ORIGINAL ARTICLE

Sarcopenia and polypharmacy: A cross-sectional study among community-dwelling older adults in Saudi Arabia

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Abstract. Background and Aim: Sarcopenia, characterized by the progressive loss of muscle mass, strength, and function, is prevalent among older adults, often exacerbated by polypharmacy, defined as the concurrent use of five or more medications. This study aimed to investigate the prevalence of sarcopenia and its association with polypharmacy in community-dwelling older adults in Saudi Arabia. Methods: A cross-sectional study was conducted with a required sample size of 245,0 based on a 65% prevalence rate of sarcopenia among older adults in Saudi Arabia. A total of 267 participants, attending outpatient clinics at Imam Abdulrahman bin Faisal University and King Fahad Hospital, were assessed for sarcopenia using a Jamar hydraulic handheld dynamometer to measure handgrip strength. Results: The prevalence of sarcopenia was found to be 31.8%, significantly higher among individuals taking five or more medications (47.9%) compared to those on fewer medications (22.3%) (p < 0.001). There was no significant association between sarcopenia and falls in the previous 12 months. Patients with sarcopenia had a higher median age (69 years) than those without (64 years). Additionally, the mean body mass index (BMI) was lower in the sarcopenic group (25.9 kg/m²) compared to non-sarcopenic individuals (27.6 kg/m²) (p = 0.04). A higher prevalence of sarcopenia was noted in females (46.4%) versus males (26.2%). Conclusion: This study highlights a strong association between polypharmacy and increased risk of sarcopenia among older adults in Saudi Arabia, emphasizing the need for careful medication management in this population. (www.actabiomedica.it)

Key words: prevalence, strength, medications, geriatrics

Introduction

Sarcopenia is the reduction of skeletal muscle mass and strength occurring in various physiological and pathological processes that include age progression, inactivity, chronic conditions, malignancy progression, and deficiency of nutrients. Sarcopenia not only affects motor activity, respiratory, and swallowing functions but also impacts the immune response resulting in compromised functions in multiple bodily

systems for those patients when faced with infections such as during trauma or surgeries (1). The latest findings from the Berlin Aging Study II have shown that the use of multiple medications, a common occurrence among older adults, is linked to the onset of sarcopenia in older individuals who live in the community (2). Accordingly, multiple studies have defined polypharmacy as the simultaneous utilization of five or more medications (3–6). In the older adult population, it has been demonstrated that polypharmacy, especially

when it includes corticosteroids, is linked to muscular weakness and low levels of lean mass (3). Also, a recent scoping review of the existing literature revealed a clear association between polypharmacy and sarcopenia in older individuals residing in the community (7). Muscle weakness is sarcopenia's most prevalent symptom. Other symptoms can include decreased muscle size, poor balance and falls, difficulty performing daily activities, and loss of stamina (8). In order to diagnose sarcopenia, it was found that there is a strong relationship between overall muscle function and handgrip strength which can be measured by using a Jamar hydraulic handheld dynamometer and expressed in kilograms (kg) (7). Handgrip strength is a simple, fast, and reliable measurement to assess the maximum voluntary force and hand injuries. It indicates overall muscular strength, muscle mass, walking performance, and nutritional status (9). The association between sarcopenia and polypharmacy has garnered increasing attention in recent years. For instance, a systematic review and meta-analysis revealed that older adults with polypharmacy had a significantly higher prevalence of sarcopenia (odds ratio: 1.65) compared to those without sarcopenia (12). This suggests that the presence of sarcopenia may contribute to the complexity of medication management in older adults. Polypharmacy itself can be a contributing factor to the development or exacerbation of sarcopenia. Certain medications can lead to muscle wasting or functional decline as side effects. For example, drugs such as corticosteroids and some antipsychotics have been implicated in inducing sarcopenia (13). Therefore, careful consideration must be given to the prescribed medications to older adults, particularly those diagnosed with or at risk for sarcopenia. The prevalence of sarcopenia among Saudi older adults was estimated to be 65% in 2019 (14). To the knowledge of the authors, no previous studies have investigated the association between sarcopenia and polypharmacy in the Gulf region, although numerous international studies have addressed this issue. Therefore, the current study aimed to investigate the prevalence of sarcopenia and its association with polypharmacy in older adult patients in the eastern province of Saudi Arabia, aiming to fill this critical research gap and enhance management strategies for older patients in the region.

