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Original Research

# Sarcopenia Screened with SARC-F and Subjective Memory Complaints Are Independently Associated with Increased Risk of Incident Dementia among Cognitively Unimpaired Older Adults

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## Abstract

OBJECTIVES: The main aim of this study was to examine the association of sarcopenia and subjective memory complaints with the incidence of dementia in a population-based cohort of cognitively unimpaired older adults.

DESIGN: Three-year longitudinal study.

SETTINGS AND PARTICIPANTS: A total of 2163 community-dwelling persons aged 65 years or older who participated in the National Health Interview Survey in Taiwan, 2017.

MEASUREMENTS: Sarcopenia was determined based on SARC-F, a self-reported symptom-based questionnaire that includes five components: strength, assistance walking, rise from a chair, climb stairs, and falls. Two questions ("Do you have difficulties with your memory or attention?" and "Do you have difficulties with your memory only or attention only or both?") were used to screen for subjective memory complaints (SMCs). The incidence of dementia was determined by data linkage to the Taiwan National Health Insurance claims database from 2018 to 2020.

RESULTS: Among the 2163 participants without dementia at baseline, 135 had incident dementia during the 3-year follow-up, giving a crude incidence rate of 6.2% (135/2163). Compared to participants free from sarcopenia and SMCs, the adjusted hazard ratio for incident dementia was 1.83 (95% confidence interval [CI]: 1.23–2.72) for SMCs alone, 2.40 (95% CI: 1.17–4.93) for sarcopenia alone, and 2.49 (95% CI: 1.21–5.11) for coexisting SMCs and sarcopenia.

CONCLUSIONS: Our results indicate that sarcopenia screened with SARC-F and SMCs independently predict the cognitively unimpaired older adults at risk of incident dementia. Our findings highlight the importance of screening not only for cognitive but also muscle deficits to identify those at increased risk of incident dementia.

*Key words: Sarcopenia, subjective memory complaints, dementia, Taiwan.*

## Introduction

Sarcopenia is common in older populations, and is characterized by the loss of muscle mass and strength as well as muscle function (1-4). Sarcopenia in older adults is associated with adverse outcomes including poor quality of life, hospitalization, impaired physical function, and mortality (5-7). A systematic review and meta-analysis showed that the prevalence of mild cognitive impairment (MCI) is high in patients with sarcopenia, suggesting sarcopenia as a risk factor (8). However, few studies have examined the relationship between sarcopenia and incident dementia among community-dwelling cognitively unimpaired older adults.

Subjective memory complaints (SMCs) refer to self-perceived memory deficits in everyday life. Older adults with SMCs have increased rates of white matter lesions and temporal lobe atrophy, which are associated with dementia (9, 10). Moreover, SMCs may be an early indicator of cognitive decline in the preclinical stage of Alzheimer's disease (11-13). Recently, Lin et al. (14) conducted an investigation of older outpatients with SMCs and found that slower performance in the gait speed test was associated with worse performance in memory, attention, language, and executive function. Al-Sari et al. (15) performed a 2-year prospective study based on a cohort of older women recruited from primary care and found that participants with SMCs at baseline had an increased risk of falls. Slower gait speed and falls are common health consequences of sarcopenia (16, 17). These observations prompted us to consider whether there is a vulnerable subgroup of older adults with SMCs with comorbid sarcopenia, and whether sarcopenia is prevalent among community-dwelling older people with SMCs.

Using the SARC-F questionnaire, Wu et al. (5) found that the prevalence of sarcopenia was 6.1% among community-dwelling Taiwanese adults aged ≥ 56 years. Similar findings were also reported by Wu et al. (18), who analyzed data from five cohort studies of community-dwelling older Taiwanese adults. Using European Working Group on Sarcopenia in Older People (EWGSOP) criteria, the authors found that the prevalence of sarcopenia in older adults ranged from 3.9% to 7.3%. However, the epidemiology of sarcopenia among older people with SMCs has not been adequately characterized. It has been reported that the prevalence of SMCs in community-dwelling cognitively unimpaired Taiwanese adults aged ≥ 65 years is 33.7% (19), consistent with reports from other populations (20). Li et al. (21) analyzed data from a 5-year prospective study of a national sample of Taiwanese adults aged ≥ 65 years and found that the incidence rate of dementia was 22.4 per 1000 person-years. Little is known about the interrelationship among sarcopenia, SMCs, and incident dementia in cognitively unimpaired

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older adults. Understanding this interrelationship in baseline cognitively unimpaired older adults could aid the development and implementation of strategies for reducing incident dementia in this population.

