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**RESEARCH**

# Association of sarcopenia with age-related macular degeneration in the very elderly

## Çok yaşlılarda sarkopeni ile yaşla ilişkili makula dejenerasyonu arasındaki ilişki

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**Abstract**

**Purpose:** The aim of this study was aimed to investigate the association between age-related macular degeneration and sarcopenia in the oldest-old population, constituting individuals aged ≥80 years.

**Materials and Methods:** This retrospective study was conducted in the ophthalmology and geriatric departments of a training and research hospital in 2023 and 2024. Participants aged ≥80 years who were admitted to the ophthalmology outpatient clinic for any reason were included in the study.

**Results:** The study population comprised 311 individuals aged 80 years or older and the prevalence of age-related macular degeneration was 20.5% (n=64). The mean age of the patients diagnosed with age-related macular degeneration (AMD) was 85.9 years (±3.8), while the mean age of the control group was 85.8 years (±3.9). Of the patients diagnosed with age-related macular degeneration, 34 were female and 30 were male. The Deyo-Charlson Comorbidity Index (D-CCI) values were 1.77 in the age-related macular degeneration group and 1.85 in the control group. The prevalence of sarcopenia was significantly higher in patients with age-related macular degeneration (89.1% vs. 52.6%).

**Conclusion:** This study demonstrates that sarcopenia is independently associated with age-related macular degeneration in the oldest-old population. These findings highlight the significance of sarcopenia management in the prevention and management of age-related macular degeneration.

**Keywords:**. Sarcopenia, age-related macular degeneration, oxidative stress, inflammation, older adults

**Öz**

**Amaç:** Bu çalışmada yaşa bağlı makula dejenerasyonu ile sarkopeni arasındaki ilişki en yaşlı popülasyonda (80 yaş ve üzeri) araştırılmıştır.

**Gereç ve Yöntem:** Bu retrospektif çalışma, 2023-2024 yılları arasında bir eğitim araştırma hastanesinin oftalmoloji ve geriatri bölümünde yürütülmüştür. Herhangi bir nedenle oftalmoloji polikliniğine başvuran 80 yaş ve üzeri katılımcılar bu çalışmaya dahil edilmiştir.

**Bulgular:** Çalışma popülasyonu 80 yaş ve üzeri 311 bireyden oluşmuştur ve yaşa bağlı makula dejenerasyonunun yaygınlığı %20,5'tir (n=64). Yaşa bağlı makula dejenerasyonu olan hastaların yaş ortalaması 85.9 (±3.8) iken kontrol grubunun yaş ortalaması 85.8(±3.9) idi. Yaşa bağlı makula dejenerasyonu olan hastaların 34 ü kadın, 30 u erkekti. Deyo-Charlson comorbidity index (D-CCI) değerleri yaşa bağlı makula dejenerasyonu grubunda 1.77 iken kontrol grubunda 1.85 idi. Sarkopeni prevalansının yaşa bağlı makula dejenerasyonu hastalarında belirgin şekilde daha yüksek olduğu gözlemlendi (%89,1'e karşı %52,6).

**Sonuç:** Çalışmamız, sarkopeninin en yaşlı bireylerde yaşa bağlı makula dejenerasyonu ile ilişkili bağımsız bir değişken olduğunu göstermektedir. Bu bulgular, sarkopeni yönetiminin yaşa bağlı makula dejenerasyonunun önlenmesi ve yönetimindeki önemini vurgulamaktadır.

**Anahtar kelimeler**: Sarkopeni, yaşa bağlı makula dejenerasyonu, oksidatif stres, inflamasyon, yaşlı birey

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## INTRODUCTION

Age-related macular degeneration (AMD) has a significant global impact, affecting millions of individuals, and it is the leading cause of irreversible vision impairment in the oldest-old adult population of ≥80 years[1]. The increasing number of oldest-old individuals in society is indicative of an ongoing exponential rise in the prevalence of AMD among the geriatric population. The visual effects of AMD may exacerbate the already challenging health concerns and comorbidities of the elderly population and seriously affect quality of life. For older patients, visual impairment inevitably leads to an increased risk of falls, depression, and inability to perform activities of daily living such as eating, working, and dressing.