Methods

Study design and population

This cross-sectional observational study was conducted from October 2023 to April 2024 at the outpatient settings of King Fahad Hospital of the University (KFHU) and Imam Abdulrahman bin Faisal University's Family and Community Medicine Center (FCMC). The study protocol was approved by the Institutional Review Board (IRB) of Imam Abdulrahman bin Faisal University, Dammam (IRB-2023-01-390). A consent form was signed by all patients prior to their participation. Data collection adhered to patient confidentiality following the Declaration of Helsinki. This study followed the guidelines of Strengthening the Reporting of Observational studies in Epidemiology (STROBE). Saudi and non-Saudi male and female patients in the outpatient department (OPD), their ages are 60 years and older were included in the study. Patients who were diagnosed with dementia, neuromuscular disorders, disabilities, or cancer were excluded. A convenience sampling technique was employed, facilitated by six trained research assistants. Patient lists from the outpatient department were utilized, and every fourth patient was approached for participation.

Sample size calculation

The minimum required sample size was calculated to be 245. This was based on a prevalence of 65% of sarcopenia among the Saudi older adults in 2019 (14), with a precision of 5% and at an alpha level of 0.1. Sample size calculation was performed in Epi info 7.0. (15).

Data collection procedure

The patients' lists were obtained from the outpatient department, asking them if they were willing to participate, and performing face-to-face interviews. All data collectors received unified instructions on gathering the data to ensure consistency and minimize variations in the results. The interview gathered information on age, gender, weight, height, the number and

names of medications taken, and specific comorbidities such as neuromuscular diseases, cancer and disabilities were excluded from this study to minimize confounding variables that could independently affect muscle mass and function, thereby ensuring a more homogeneous sample for assessing the prevalence of sarcopenia.

Sarcopenia assessment

Sarcopenia was assessed by measuring hand grip strength, considered the gold standard for evaluating muscle strength. Hand grip strength was measured using the Jamar hydraulic handheld dynamometer, a validated device that provides an objective assessment of physical capability. The measurement protocol was as follows:

- 1. Patients were seated upright in a comfortable chair, with hips and knees flexed at 90°, shoulder adducted, elbow flexed at 90°, forearm in a neutral position, and wrist in a neutral position.
- 2. Patients were instructed to exert maximum force by squeezing the dynamometer handle with their dominant hand for 3-5 seconds.
- 3. This procedure was repeated three times for each patient, with a 15-second rest between trials. The final value was calculated as the mean of the three trials.
- 4. The assessment was blinded, meaning patients were not shown their readings during the hand grip measurement. Uniform instructions were provided to all patients.

A cutoff value of low handgrip strength is (18 kg in women and 25.5 kg in men) which is considered an indicator of low muscle strength, and functions as a clinical marker of poor mobility as well as a better predictor of clinical outcome of low muscle mass (9–11).

Statistical analysis

For descriptive statistics, medians and interquartile ranges [IQR] were estimated for continuous variables given their non-normal distribution, while frequencies and proportions were used to characterize categorical variables. The outcome of interest, sarcopenia status, was presented as a categorical (Yes/No) variable. Two-sample Wilcoxon Test was used to test for significant differences in the medians of age and BMI by sarcopenia status. The Chi-Square Test was used to test for significant differences in the proportions of sarcopenia across the categorical variables of sex, medication count, and falls per past year. Multivariate logistic regression was used to test the association between patients' sarcopenia status as the independent variable and the different variables controlled for in the model. The regression model was adjusted for potential confounders determined a priori using theoretical knowledge and prior literature. Factors adjusted for in the model included age, BMI, sex, and falls per past year. A significant level was set at p = 0.05. Analyses were performed using Stata© software version 18 (StataCorp, College Station, TX).

Results

A total of 267 older patients were included in the research. Initially, 326 patients were enrolled. Duplicate entries were identified and removed to ensure that each participant was represented only once. Patients with incomplete data, specifically those lacking either weight or height measurements, were also excluded. The patients' baseline characteristics are summarized in Table 1. The study included a total number of 267 patients, with a median age of 65 years (Interquartile Range [IQR]: 62-70) and a mean body mass index (BMI) of 27.3 kg/m² [IQR: 24.5-30.3]. Most patients were male (74.2%), while females comprised 25.8% of the study cohort. Regarding medication use, 64% of the patients reported taking less than five medications, while 36% reported taking five or more. Additionally, 21% of patients reported experiencing fall incidents within the past year, while the majority (79.0%) reported no fall history. Unadjusted differences in patients' characteristics by sarcopenia status along with sarcopenia prevalence are presented in Figure 1 (A-B). Differences in the medians of age and BMI can be seen in Figure 1-A, indicating that patients with