Most research on sarcopenia or SMCs has been conducted on convenience samples of community-dwelling populations or hospital-based outpatients. However, there have been no nationwide studies on the relationship between sarcopenia and SMCs and incident dementia in older people. In view of these considerations, we analyzed data from a 3-year prospective study of a national sample of community-dwelling cognitively unimpaired older adults in Taiwan. The aims of the present study were two-fold. First, we described the prevalence of sarcopenia assessed by SARC-F among older people with and without SMCs. Second, we determined whether sarcopenia screened with SARC-F and SMCs are independently associated with increased risk of incident dementia among community-dwelling cognitively unimpaired older adults. We hypothesized that sarcopenia screened with SARC-F and SMCs would be independently associated with an increased risk of incident dementia.

## Methods

### *Study population*

This was a prospective study involving participants of the National Health Interview Survey (NHIS) in Taiwan, 2017. The NHIS was designed to be carried out every 4 years since 2001 in Taiwan. The sample design of the 2017 NHIS is similar to that of the 2013 NHIS, which has been detailed previously (22) and is on the NHIS website (http://nhis.nhri.org.tw/). In summary, the survey sample was drawn from the National Registry Database via multistage stratified sampling. All study participants provided written informed consent.

There were a total of 3178 individuals aged 65 years and older; 187 were excluded due to pre-existing dementia or Parkinson's disease diagnosis, 31 participants died in 2017, and 445 were excluded due to missing data on the Mini-Mental State Examination (MMSE) and for assessments of sarcopenia and SMCs. Of the remaining 2515 participants, we further excluded 352 participants who were diagnosed as cognitively impaired (MMSE score < 18 for participants who were illiterate and had no schooling, <21 for those with 1–6 years of education, and <25 for those with ≥7 years of education) (23, 24). This resulted in 2163 eligible participants for the analyses.

The study cohort was followed until the date of dementia diagnosis, death, or the end of the study period (31 December 2020). The incidence of dementia was determined by data linkage to the Taiwan National Health Insurance (NHI) claims database from 2018 to 2020. Deaths were confirmed by the computerized data files of the National Register of Deaths. Dataset linkage and statistical analyses were performed at the Data Science Center of the Ministry of Health and Welfare. This study was approved by the relevant institutional review board.

### *Measures*

#### *Assessment of incident dementia*

In this study, the outcome was incident dementia, which was defined according to the International Classification of Disease, Tenth Edition, Clinical Modification codes F00, F01, F02, F03, and G30 in the NHI claims database. Participants were considered to have incident dementia if the diagnosis occurred at least three times in outpatient visits or at least once in an inpatient setting. The date of the first dementia claim was defined as the date of dementia diagnosis. This definition was adopted from previous studies on dementia using the NHI claims database in Taiwan (21).

#### *Assessment of sarcopenia, SMCs, and baseline characteristics*

Sarcopenia was determined based on SARC-F, a self-reported symptom-based questionnaire that includes five components: strength, assistance walking, rise from a chair, climb stairs, and falls. Strength was assessed by asking individuals how much difficulty they had lifting or carrying 4.5 kg. Assistance walking was assessed by asking individuals how much difficulty they had walking between rooms. Rise from a chair was assessed by asking individuals how much difficulty they had transferring from a bed. The ability to climb stairs was assessed by asking individuals how much difficulty they had climbing a flight of 10 steps. Responses of "no difficulty," "some difficulty," or "a lot of difficulty or unable to do," were given a score of 0, 1, and 2, respectively. Falls were scored 0 for individuals who reported no falls in the past year, 1 for individuals who reported falling 1–3 times in the past year, and 2 for individuals who reported falling four or more times in the past year. SARC-F scores range from 0 to 10. Participants with scores ranging from 4 to 10 are defined as having sarcopenia (5, 25, 26).

