International Psychogeriatrics (2023), 35:12, 686–688 © International Psychogeriatric Association, 2023
doi:10.1017/S1041610223000108

COMMENTARY

Identifying sarcopenia in older adults and its impact on late-life depression

Commentary on "Association Between Lean Muscle Mass and Treatment-Resistant Late-life Depression in the IRL-GRey Randomized Controlled Trial" by Ainsworth *et al.*

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Depression is a common illness, affecting an estimated 5.7% of people older than 60 years of age (World Health Organization, 2017), with a high level of associated morbidity, mortality, and health care utilization (American Psychiatric Association 2013). Sarcopenia, a known risk factor for depression, falls, and increased disability (Fielding *et al.*, 2011), is also highly prevalent in 20% of people aged 65 years, increasing to 50–60% in people aged 80 years and over. Primary sarcopenia is characterized by age-related loss of muscle mass and function, while secondary sarcopenia is attributable to another health condition (Pilati *et al.*, 2022). The etiology of age-related sarcopenia is complex with multiple contributing factors, including genetics, nutrition, physical activity, hormones, and inflammation (Fielding *et al.*, 2011). Our editorial provides a broader context to Ainsworth's article in the current issue of IPG, hypothesizing that low appendicular skeletal muscle mass is associated with older age, greater physical comorbidity, greater severity of depression, and poor treatment response (Ainsworth *et al.*, 2022).

Early clinical definition and diagnostic criteria for sarcopenia developed by the European Working Group in 2009 (Cruz-Jentoft *et al.*, 2010) were based on literature reviews and expert consensus, but later refined by inclusion of appendicular lean muscle mass, muscle strength, and physical functioning by the European Working Group on Sarcopenia in Older People (EWGSOP), the Asian Working Group for Sarcopenia (AWGS), and the International Working Group on Sarcopenia (IWGS) (Fielding *et al.*, 2011).

The EWGSOP defines sarcopenia as the presence of low muscle mass plus either low muscle strength or low physical performance. They caution that low muscle mass alone should not be used to diagnose sarcopenia, since the relationship between muscle mass and strength is not linear. The EWGSOP outlines a range of techniques which may be used for determining muscle mass. Of these, CT and MRI, often used in research settings, are considered the gold standard. Unfortunately, they have limited clinical utility due to higher cost, limited access, and risk of radiation exposure. Similarly, dual-energy X-ray absorptiometry (DEXA) has limited utility due to its lack of portability (Chien *et al.*, 2008), despite its clinical appeal due to minimal radiation exposure. Bioimpedance analysis (BIA) may be used as a more portable alternative to determine muscle mass in clinical settings (Roubenoff *et al.*, 1997). Anthropometry is not recommended, due to its higher likelihood of errors and lack of validation in older and obese populations (Cruz-Jentoft *et al.*, 2010). The EWGSOP recommends handgrip strength, measured using a handheld dynamometer, as the preferred method for measuring muscle strength in clinical settings (Cruz-Jentoft *et al.*, 2010). Handgrip strength is strongly correlated with lower limb strength, and low handgrip strength has a stronger correlation with poor clinical outcomes versus low muscle mass alone (Laurentani *et al.*, 2003). For determining physical performance, the EWGSOP recommended the Short Physical Performance Battery (SPPB) or gait speed (Cruz-Jentoft *et al.*, 2010).

The EWGSOP defines the cutoff for sarcopenia as two standard deviations below healthy young adult reference values, which differed depending on the specific measurement technique

(Cruz-Jentoft *et al.*, 2010). The sarcopenia cutoff for muscle mass is a skeletal muscle mass index (SMI) of <7.26 kg/m^2 for men and <5.5 kg/m^2 for women, when measured using DXA. The muscle mass cutoffs are instead <8.87 kg/m^2 for men and <6.42 kg/m^2 for women, when measured using BIA. The cutoff for handgrip strength is <30 kg for men and <20 kg for women. The cutoffs for physical performance are a score of ≤ 8 on the SPPB, or a gait speed of <1 m/s on a 6-m course (Cruz-Jentoft *et al.*, 2010). Combining the above recommendations, the EWGSOP suggests using gait speed and grip strength as the initial screening tools for sarcopenia in older adults, followed by muscle mass measurement if the screen was positive. The choice to start the screening process with gait speed was based on its ease of use and reliability (Abellan van Kan *et al.*, 2009).

The AWGS notes that Asian populations are likely to have different cutoffs for sarcopenia compared to European populations, due to differences in genetics, diet, and adiposity. They also found that existing European cutoffs were insufficiently sensitive for detecting low muscle mass in older Asian women. The AWGS recommended SMI cutoffs of <7.0 kg/m^2 for men and <5.4 kg/m^2 for women using DXA and <7.0 kg/m^2 for men and <5.7 kg/m^2 for women using BIA. The AWG also recommended using both gait speed and grip strength when screening for sarcopenia. Their recommended cutoffs for Asian populations were handgrip strength of <26 kg for men and <18 kg for women. For gait speed, the recommended cutoff was <0.8 m/s (Chen *et al.*, 2014).

The IWGS defines sarcopenia as appendicular skeletal muscle index (SMI) of <7.23 kg/m^2 in men and <5.67 kg/m^2 for women (less than the 20th percentile compared to healthy young adults), combined with a gait speed of <1 m/s. The IWGS also noted that the relationship between muscle mass and force production becomes less reliable with advanced age. Furthermore, muscle weakness is a stronger predictor of mortality in the elderly than low muscle mass alone (Fielding *et al.*, 2011).

