Clarifying the relationship between sarcopenia and depression in geriatric outpatients

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ABSTRACT
Objective: We investigate the relationship between sarcopenia components and depression in geriatric outpatients, considering the effects of potential confounding factors.

Methods: Adults ≥60 years of age were selected from outpatient clinics. Muscle strength was assessed using handgrip strength (HGS) measured using a hydraulic hand dynamometer and chair stand test (CSST). Physical performance was evaluated by usual gait speed (UGS), nutritional status, and frailty were screened by mini-nutritional assessment (MNA) questionnaire and FRAIL scale. Depression was diagnosed through a psychiatric interview and the administration of the Geriatric Depression Scale (GDS).

Results: Participants with depression were similar to participants without depression regarding age (p = .055), education (p = .095), frailty (p = .857), and HGS scores (p = .053). The group with depression had longer CSST duration (p = .023), slower UGS (p = .027), and more malnutrition (p = .001). Multivariate regression analysis revealed that only the malnutrition was independently associated factor with depression after adjusting for confounding factors.

Conclusions: Depression is associated with malnutrition and some components of sarcopenia in geriatric outpatients. Our results revealed that sarcopenia might be associated with depression through malnutrition. If malnutrition lasts for a long time, sarcopenia may become evident in the later stages of depression.

INTRODUCTION
Depression is a common and important health concern among older adults [1]. Studies have reported that up to 38% of older adults may have depressive symptoms [2]. Depression cannot be considered a normal process of aging. Gender, physical activity, nutrition, and socioeconomic status have been reported to be associated with depression in older adults [3–5]. Geriatric depression is strongly associated with negative outcomes related to the presence of medical comorbidities, cognitive deficits, poor functioning, increased suicide risk, and overall mortality [2]. Clinicians treating chronic disorders may be preoccupied with treating the medical condition and overlook screening and treatment for depression. Therefore, awareness of geriatric depression is crucial; it should be recognized and treated [6].

Sarcopenia is defined as a muscle disease that can develop acutely or chronically with the recommendations of the European Working Group on Sarcopenia in Older People (EWGSOP) [7]. It can be seen at any age, but it is more common in older adults. With the last recommendations of EWGSOP 2, it was aimed to facilitate the diagnosis of sarcopenia. According to the report, sarcopenia is a syndrome characterized by low levels of measures for three parameters: (1) muscle strength, (2) muscle quantity/quality, and (3) physical performance as an indicator of severity [7].

Sarcopenia is associated with negative consequences in many health-related areas, which may lead to immobility, decreased functionality in daily life,
decreased quality of life, falls, and long-term hospitalizations in care institutions [7]. Physical well-being, particularly, muscle strength – estimated by handgrip strength (HGS) – may increase health-related quality of life and is, therefore, an important source in maintaining well-being during old age [7]. Chang et al. suggested that sarcopenia plays a role in the pathophysiology of depression [8]. On the other hand, the results of the studies investigating the relationship between sarcopenia and depression are controversial. Some researchers found no relationship between sarcopenia and depression in older adults [9–13]. However, other researchers suggested an association with depressive symptoms and diagnosis of sarcopenia [5,14–21]. All these studies evaluated depression with a screening scale. Therefore, further research has been recommended to uncover the relationship between depression and sarcopenia components [8].

In this study, we aimed to investigate the relationship between the components of sarcopenia and depressive disorders in geriatric outpatients aged 60 and over, considering the possible confounding factors.

Methods

Study design and participants

This study was designed in a cross-sectional structure between 1 February 2019 and 1 February 2020. Participants were recruited from geriatric population aged 60 years or older who were admitted to the psychiatry and neurology outpatient clinics of Izmir Bozyaka Training and Research Hospital. At the beginning of this study, some exclusion criteria were determined. Patients with a clinical diagnosis or suspicion of dementia or mild cognitive impairment, stroke or Parkinson's disease or other neurodegenerative disease, previous depression diagnosis or antidepressant medication use, mental retardation, morbid obesity (body mass index [BMI] ≥ 40 kg/m²), substance abuse in the last 6 months, thyroid disease, first degree relatives or close friend loss (to rule out mourning), a negative life event experience recently (to rule out reactive depression), bedridden, and conditions that might interfere with HGS assessment (e.g. hand osteoarthritis, stroke, peripheral artery disease, or neuropathy) were excluded from this study.