sarcopenia had a significantly higher median age of 69 years compared to 64 years for those without sarcopenia (p < 0.001). For BMI, patients with sarcopenia had a mean BMI of 25.9 kg/m², which is significantly lower than that of people without sarcopenia, 27.6 kg/m² (p = 0.04). Additional characteristics of the patients and the prevalence of sarcopenia are displayed in Figure 1-B. Out of the total of 267 patients, 85 (31.8%) were identified as having sarcopenia using the appropriate dynamometer cut points. Sex was found to be significantly associated with having sarcopenia, as 46.4% of females were affected compared to 26.2% of males (p = 0.003). Additionally, the

Table 1. Baseline Characteristics of Study Participants (n=267)

Characteristic	Median [IQR] or Number (%)			
Age (in years)	65 [62 - 70]			
BMI (in kg/m²)	27.3 [24.5 - 30.3]			
Sex				
Male	198 (74.2)			
Female	69 (25.8)			
Medications Count				
<5	171 (64.0)			
≥5	96 (36.0)			
Falls past year				
No Falls	211 (79.0)			
1-3 Falls	56 (21.0)			

Abbreviations: BMI: Body Mass Index

prevalence of sarcopenia was notably higher among those taking five or more medications (47.9%) compared to those taking fewer than five medications (22.3%) (p < 0.001). In contrast, there was no significant association between falls in the last year and sarcopenia status (p = 0.705), as 33.3% of patients with 1-3 falls had sarcopenia, compared to 30.8% of those with no falls. The results of the fully adjusted logistic regression model that examines the association between medication count or polypharmacy as a primary exposure and the outcome of sarcopenia are displayed in Table 2. Important variables adjusted for in the model included age, BMI, sex, and falls over the last year. In terms of the odds of having sarcopenia, patients with polypharmacy (≥5 medications) had a significantly higher likelihood (OR = 2.72, 95% CI: 1.51– 4.87, p=0.001) compared to those taking less than five medications. Additionally, it was found that every additional year of age was significantly associated with a higher likelihood of sarcopenia among male patients (OR = 1.11, 95% CI: 1.06-1.17, p <0.001). Moreover, female patients were found to have more than twice the odds of being sarcopenic compared to males (OR = 2.29, 95% CI: 1.23-4.29, p=0.009). On the other hand, BMI had an inverse relationship, although not significant, association with sarcopenia (OR=0.95, 95% CI: 0.90-1.01, p=0.081). Lastly, regarding fall history in the past year, patients with 1-3 falls did not have significantly different odds of having sarcopenia than those without falls (OR = 0.89, 95% CI: 0.44–1.81, p=0.757).

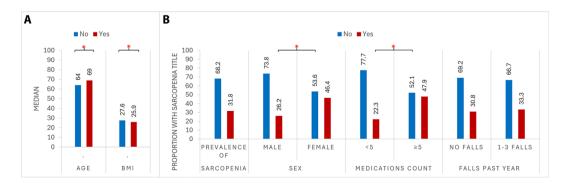


Figure 1 (A-B). Differences in participants' Characteristics by Sarcopenia Status (Yes/No) (n=267). Note: (*) Denotes significant differences in median age and BMI by sarcopenia status (Wilcoxon Two-Sample Test), and in sarcopenia proportions by sex, medication count, and falls in the past year (Chi-Square Test).

Table 2. Multivariate Regression Analysis Results for the Odds of Having Sarcopenia among participants (n=267)

Variables	Adjusted OR ^a	95% CI	P-value
Medications Count			
<5	Reference	-	-
≥5	2.72	(1.51 - 4.87)	0.001
Age (in years)	1.11	(1.06 - 1.17)	<0.001
BMI (in kg/m ²)	0.95	(0.9 - 1.01)	0.081
Sex			
Male	Reference	-	-
Female	2.29	(1.23 - 4.29)	0.009
Falls past year			
No Falls	Reference	-	-
1-3 Falls	0.89	(0.44 - 1.81)	0.757

Note: a: Adjusted odd ratios. Model adjusted for: age, Body Mass Index (BMI), sex, falls per past year.