In this study, SMCs were assessed in the self-report questionnaire by two questions. The first question was "Do you have difficulties with your memory or attention?" The response categories were "no difficulty," "some difficulty," "much difficulty," or "completely unable." Participants responding with "some difficulty," "much difficulty," or "completely unable," were asked a second question, "Do you have difficulties with your memory only or attention only or both?" The response categories were "memory alone," "attention alone," or "both memory and attention." SMCs were defined as reporting some difficulty, much difficulty, or being completely unable to use their memory alone or both their memory and attention. The same approach to screen for SMCs in this study was shown to be predictive of incident dementia in our previous study of older adults (21).

Demographic and health information such as age, sex, years of education, marital status (married or living with partner; yes/no), smoking status (current or former smoker; yes/no), and the presence of other chronic conditions such as hypertension, diabetes, stroke, and heart disease were

**Table 1.** Baseline characteristics of the study participants by dementia incidence

| | Overall (N = 2163) | Incident Dementia | | P-value[a] |
|---|---|---|---|---|
| | | No (N = 2028) | Yes (N = 135) | |
| | N (%) | | | |
| Age (%) | | | | <0.0001 |
| 65–74 years | 1456 (67.3) | 1403 (69.2) | 53 (39.3) | |
| 75+ years | 707 (32.7) | 625 (30.8) | 82 (60.7) | |
| Sex (% female) | 1095 (50.6) | 1022 (50.4) | 73 (54.1) | 0.4077 |
| Education (%) | | | | 0.0306 |
| 0 years | 360 (16.6) | 333 (16.4) | 27 (20.0) | |
| 1–6 years | 1031 (47.7) | 957 (47.2) | 74 (54.8) | |
| 7+ years | 772 (35.7) | 738 (36.4) | 34 (25.2) | |
| Marital status (% married or living with partner) | 1461 (67.6) | 1380 (68.1) | 81 (60.0) | 0.0521 |
| Current or former smoker (% yes) | 509 (23.8) | 477 (23.8) | 32 (24.4) | 0.8634 |
| Depressive symptoms (% yes) | 194 (9.0) | 170 (8.4) | 24 (17.8) | 0.0002 |
| Hypertension (% yes) | 1057 (49.3) | 989 (49.2) | 68 (50.8) | 0.7295 |
| Diabetes (% yes) | 482 (22.4) | 445 (22.0) | 37 (27.4) | 0.1448 |
| Stroke (% yes) | 92 (4.3) | 85 (4.2) | 7 (5.3) | 0.5591 |
| Heart (% yes) | 354 (16.4) | 330 (16.3) | 24 (17.8) | 0.6580 |
| Sarcopenia (% SARC-F score ≥ 4) | 152 (7.0) | 129 (6.4) | 23 (17.0) | <0.0001 |
| SMCs (% yes) | 667 (30.8) | 606 (29.9) | 61 (45.2) | 0.0002 |

a. Categorical variables were compared using Pearson's chi-square test. SMCs: Subjective memory complaints.

obtained from the questionnaires. For each disease, participants were asked whether the diagnosis had been confirmed by a medical professional. Depressive symptoms were assessed by the 10-item version of the Center for Epidemiologic Studies Depression Scale (27, 28). Participants with scores ranging from 10 to 30 were defined as having depressive symptoms.