Ethical permission was obtained from the local ethics committee for this research (Ethics committee number: 16.01.2019–12). This study was conducted according to guidelines in the Declaration of Helsinki. Informed consent was obtained from all participants. A total of 247 participants were evaluated for this study. After the exclusion criteria, 204 participants were included in this study.

Sociodemographic and medical history characteristics, such as age, gender, marital status, educational status (recorded in years), with whom they lived, perceived economic status, smoking status, medications, and comorbidities reported by the individual, were recorded. BMI was calculated as weight (kg) divided by height (m) squared.

Assessment of depressive disorder

Geriatric Depression Scale (GDS) was developed to investigate symptoms of depression in the geriatric population [22]. Depression was assessed with the help of the Turkish version of GDS [23]. It comprises 30 self-rating questions with either yes or no response. Item scores are summed, resulting in a possible total score of 0–30. High scores represent more severe depression. In the total score of this scale, it is suggested that those between 0 and 9 points should be evaluated as no depression, between 9 and 14 points as depression, and above 14 points as severe depression [22]. Depression score was determined with this scale and the diagnosis of depression of all participants was decided by a psychiatrist with a structured interview (Structured Clinical Interview for the Diagnostic and Statistical Manual – SCID-V) [24].

Assessment of components of sarcopenia

We assessed skeletal muscle strength and physical performance tests. Skeletal muscle strength was evaluated using both hand grip strength (HGS) and chair stand test (5-times sit-to-stand- CSST) as suggested by EWGSOP 2 consensus report [7]. HGS was measured with a Jamar hydraulic hand dynamometer (Trademark: Baseline Hydraulic Hand Dynamometer, Model: 12-0240 standard) by a single neurologist using validated protocol [25]. HGS was measured in sitting position, elbow in 90° flexion, and wrist in a neutral position. Participants were asked to apply the maximum HGS three times with both left and right hands. It was ensured that rest intervals between measurements were at least 30 s. We recorded the highest score of HGS as grip strength. Low HGS thresholds were defined according to the national data (<22 kg and <32 kg for females and males, respectively) [26].

CSST was performed to assess the muscle strength of the lower limb. Participants were asked to sit and stand from a chair five times as quickly as possible,
keeping arms folded across the chest. Participants had to rise to a full standing position each time they stood up and sit all the way down each time. A completion time >15 s for five rises reflected impaired CSST [7]. Physical performance was assessed by four-meter gait speed (usual gait speed [UGS]). Decreased UGS was defined as if gait speed /C20 /C20 0.8 m/s [27].

Assessment of malnutrition and frailty

Nutritional status was assessed by a full mini-nutritional assessment (MNA) questionnaire. An MNA score <17 was assessed as malnutrition (MN), with an MNA score of 17–23.5 as at risk of MN (MNR) and ≥24 as normal nutritional status [28]. Frailty was assessed by the FRAIL scale, which consists of five questions on Fatigue, Resistance, Ambulation, Illness and Loss of Weight. Scores ranged from 0 to 5, where 3–5 represented frailty and 1–2 represented pre-frailty [29].

Procedure

After giving written informed consent, each person was interviewed with the SCID to determine psychiatric diagnosis by the psychiatrist. Sociodemographic data form, GDS, MNA, and FRAIL scale were completed by psychiatrists. Then the participants were directed to the neurologist. Neurologists were not aware of the participants’ depression status. Participants were tested for HGS, CSST and UGS by the neurologist. All measurements were constantly applied by the same researcher to ensure that there was no difference between practitioners.