Discussion

Our study highlights the prevalence of sarcopenia among older adults aged 60 years and above, revealing that approximately one-third of the sample is affected by this condition. We focus on the significant association between polypharmacy and sarcopenia, finding that patients taking five or more medications are nearly three times more likely to have sarcopenia compared to those prescribed fewer than five medications. In addition to polypharmacy, age emerged as a critical factor, with each additional year of age associated with an 11% increase in the likelihood of developing sarcopenia. Our findings demonstrate a clear correlation between age and the prevalence of sarcopenia, with a median age of 69 years for patients diagnosed with the condition, in contrast to a median age of 64 years for those without sarcopenia (p < 0.001). Interestingly, females exhibited more than twice the odds of developing sarcopenia, suggesting that genderspecific factors may contribute to the higher prevalence observed in women. Furthermore, body mass index (BMI) displayed a slight inverse association with sarcopenia. Notably, a history of falls in the past year did not reveal a significant association with sarcopenia. Globally, Studies from Brazil, Europe, and Asia show prevalence rates ranging from 1% to 50%, with community-dwelling older adults' populations typically reporting lower rates compared to institutionalized or hospitalized groups. For instance, the prevalence in Brazil is around 17% for community-dwelling adults aged 60 years and older (19). Similarly, in China, community-dwelling men and women aged 60 years and above show prevalence rates of 12.9% and 11.2%, respectively, compared to higher rates in hospitalized individuals (29.7% in men and 23% in women) (20). In Europe, community prevalence is generally lower, such as 6% in the UK (19). In Saudi Arabia, sarcopenia appears notably more prevalent than global averages, particularly among community-dwelling older adults. Studies conducted in Riyadh and other regions report prevalence rates as high as 65.7% among prefrail community-dwelling older adults, with women (71.9%) being disproportionately affected compared to men (59.1%) (14). Similarly, another study highlights that 84% of sarcopenic individuals in Saudi Arabia were women, a stark contrast to the lower prevalence. Recent studies have highlighted the significant association between polypharmacy and the onset of sarcopenia. Tanaka et al. found that the combination of polypharmacy and the use of potentially inappropriate medications significantly increased the risk of developing sarcopenia (21). Specifically, those patients on five or more medications alongside PIMs had more than double the risk of developing sarcopenia compared to those not on such medication regimens (21). The findings of Tanaka et al. are consistent with our findings. In addition to medication-related risks, sarcopenia itself has been linked to other adverse health outcomes (21). The relationship between sarcopenia and polypharmacy has garnered increasing attention due to its implications for geriatric health outcomes. A systematic review by Prokopidis et al. analyzed data from 29 studies, concluding that individuals with sarcopenia exhibited a 65% higher prevalence of polypharmacy (odds ratio [OR]: 1.65) compared to those without sarcopenia (22).

This robust analysis underscores the critical intersection between medication management and muscle health in aging populations. Kuzuya introduced the

concept of drug-related sarcopenia as a significant contributor to muscle loss in older adults undergoing polypharmacy regimes—highlighting that certain medications can induce adverse effects on skeletal muscle mass, other medications can alter neurotransmitter levels, affecting balance and coordination, which are crucial for maintaining muscle mass, and other drugs are associated with increased systemic inflammation, which can accelerate muscle degredation leading to further complications such as frailty and increased fall risk (23). Aging encompasses a multifaceted interplay of physiological, psychological, and environmental changes that significantly contribute to muscle loss and increased medication use among older adults. Physiologically, sarcopenia—characterized by the involuntary loss of muscle mass and strengthcommonly begins around age 30 and accelerates after age 60, with estimates indicating a reduction of 3-5% in muscle mass per decade (3). This condition profoundly affects physical function, elevating the risk of falls and disability. Concurrently, hormonal alterations particularly decline in anabolic hormones such as testosterone and growth hormone, hinder muscle protein synthesis, while metabolic changes diminish the body's capacity to synthesize protein, resulting in a negative protein balance and heightened insulin resistance (22). The likelihood of developing sarcopenia decreases by 1% for every 1 unit increase in BMI. This finding aligns with existing literature suggesting that higher BMI may serve as a protective factor against sarcopenia in older adults. This protective effect is often attributed to better nutritional reserves and increased overall body mass, which could help preserve muscle mass. Several studies support this inverse relationship between BMI and sarcopenia. For instance, a study by Curtis et al. showed a negative association between BMI and the risk of sarcopenia in community-dwelling older adults' populations (24). Similarly, a study by Lau et al. found that a lower BMI was significantly correlated with a higher likelihood of sarcopenia in older Chinese adults (25). Additionally, a study by Sung et al. found that low BMI is a significant predictor of sarcopenia, likely due to the correlation between body weight and muscle mass (26). Moreover, Suzuki et al. noted that individuals with higher BMI, while

