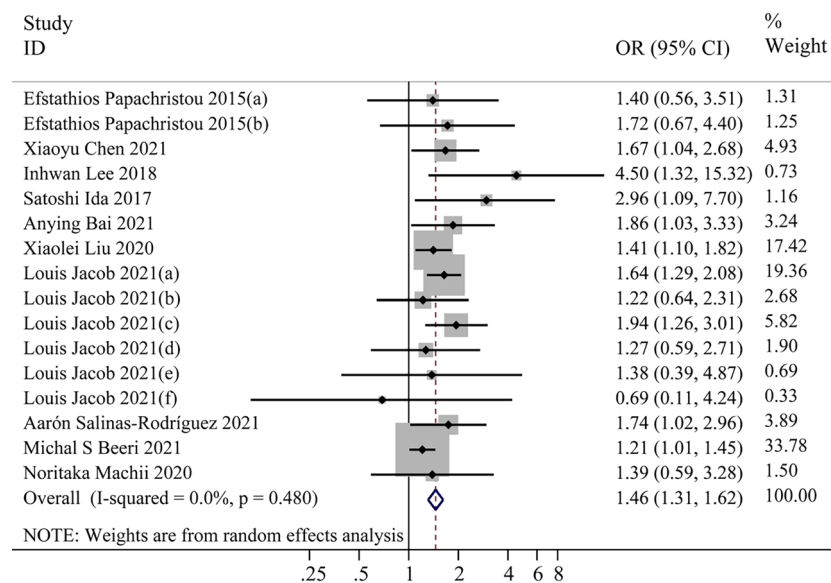
Figure 4 Forest plot of the adjusted odds ratios (ORs) between sarcopenia and mild cognitive impairment. CI, confidence interval.

Table 4 Univariate meta-regression of MCI prevalence and correlation between MCI and sarcopenia in subgroups

Variable	β (95% CI)	SE	P
Prevalence of MCI			
Study design: cross-sectional study vs. cohort study	0.117 (−0.297 to 0.532)	0.186	0.542
Study population: community-dwelling participants vs. non-community-dwelling participants	−0.080 (−0.345 to 0.184)	0.119	0.515
Sarcopenia assessment: AWGS vs. other	−0.038 (−0.303 to 0.226)	0.119	0.754
MCI assessment: MoCA vs. other	0.088 (−0.328 to 0.504)	0.187	0.648
Mean age (continuous)	0.004 (−0.013 to 0.022)	0.008	0.590
Natural log of odds ratio for MCI			
Study design: cross-sectional study vs. cohort study	0.236 (0.012–0.472)	0.110	0.049
Study population: community-dwelling participants vs. non-community-dwelling participants	−0.163 (−0.589 to 0.262)	0.198	0.423
Sarcopenia assessment: AWGS vs. other	0.073 (−0.254 to 0.399)	0.152	0.640
MCI assessment: MMSE vs. other	−0.241 (−0.482 to 0.001)	0.113	0.051
Gender: male vs. other	0.025 (−0.728 to 0.778)	0.351	0.945

Abbreviations: AWGS, Asian Working Group for Sarcopenia; CI, confidence interval; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; SE, standard error.

and sarcopenia. First, sarcopenia shares common risk factors with cognitive impairment, such as cerebrovascular diseases, diabetes and hypertension.[30,34,35] Additionally, the chronic state of inflammation caused by immunosenescence and the increased secretion of cytokines may have detrimental consequences. High levels of interleukin (IL)-6, IL-1, tumour necrosis factor-α and C-reactive protein have been studied as potential pathophysiological mechanisms underlying sarcopenia. Dysregulation of the inflammatory pathway may simultaneously be involved in the pathophysiological mechanisms of MCI.[36,37] Last, epidemiological studies demonstrate that the Mediterranean diet with high-quality protein intake may reduce the risk of MCI. The equilibrium between muscle protein synthesis and muscle protein levels may be a major contributor to the aetiology of muscle atrophy in patients with sarcopenia.[38–40] Therefore, insufficient nutritional supplementation may also be one of the reasons for the co-occurrence of MCI and sarcopenia.

Our results also demonstrated that the prevalence of MWS (20.5%) is higher than that of the prevalence of SWM (9.1%). This may be related to the following reasons. Sarcopenia is primarily due to low muscle strength.[41] Inactivity and inadequate rehabilitation programmes for sarcopenia may further reduce the amount of physical activity. Past studies have shown that physical activity promotes cognitive improvement and stability; however, resistance training programmes are still seriously underutilized.[42,43] It has also been suggested that brain atrophy and loss of muscle mass may co-occur in patients with sarcopenia.[35,44] These pathophysiological mechanisms are thought to predispose patients with sarcopenia to cognitive decline. On the other hand, patients with MCI have little limitation in physical activity.[45,46] Cognitive decline may lead to loss of appetite and decreased food intake. However, protein-energy malnutrition is often more pronounced after the onset of dementia and is less pronounced in patients with MCI.[43,47] Thus, patients with MCI are less likely to develop sarcopenia due to low activity and malnutrition.