Statistical analysis

Data were analyzed by IBM SPSS Statistics version 21 for Windows (SPSS Inc., Chicago, IL). The normality of the variables was analyzed using visual methods (histograms and probability plots) and Kolmogorov–Smirnov tests. Descriptive statistics were given as means ± standard deviations, median (minimum–maximum values), and interquartile range or percentages as appropriate. A chi-square test was run to compare categorical variables. Groups with/without depression were compared with independent sample t-test or Mann–Whitney U test as necessary. The variables detected as significant in univariate analyses were analyzed with regression analyses. Determining the multicollinearity among the possible regression analyses, independent variables were checked with Pearson, Spearman, or Kendall’s tau-b correlation analyses. Then binary logistic regression analysis was run to assess factors independently associated with depression. A p value of <.05 was accepted as statistically significant. We reported multivariate associations as odds ratio (OR) with 95% confidence interval (CI).

Results

A total of 204 older participants (138 females, 66 males; mean age: 68.7±5.2 years) were included in the analyses. Sixty-two percent were married, 33%
were widowed, and 5% were single. All participants were community-dwelling older adults. Seventy-two percent of participants (n = 147) defined their socioeconomic status as medium level, while 25% (n = 50) participants stated as a lower level. Most of the participants lived with their spouses (56%, n = 114). There were 42 (21%) participants living with their children and 40 (20%) living alone. There was no significant difference between depressive and non-depressive groups concerning socioeconomic status and whom they lived (p > .05). The median value of the education period of the participants was five (0–16) years. Eleven percent of the participants were current smokers (n = 22). The most common physical diseases were hypertension (55%, n = 113), diabetes mellitus (33%, n = 67), cardiovascular disease (17%, n = 34), chronic obstructive pulmonary disease (4%, n = 8), and cancer (2%, n = 4). The median number of chronically used drugs was two (0–5). The median number of chronic diseases was one (0–5). Details of the sociodemographic and clinical characteristics of the participant data and the comparison of those with and without depression are given in Table 1.

The participants’ GDS median score was 11 (0–29). As a result of the clinical interview, the clinical diagnosis of depression was confirmed in 69 (34%) people. There were 53 (38%) women and 16 (24%) men with clinical depression. There was a difference between gender in terms of depression (p < .05).

The average HGS value was 21.9 ± 5 kg in women and 35.3 ± 7.2 kg in men. The prevalence of low HGS was 43% (n = 82). The participants’ mean CSST test time was 11.4 ± 2.3 s. Five percent (n = 7) of those had long CSST time. In women, this rate was 6% (n = 6); and 2% (n = 1) in males. The average UGS of the participants was 0.79 ± 0.15 m/s [min: 0.4 – max: 1.3].

The MNA mean score was 25.1 ± 3. The MNA median score was 26 [13–30]. More than one in five of the participants were classified as at MNR (21.2%) or MN (0.5%). According to the FRAIL scale, 87 (64.4%) participants were prefrail or frail, 48 (35.6%) participants were robust. The comparison of those with and without depression according to the risks of HGS, CSST, UGS, frailty, and malnutrition is given in Table 1.

**Table 2.** Results of multivariate regression analysis: association between depression and malnutrition after adjustment for confounders.

| Model 1 | Model 2 | Model 3 | Model 4 |
|---------|---------|---------|---------|
| Gender | 1.908 [0.897–4.057] | 1.924 [0.907–4.084] | 2.023 [0.679–6.029] | 1.619 [0.394–6.650] |
| MN or MNR | 0.191 [0.095–0.386]* | 0.201 [0.099–0.408]* | 0.187 [0.092–0.380]* | 0.240 [0.090–0.637]*** |
| CSST | 0.291 [0.065–1.314] | 0.350 [0.050–1.879] | _ | _ |
| UGS | 0.254 [0.026–2.495] | _ | _ | _ |
| HGS | 1.001 [0.943–1.062] | 0.982 [0.904–1.066] | _ | _ |

Model 1: adjusted for gender, MN or MNR, CSST. Model 2: adjusted for gender, MN or MNR, UGS. Model 3: adjusted for gender, MN or MNR, HGS. Model 4: adjusted for gender, MN or MNR, CSST, UGS, and HGS.