### *Statistical analyses*

We used the Pearson's chi-square test to examine factors associated with incident dementia. Subdistribution hazard models were used according to the methods of Fine and Gray to examine the association among sarcopenia, SMCs, and incident dementia while taking into account death as a competing risk (29, 30). To assess the independent associations between the presence of SMCs and sarcopenia and incident dementia, we fit SMCs and sarcopenia separately (Model 1 and Model 2) and simultaneously (Model 3 and Model 4) in the subdistribution hazard model. All models were adjusted for age, sex, education, marital status, smoking status (current or former smoker), depressive symptoms, hypertension, diabetes, stroke, and heart disease. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for incident dementia were estimated. All analyses were conducted using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

## Results

Figure 1 presents the flowchart of the study participants. Of the 2163 participants aged ≥ 65 years, 135 participants had incident dementia during the 3-year follow-up, giving a crude incidence rate of 6.2% (135/2163). The baseline characteristics of the older adults with and without incident dementia are presented in Table 1. Participants with incident dementia were more likely to be older, with lower education years, depressive symptoms, sarcopenia, and SMCs.

**Figure 1.** Flowchart of study participants

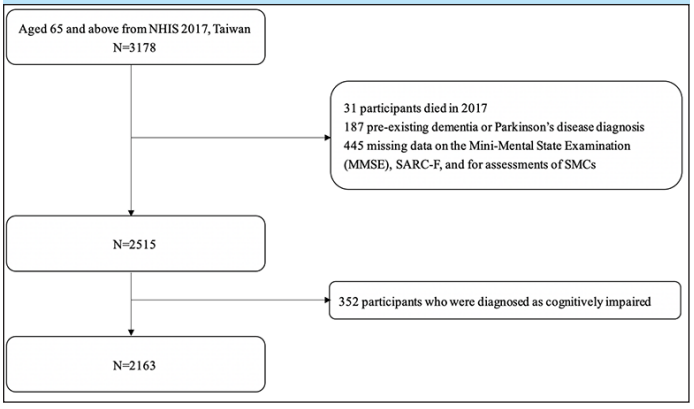


Table 2 presents the distribution of sarcopenia assessed by SARC-F and its components of older adults by SMCs. The distributions of baseline sarcopenia and its components were significantly different between participants with and without SMCs. The prevalence of sarcopenia assessed by SARC-F was 12.0% and 4.8% in those with and without SMCs, respectively. Participants with SMCs were more likely to have muscle weakness; difficulty walking, rising from a chair, and climbing stairs; and to report falls.

**Table 2.** Distributions of sarcopenia and its components of study participants by subjective memory complaints

| | Overall (N = 2163) | SMCs | | P-value[a] |
|---|---|---|---|---|
| | | No (N = 1496) | Yes (N = 667) | |
| | N (%) | | | |
| Sarcopenia (SARC-F score ≥ 4) | 152 (7.0) | 72 (4.8) | 80 (12.0) | <0.0001 |
| Strength | | | | <0.0001 |
| No difficulty | 1714 (79.2) | 1277 (85.4) | 437 (65.5) | |
| Some difficulty | 249 (11.5) | 129 (8.6) | 120 (18.0) | |
| Much difficulty or unable to carry out | 200 (9.3) | 90 (6.0) | 110 (16.5) | |
| Assistance walking | | | | <0.0001 |
| No difficulty | 2018 (93.3) | 1421 (95.0) | 597 (89.5) | |
| Some difficulty | 93 (4.3) | 45 (3.0) | 48 (7.2) | |
| Much difficulty or unable to carry out | 52 (2.4) | 30 (2.0) | 22 (3.3) | |
| Rise from a chair | | | | <0.0001 |
| No difficulty | 2099 (97.0) | 1470 (98.3) | 629 (94.3) | |
| Some difficulty | 46 (2.1) | 16 (1.1) | 30 (4.5) | |
| Much difficulty or unable to carry out | 18 (0.8) | 10 (0.7) | 8 (1.2) | |
| Climb stairs | | | | <0.0001 |
| No difficulty | 1730 (80.0) | 1293 (86.4) | 437 (65.5) | |
| Some difficulty | 270 (12.5) | 125 (8.4) | 145 (21.7) | |
| Much difficulty or unable to carry out | 163 (7.5) | 78 (5.2) | 85 (12.7) | |
| Falls | | | | 0.0078 |
| No falls | 2022 (93.5) | 1415 (94.6) | 607 (91.0) | |
| 1–3 times | 134 (6.2) | 77 (5.2) | 57 (8.6) | |
| 4 or more times | 7 (0.3) | 4 (0.3) | 3 (0.5) | |

a. Categorical variables were compared using Pearson's chi-square test. SMCs: Subjective memory complaints.