Our meta-analysis subgroup analyses revealed significant heterogeneity in MCI measurement methods, diagnostic criteria for sarcopenia, study demographics and study design. The prevalence of MWS and SWM defined by the SARC-F-J criteria was found to be the highest, whereas the AWGS approach and EWGSOP guidelines reflected the lowest associated prevalence. Additionally, the correlation between MCI and sarcopenia was calculated to be higher using the SARC-F-J criteria. As such, the use of different diagnostic tools may lead to different prevalence estimates of MWS and SWM or the correlation between MCI and sarcopenia. Previous studies have clearly demonstrated that the sensitivity of the SARC-F-J for the assessment of sarcopenia is low,[12] and other studies that used SMM also mentioned that these methods lacked objective measurement data and direct assessments[11]; thus, caution is advised with using non-objective muscle strength and mass to assess sarcopenia. The EWGSOP approach to diagnosing sarcopenia reported a lower prevalence than the FNIH and AWGS-defined guidelines, indicating that this method considering low muscle mass combined with low muscle strength objectively was stricter than that of a single metric, which is similar to what was previously reported with Yang et al.'s study.[48] Because dual-emission X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) has a higher sensitivity for the diagnosis of sarcopenia,[49,50] there is potential that in the future, there will be more studies using more objective methods to assess sarcopenia to further discuss the relationship of sarcopenia and MCI.

Notably, heterogeneous MCI assessment tools also affected our results. All of these approaches (except for the TYM test and the MMSE) were able to detect that sarcopenia may be a risk factor for MCI. However, the results of using the TYM, SPMSQ and MMSE methods to assess cognition appear to be unreliable. This may be related to the limitations of these scales themselves. The TYM test, a simple 10-task self-assessment cognitive screening instrument, has been reported to reduce the specificity of MCI and thus is usually not

a recognized diagnostic method for MCI.[23] Similarly, the SPMSQ involves using a 10-item short portable mental state questionnaire, whose instrument might introduce potential problems with subjective bias associated with questionnaire surveys.[13] A meta-analysis of diagnostic accuracy studies clearly indicate the MoCA to be superior to MMSE in discriminating between individuals with MCI and no cognitive impairment or MCI and healthy elderly individuals.[51] Therefore, TYM, SPMSQ and MMSE may lack comparative advantages in the assessment of MCI. In our study, whether SWM, MWS or their correlations, the results of the MoCA assessment remained at a neutral level, indicating the stability of the scale. This is consistent with other research findings,[52] and as such, we recommend the use of the MoCA scale for future MCI studies.

Last but not least, there was no significant heterogeneity between the main studies despite how the included studies had various differences in countries, settings, diagnostic methods, measurement approaches, diagnostic thresholds and unreported comorbidities in our causal analysis of sarcopenia and MCI. Our study had several limitations. First, our search strategy was limited to English-only studies, which could have excluded high-quality, non-English studies. Next, the number of studies was low, and most of our included studies consisted of cross-sectional designs. We further discovered that in the study-type subgroup analysis, the prevalence of SWM in cohort studies (13%) was higher than that in cross-sectional studies (7.8%); thus, this likely skewed the results. Seven of the cross-sectional studies we included also did not meet high-quality criteria; however, this was not found to be significant in our sensitivity analyses. Nevertheless, more high-quality longitudinal studies in the future that explore the association between sarcopenia and MCI and its underlying mechanisms would be beneficial. Finally, no classification of cut-off values for MCI and sarcopenia has been well established yet; in other words, no attention was paid to the impact of their severity on the results. Future studies that are able to explore and stratify different degrees of sarcopenia would be helpful for the improvement of outcome assessments.

Conclusion and future direction

In conclusion, our meta-analysis reveals that the prevalence of MWS and SWM is high. Furthermore, there is a significant association between sarcopenia and MCI. Based on our subgroup analyses, we found that the heterogeneity of the evaluation criteria of MCI or sarcopenia, populations and study designs was high. Our results suggest that clinicians should have a low threshold to screen for MCI in patients with sarcopenia and researchers should continue to work on recognizing the mutual influence of MCI and sarcopenia in the future of elderly care and management work. These measures may facilitate the earlier identification of sarcopenia and MCI, thereby delaying disease progression, improving the quality of life of the elderly and reducing social and economic burdens. Prospective cohort studies of large sample size should be conducted to further unify measurement tools for MCI and sarcopenia and to establish a global consensus for the diagnostic criteria. Additionally, some well-designed basic science studies are also warranted to explore the underlying pathophysiological mechanisms of MCI and sarcopenia.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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