MN: malnutrition; MNR: risk of malnutrition; CSST: chair stand test; UGS: usual gait speed; HGS: hand grip strength
*significant p values. **p < .001, ***p = .004.

**Associated factors with depression results of univariate analysis**

Between the participants diagnosed with depression and those without depression, age (p = .055), duration of education (p = .095), frailty (p = .857), number of drugs used (p = .175), number of chronic diseases (p = .217), and HGS score (p = .053) were not statistically significantly different. The rate of female gender was higher in individuals with depression (p = .045). The group with depression had a higher proportion of those with a CSST duration longer than 15 s (p = .023), slower gait speed (p = .027), and a higher prevalence of MNR or MN than the group without depression (p = .001). Univariate analysis between depression and other independent factors is shown in Table 1.

When we divide the depression group into three groups (no depression, depression, and severe depression) concerning the severity of depression symptoms, there was no difference between the groups about the comparison of sarcopenia parameters (HGS [p = .190], CSST [p = .074], UGS [p = .600]). The only difference between the groups concerning depression score was poor nutritional status (MN or MNR) (p = .001).

**Results of multivariate regression analysis**

Variables that were associated with depression in univariate analysis (p < .05) were used as independent variables in regression analysis. Depression was a dependent variable, while gender, presence of MN or MNR, and components of sarcopenia were independent variables. Each component of sarcopenia (HGS, UGS, and CSST) was added separately and consecutively in four different regression models (Table 2).
Although numeric HGS values did not show a statistically significant association with depression in univariate analysis ($p = .053$), it was included in the model because of its clinical relevance. Multivariate regression analysis showed that poor nutritional status (MN and MNR) was independently associated with depression after adjustment for confounders in all models (OR 0.240, 95% CI: 0.090–0.637, $p = .004$). UGS ($p = .241$), HGS ($p = .890$), and CSST ($p = .123$) were not associated with depression in regression analysis models.

**Discussion**

In this cross-sectional study, we observed that there was an independent association between depression and malnutrition in geriatric outpatients. The relationship between components of sarcopenia and depression disappeared after adjustment for confounders. Malnutrition remained a significant associated factor for depression in all regression models. Our results from this study suggest that the relationship between sarcopenia and depression may be indirectly related through malnutrition.

Previous studies reported that sarcopenia and depression seem to share several common risk factors. Decreased physical activity [30,31], increased oxidative stress [32,33], increased falling risk, which caused immobility [34,35], malnutrition [4,36], and dysregulated hormonal cycles [37,38] were some of the common risk factors suggested [39] in the literature. While some articles in recent years report the relationship between sarcopenia components and depression [5,14–21], some of them reported that there is no relationship between sarcopenia components and depression [9–13]. We think there are several points to discuss our results here. First, the different results in previous studies may be because different methods were used in the diagnosis of sarcopenia. Association between depression and sarcopenia was assessed concerning either HGS, muscle mass and muscle function or a combination of them as sarcopenia diagnosis in previous studies. In our study, the muscle mass of the participants was not evaluated. However, most of the previous studies reported a relationship between depression and impaired HGS or muscle performance [5,9,11,16,21] but not between depression and low muscle mass [12,19,20]. Here, we comment that the lack of motivation caused by depression might cause impaired physical performance tests. To our knowledge, two studies reported a relationship between depression and sarcopenia, which were defined based on low muscle mass [14,15]. However, they did not assess nutritional status as a confounding factor.