Table 3 presents the adjusted HR and 95% CIs for incident dementia. In subdistribution models, after adjustment for age, sex, education, marital status, smoking status (current or former smoker), depressive symptoms, hypertension, diabetes, stroke, and heart disease, compared to those participants free from sarcopenia and SMCs, the adjusted HR for incident dementia was 1.83 (95% CI: 1.23–2.72) for SMCs alone, 2.40 (95% CI: 1.17–4.93) for sarcopenia alone, and 2.49 (95% CI: 1.21–5.11) for coexisting SMCs and sarcopenia.

## Discussion

Our study found a high prevalence of sarcopenia screened with SARC-F in participants with SMCs among community-dwelling cognitively unimpaired older people. Moreover, our results confirmed our hypothesis that sarcopenia screened with SARC-F and SMCs are independently associated with increased risk of incident dementia. These findings highlight that cognitive assessment for dementia screening alone may not be enough. The prevention or early detection of sarcopenia should also be emphasized for cognitively unimpaired older adults.

Our study differs from prior research on the association between sarcopenia and incident dementia by taking into account the effects of SMCs. Our results confirm that sarcopenia assessed by SARC-F is more prevalent in participants with SMCs (12.0%) compared to their peers without SMCs (4.8%). Moreover, participants with SMCs were more likely to have poor muscle performance in all components of the SARC-F scale than participants without SMCs. It is notable that among participants with SMCs, as many as 34.5%, 10.5%, and 34.5% experienced difficulties lifting or carrying 4.5 kg, walking between rooms, and climbing a flight of 10 steps, respectively. These findings suggest that poor muscle performance and cognitive defects could be related to each other in the preclinical stage of cognitive impairment. After adjustment for other factors, our data indicated that either sarcopenia alone (HR: 2.40; 95% CI: 1.17–4.93) or SMCs alone (HR: 1.83; 95% CI: 1.23–2.72) was associated with an increased risk of developing dementia. These findings suggest that although sarcopenia and SMCs may be related to each other, they maintain an independent pathogenic role during the development of dementia. Therefore, screening programs for dementia should target both muscle and cognitive defects. Further investigations are needed to examine the prospective association between sarcopenia and SMCs in older adults to provide greater insights into the interdependent pathways among muscle health, cognitive function, and incident dementia.

In this study, we used SARC-F to identify older adults

**Table 3.** Adjusted hazard ratios and 95% confidence intervals for 3-year incidence of dementia in the study cohort by absence or presence of subjective memory complaints and sarcopenia status at baseline

| | Model 1 | Model 2 | Model 3 | Model 4 |
|---|---|---|---|---|
| | Adjusted HR* (95% CI) | Adjusted HR* (95% CI) | Adjusted HR* (95% CI) | Adjusted HR* (95% CI) |
| SMCs | | - | | - |
| No | Ref | | Ref | |
| Yes | 1.72 [1.20,2.48] | | 1.67 [1.15,2.42] | |
| Sarcopenia | - | | | - |
| No | | Ref | Ref | |
| Yes | | 1.86 [1.09,3.19] | 1.74 [1.00,3.01] | |
| SMCs/Sarcopenia | - | - | - | |
| No/No | | | | Ref |
| Yes/No | | | | 1.83 [1.23,2.72] |
| No/Yes | | | | 2.40 [1.17,4.93] |
| Yes/Yes | - | - | - | 2.49 [1.21,5.11] |

*Adjusted for age, sex, education, marital status, current or former smoker, depressive symptoms, hypertension, diabetes, stroke, and heart disease. HR: Hazard ratio; CI: Confidence interval; SMCs: Subjective memory complaints.

suffering from sarcopenia. Previous studies have indicated that the components of SARC-F are expected to be associated with poor muscle function (6). Our finding that sarcopenia is associated with incident dementia is in accordance with the results reported by Beeri et al. (31), although different measures of sarcopenia were used. The authors performed an average 5.6-year longitudinal study of 1175 community-dwelling older adults without dementia, using criteria based on assessments of both muscle mass and function. The authors found that poor muscle function based on grip strength was related to incident Alzheimer's dementia, incident MCI, and the rate of cognitive decline.