Ainsworth *et al.* conducted a secondary analysis of the Incomplete Response in LLD: Getting to Remission (IRL-GRey) study. Patients over age 60 with at least a moderately severe acute episode of Major Depressive Disorder received open-label treatment with venlafaxine up to 300 mg daily for 24 weeks in phase one. Patients who did not remit after phase one were randomized to adjunctive aripiprazole up to 15 mg daily versus placebo for another 12 weeks, as phase two (Ainsworth *et al.*, 2022). DEXA scans were conducted for 178 participants at the start of phase two, with 175 participants repeating a DEXA scan at the end of phase two. Results from DEXA scans were used to determine body composition and lean muscle mass. The appendicular skeletal muscle indices (ASMI) were calculated by dividing average appendicular skeletal muscle mass (ASM) in kilograms (kg) by the square of height (h^2). Low ASMI was defined as <7 kg/m^2 for males and <5.5 kg/m^2 for females and was present in 12.4% of study participants (Ainsworth *et al.*, 2022).

By conducting multivariate linear regression analysis, Ainsworth *et al.* identified several factors that were independently associated with improvement of symptoms of Major Depressive Disorder in the IRL-GRey study. Current or previous marriage, higher baseline depression symptom severity, and treatment with aripiprazole were independently associated with improvement in depression in phase two ($p < 0.05$). However, there was no significant association found between low ASMI and improvement in depressive symptoms, for either the treatment or the control group. Ainsworth also found older age and female sex to be independently associated with low ASMI ($p < 0.05$), but not baseline depression symptom severity (Ainsworth *et al.*, 2022).

There are several possible explanations for the lack of significant association between low muscle mass and responsiveness to depression treatment in Ainsworth's study. As noted by the European, Asian, and International Working Groups on sarcopenia, muscle mass alone correlates poorly with muscle strength and functional outcomes. All three major diagnostic standards use a combination of muscle mass as well as muscle strength and functional status to diagnose the presence of sarcopenia (Chen *et al.*, 2014; Cruz-Jentoft *et al.*, 2010; Fielding *et al.*, 2011). Therefore, it is likely that low muscle mass on DEXA alone was not adequately identifying cases of sarcopenia in the IRL-GRey study. Furthermore, the specific pathophysiological link between sarcopenia and depression has not been established (Pilati *et al.*, 2022). Sarcopenia may be correlated with depression in older adults, but it may or may not impact prognosis or treatment response.

Much of the existing literature has been focused on the definition and diagnosis of sarcopenia, but research is lacking in the prevention and treatment of sarcopenia in older adults (Fielding *et al.*, 2011). The EWGSOP recommends further research be dedicated to determining the role of nutrition,

https://doi.org/10.1017/S1041610223000108 Published online by Cambridge University Press

exercise, and pharmacotherapy in the prevention and treatment of sarcopenia (Cruz-Jentoft *et al.*, 2010). The AWGS notes that aerobic exercise can significantly increase muscle mass and strength in older adults. However, there is no consensus on the optimal exercise regimen, and the impact of exercise on depression in sarcopenic older adults requires further study (Chen *et al.*, 2014). Potential pharmacotherapies exist for sarcopenia, such as androgen therapy or growth hormone therapy. Ultimately, the AWGS notes that no pharmacotherapies have sufficient evidence for the treatment of sarcopenia, and a combination of physical exercise and nutritional supplementation is more likely to be effective (Chen *et al.*, 2014).

The link between sarcopenia and depression in older adults requires further study, both to establish the link more definitively through longitudinal studies, and to better understand the potential underlying mechanisms (Fielding *et al.*, 2011). Furthermore, it remains to be seen whether sarcopenia impacts rates of response to antidepressants. Sarcopenia can be detected in clinical settings with modest investments in diagnostic equipment (Chien *et al.*, 2008). The path forward must investigate if assessment of sarcopenia can identify older adults at risk for developing depression, change treatment of geriatric depression, or alter antidepressant response.

Conflict of interest

None.

Description of authors' roles

The authors, Song Yang Yu and Kiran Rabheru, equally contributed to the manuscript, revised, read, and approved the submitted version.

References

Abellan van Kan, G. *et al.* (2009). Gait speed as a marker of adverse outcomes. *J Nutr Health Aging*, 13, 881–889.

Ainsworth, N. *et al.* (2022). Association between lean muscle mass and treatment-resistant late-life depression in the IRL-GRey randomized controlled trial. *Int Psychogeriatr* (in press).

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders*. 5th, https://doi.org/10.1176/appi.books.9780890425596.

Chen, L. K. *et al.* (2014). Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc*, 15, 95–101.

Chien, M. Y., Huang, T. Y. and Wu, Y. T. (2008). Prevalence of sarcopenia estimated using a bioelectrical impedance analysis prediction equation in community-dwelling elderly people in Taiwan. *J Am Geriatr Soc*, 56, 1710–1715.

Cruz-Jentoft, A. J. *et al.* (2010). Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing*, 39, 412–423.

Fielding, R. *et al.* (2011). Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, aetiology, and consequences. *J Am Med Dir Assoc*, 12, 249–256.

Laurentani, F. *et al.* (2003). Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol*, 95, 1851–1860.

Pilati, I., Slee, A. and Frost, R. (2022). Sarcopenic obesity and depression: a systematic review. *J Frailty Aging*, 11, 51–58.

Roubenoff, R. *et al.* (1997). Application of bioelectrical impedance analysis to elderly populations. *J Gerontol A Biol Sci Med Sci*, 52, M129–136.

World Health Organization. (2017). Mental health of older adults [Fact sheet], Available at: https://www.who.int/news-room/fact-sheets/detail/mental-health-ofolder-adults.

https://doi.org/10.1017/S1041610223000108 Published online by Cambridge University Press