Second, the diagnosis of depression was made by a psychiatrist with a clinical interview in our study. Depression is a mental illness suggested to be diagnosed clinically [40]. If the screening is positive for possible depression, it is recommended that the diagnosis should be confirmed using the SCID-V or semi-structured interview to detect high agreement among investigators [24]. Depressive symptoms may overlap with mood changes caused by life events (such as mourning). In addition, there are many medical conditions that may cause depressive symptoms [41]. When examining the direct relationship between depression and sarcopenia, these conditions should be excluded. Despite this, many studies have been conducted with depression screening scales and conditions that may cause depressive symptoms have not been excluded [5,12–21]. Our preference for strict exclusion criteria while selecting the participants might be the reason why we did not find an independent relationship between sarcopenia components and depression. To our knowledge, there is no study investigating the relationship between sarcopenia and geriatric depressive disorder diagnosed by a clinical interview by a psychiatrist. Third, in our study, we included only participants with new and first diagnosed depression and without current antidepressant medication. Because the depressive symptoms of these patients are not repetitive and not for a long time, we assume that the malnutrition and limitation of movement due to depression do not last long. This suggests that sarcopenia has not yet occurred in these patients and may explain why it is not independently associated with depression. Also, being under antidepressant treatment and/or the number of depressive episodes may be a factor in the relationship between sarcopenia and depression in previous studies that reported a relationship between them. To our knowledge, none of the previous studies had these inclusion criteria similar to ours. Therefore, we cannot compare our results in this respect.

Malnutrition is associated with both sarcopenia and depression [4,36,42–44]. Malnutrition is a challenging public health concern among older adults and has severe unfavorable effects on health and one of its correctable causes is depression [4,45]. It has been suggested to start treatment as soon as possible in older adults with depression and/or malnutrition [46,47]. Several studies have indicated that depression was a major factor contributing to weight loss in older adults and malnourished patients had higher
depression scores [5,48]. When we compare our research with studies investigating the relationship between sarcopenia and depression, an association was found between depression and sarcopenia in those with a similar mean age and community-dwelling as in our study [5,14,16,18]. However, in these studies, malnutrition was not evaluated except Wang et al. [18]. Wang et al. reported that MNA scores were lower in patients with depression compared to the non-depressed group in their study examining the relationship between sarcopenia and depressive symptoms. However, malnutrition was not included in regression analysis even it was associated with depression in their univariate analysis [18]. Undernutrition might also precipitate depressive symptoms [49].

To our knowledge, the potential mediating effect of malnutrition in the relationship between sarcopenia and depression has not been studied empirically. The relationship between sarcopenia and depression may be mediated by malnutrition and is an important confounding factor [5].

From a general perspective, our results showed that depression and malnutrition and sarcopenia are related to each other in older adults. Malnutrition and sarcopenia are two geriatric syndromes that have been stated to be associated with frailty [50]. Moreover, it has been suggested that sarcopenia screening tools can also be used as a frailty screening tool [51]. Frailty has been known to be associated with increased mortality [52]. Therefore, it is noteworthy to screen these interrelated situations (depression, malnutrition, and sarcopenia) simultaneously in older adults.

This study has several limitations. The skeletal muscle mass was not considered to confirm the diagnosis of sarcopenia. Only probable sarcopenia cases were evaluated in this study. The cross-sectional study design limited the ability to establish a causal relationship of depression and component of probable sarcopenia. Depressed participants may not be able to fully squeeze HGS due to lack of motivation. Therefore, participants with depression may have low HGS results. To overcome this limitation, groups were compared concerning depression symptom severity according to GDS scores, and no difference was found between depression symptom severity and HGS scores. Finally, the data of our study cannot be generalized to the whole population because our sample consisted of a relatively young geriatric outpatient; the number of chronic diseases and the number of drugs they used was low and diseases, such as Parkinsonism and cognitive disorders, which are common in older adults were excluded.

Conclusions and implications

In conclusion, our study showed that clinically diagnosed depression is not independently associated with sarcopenia parameters, while a significant association is observed with poor nutritional status. We recommend that malnutrition should be considered as a confounding factor in future studies. Further longitudinal studies those evaluate each sarcopenia component, including muscle mass and recognize nutritional status as a confounding factor are needed to document the relation between sarcopenia and depression clearly.

Disclosure statement

The authors report no conflict of interest.

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