Our findings that SMCs are independently associated with an increased incidence of dementia are in line with previous findings (32, 33). A meta-analysis of 28 prospective longitudinal studies with a follow-up of at least 6 months reported a two-fold higher risk of incident dementia in participants with than without SMCs (33). Our findings extend prior research by demonstrating that the adjusted HRs for dementia incidence were similar when considering participants with sarcopenia in combination with SMCs (HR: 2.49; 95% CI: 1.21–5.11) or when considering participants with sarcopenia alone (HR: 2.40; 95% CI: 1.17–4.93). These results suggest that sarcopenia assessed by SARC-F is the primary driver of the association between sarcopenia in combination with SMCs and incident dementia. One possible explanation is that SARC-F is a broad measure of health and function that could identify persons suffering from sarcopenia and adverse outcomes in persons with sarcopenia (6). Kim et al. (34) investigated the effects of sarcopenia on cortical thickness, white matter hyperintensity, and subcortical volumes in cognitively normal older adults. The authors found cortical thickness reduction and white matter hyperintensity changes in patients with sarcopenia compared with the control group. Moreover, they found a significant correlation between cortical thickness and white matter hyperintensity and muscle function and strength in sarcopenia. These observations provide possible neurobiological mechanisms underlying our finding of the association between sarcopenia and incident dementia in cognitively unimpaired older adults.

This study had some limitations. Our observational study design limits causal interpretations of the findings. Although the initial sample of 3178 is a nationally representative sample of adults aged ≥ 65 years, our analytic sample could be biased as the included participants were limited to those who had complete data for the assessments of sarcopenia and cognition. Comparison of characteristics between respondents who were included (N = 2163) and excluded (N = 445) suggests that our sample could be biased toward individuals who are younger, males, have a higher education level, and are married or living with a partner (Supplementary Table 1). Thus, the observed dementia incidence rate may be an underestimate. Additionally, the association of sarcopenia and SMC with dementia incidence may be underestimated. The sarcopenia condition assessed by the SARC-F was based on self-reporting, and therefore recall bias was unavoidable.

The present study also had several strengths, including that we investigated the prevalence of sarcopenia assessed by SARC-F or SMCs in a population-based national sample of older adults. We found that 7.0% and 30.8% of Taiwanese cognitively unimpaired adults aged ≥ 65 years were suffering from sarcopenia or SMCs, respectively. It is notable that among our participants, as many as 34.2% had either sarcopenia or SMCs, or had comorbid sarcopenia and SMCs. These findings indicate that a substantial proportion of older adults have impaired muscle or cognitive function and thus may be at increased risk of dementia. Moreover, our results indicate that using simple questions to screen for sarcopenia and SMCs could identify people at higher risk of incident dementia in a relatively inexpensive manner in the preclinical stage of cognitive impairment. Previous studies have indicated that the early identification of sarcopenia by SARC-F and resistance

training and nutritional intervention may result in improved muscle function (35, 36). We suggest that healthcare providers inquire about muscle performance and memory problems in their older patients at regular clinic visits to identify individuals who would most benefit from interventions aimed at preventing dementia.

## Conclusions

In summary, our results contribute to the literature by providing new data on the association of sarcopenia and SMCs with incident dementia in a population-based sample of community-dwelling cognitively unimpaired older adults in Taiwan. Our findings highlight the importance of screening not only for cognitive but also muscle deficits to identify those at increased risk of incident dementia. We believe that our findings will promote further efforts to design and implement interventions aimed at preventing incident dementia in individuals with poor cognitive or muscle performance.

*Ethical consideration:* This research complied with the ethical rules for human experimentation stated in the Declaration of Helsinki.

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*Conflict of interest:* The authors have no conflicts of interest to declare.

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