at risk for other comorbidities such as obesity, may have a lower likelihood of sarcopenia due to increased overall muscle mass (27). These studies point toward a protective role of increased BMI, potentially due to higher muscle mass and fat stores, which may preserve physical function. One possible mechanism for the protective effect of higher BMI on sarcopenia could be related to mechanical loading. Increased body mass may result in higher mechanical loading on muscles, thus promoting muscle mass maintenance through increased activation of anabolic pathways such as the insulin-like growth factor-1 (IGF-1) signaling cascade (28). On top of that, a higher BMI could reflect better nutritional status, which is crucial for maintaining muscle protein synthesis and preventing muscle breakdown (28). However, it is essential to interpret these findings with nuance. While a higher BMI might reduce the risk of sarcopenia, it does not necessarily equate to better muscle quality or function. Hong and Choi highlighted that increased fat mass, particularly in the form of visceral adiposity, might still impair muscle metabolism, leading to a phenomenon known as sarcopenic obesity (29). Furthermore, Obesity has been linked with increased fat infiltration into muscle (myosteatosis), contributing to muscle weakness and functional decline (29). The discrepancy between these findings may be due to differences in population characteristics (e.g., body composition, physical activity levels, and comorbidities) or methodologies, such as the cutoffs used for defining sarcopenia and obesity. It is also essential to account for the distribution of fat and muscle mass in different individuals, as a higher BMI could represent either lean mass or fat mass. Our research revealed that women have a 46.4% higher risk of sarcopenia than men 26.2%. This was in line with a prior study done in Riyadh, Saudi Arabia, where the prevalence of sarcopenia in females living in pre-frail communities was 71.9%, greater than the male incidence of 59.1% (14). Similar findings were made by a Korean study, which discovered that the prevalence of sarcopenia was 19.2% in males and 26.4% in females (30). Because of menopause and lower blood levels of estrogen, women lose muscular mass and strength more quickly than men do in their early years of aging. However, in a later stage of aging, men's blood levels of

insulin-like growth factor-1 and testosterone hormone decrease, leading to a faster rate of muscular function and mass loss, ultimately resulting in sarcopenia (31). In this study, the results indicate that patients who experienced 1 to 3 falls in the past year did not exhibit significantly different odds of having sarcopenia compared to those who did not experience any falls (OR = 0.89, 95% CI: 0.44–1.81, p = 0.757). A meta-analysis by Yeung et al. (2019), which included twenty-two studies investigating the association between sarcopenia and the risk of falls, revealed that 10 studies (45%) reported an increased risk of falls among patients with sarcopenia compared to those without. Conversely, the remaining 12 studies found a non-significant association between sarcopenia and falls (32), which aligns with our findings. This lack of statistical significance suggests that falls in this frequency range may not be a reliable predictor of sarcopenia in older adults. Other factors, such as levels of physical activity, comorbidities, and environmental influences, may play a more crucial role in the development of sarcopenia than the mere occurrence of falls. Additionally, the relatively small sample size or the specific characteristics of the participants may have influenced our findings. Such important findings highlight the need for policymakers to develop community-based interventions focused on nutrition, physical activity, and education about the risks associated with polypharmacy and how to prevent sarcopenia.

Strengths and limitations

A notable strength of this study is its focused assessment of sarcopenia through a standardized measure, the handgrip strength test (dynamometry). However, one of the key limitations is the use of a convenience sampling method, which may introduce selection bias. Additionally, the exclusion of certain populations, such as those with neuromuscular disorders or cancer, limits the generalizability of the findings to individuals with more complex medical profiles. The reliance on self-reported medication use may also be subject to recall bias, potentially affecting the accuracy of the data collected. In addition,

convenience sampling is prone to selection bias and lacks representativeness, which can limit the generalizability and validity of the findings.

Conclusion

In conclusion, this study highlights a significant correlation between polypharmacy and sarcopenia among community-dwelling older adults in Saudi Arabia. Individuals taking five or more medications are at a markedly increased risk of developing sarcopenia, emphasizing the need for careful medication management. Additionally, older age and female gender further elevate this risk. While BMI and fall history showed weaker associations, the findings underscore the complexities of managing sarcopenia in older adults with multiple medications. These insights can inform healthcare strategies aimed at reducing polypharmacy and promoting muscle health, ultimately improving quality of life and reducing sarcopenia-related complications.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article

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Declaration on the Use of AI: This study utilized OpenAI's ChatGPT for assistance in drafting and refining the manuscript.

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