Sarcopenia is a progressive and generalized skeletal muscle disorder involving accelerated loss of muscle function and muscle mass. It is associated with increased adverse outcomes including a higher risk of falls, the loss of functional ability, increased frailty, and an elevated risk of mortality. The term was initially employed to describe age-related loss of muscle function and mass[2]. On average, 5-13% of individuals aged 60 and older suffer from sarcopenia, with the prevalence increasing to as high as 50% in those aged ≥80 years[3]. For the past several decades, however, the term has been employed to describe loss of muscle mass without reference to function[4]. In clinical settings, according to the criteria of the European Working Group on Sarcopenia in Older Persons (EWGSOP2), an individual exhibiting low muscle mass and low muscle strength or quality should be diagnosed with sarcopenia [5]. This condition can be best conceptualized as an insufficiency or failure of skeletal muscles. The most common symptoms among patients diagnosed with sarcopenia include weakness, falls, slowness, and self-reported muscle wasting or difficulties in performing activities of daily living[6].

As the prevalence rates of both sarcopenia and AMD increase, the possibility arises that these two diseases may influence one another. In particular, the impaired nutritional status of older individuals due to sarcopenia may contribute to the progression of AMD. In addition, decreased physical activity and tendencies toward sedentary lifestyles among individuals with sarcopenia may increase the risk of AMD. Addressing the association between sarcopenia and AMD is crucial due to the impact of both diseases on overall health and quality of life in aging populations. Based on the hypothesis that sarcopenia increases the risk of developing AMD in older individuals, this study aims to fill an important gap in the literature by addressing the potential relationship between sarcopenia and AMD.A review of existing research shows that there is limited data on the co-occurrence of these two conditions, and there is insufficient information on how the effect of sarcopenia on nutritional status and physical activity levels affects the risk of AMD, especially in older individuals. By evaluating the effects of sarcopenia on the development of AMD, this study aims to fill the knowledge gap in this field and provide important implications for the planning of health services in the elderly population. The findings will contribute to the development of both prevention strategies and integrated treatment approaches.

## MATERIALS AND METHODS

### Sample

This retrospective study was conducted by reviewing the medical records of over 700 older adults who were examined in the ophthalmology and geriatrics departments of Balikesir City Hospital in 2023 and 2024. The number of individuals aged 80 years and over who were admitted to the eye clinic for any reason and met the diagnostic criteria for sarcopenia and did not have any retinal disease other than AMD was 311.

The study population excluded individuals with a history of severe neuromuscular disease, who had not been tested or whose data were not recorded in the hospital's electronic database, who were diagnosed with retinal disease other than AMD by an ophthalmologist, who had acute infectious disease, acute cerebrovascular disease, acute organ failure (renal, hepatic, cardiac or respiratory), acute metabolic and electrolyte imbalance (bleeding, acidosis or sepsis), and who were aged <80 years. In accordance with the retrospective nature of the study, the requirement for informed consent was waived.

Approval was obtained from the Ethics Committee of Balıkesir Atatürk City Hospital (Decision No: 2024/05/27 Date: 30.05.2024) before the research, which was conducted following the Declaration of Helsinki.

### Procedure

In Turkey, all individuals admitted to Turkish

hospitals are registered in the Turkish National Patient Registry, a centralized database that contains information on all hospital admissions[7], as captured in the national e-Nabız health records system. Patient-specific demographic information including date of birth and gender was obtained from the SISOFT electronic hospital registration database.

The previous electronic medical records of all analyzed patients diagnosed with AMD by optical coherence tomography performed by specialist ophthalmologist were reviewed. A specialist geriatrician performed the geriatric evaluations and diagnoses of sarcopenia. The diagnosis of probable sarcopenia was based on the observation of abnormal results in handgrip tests and/or the 5-times sit-to-stand test as part of a comprehensive geriatric assessment. Handgrip strength was evaluated using a Camry hand dynamometer and the cutoff values for low handgrip strength were based on those recommended for the Turkish population [8]. The 5-times sit-to-stand test was used to assess lower body strength. Impaired performance was defined as a cutoff time of greater than 12 seconds[9].

Medical diagnoses and comorbidities were identified using electronic medical records and the International Classification of Diseases and Related Health Problems-Tenth Revision (ICD-10). Modified Deyo-Charlson Comorbidity Index (D-CCI) scores were calculated based on comorbidities and used to determine the relative 1-year mortality risk associated with multiple comorbid conditions[10,11,12,13].

## Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was utilized to ascertain the normality of the data distribution. Baseline data were presented in accordance with the relevant statistical standards as mean ± standard deviation, median (minimum–maximum), or number (percentage). Chi-square tests were performed for independent samples comprising categorical variables (gender and sarcopenia) and independent t-tests were performed for continuous variables (D-CCI score and age).

A binary logistic regression analysis was conducted, with adjustments made in accordance with the parameters that were clinical relevant and univariate analysis. Consequently, a multivariate analysis was conducted to identify the factors associated with AMD, incorporating age, gender, and a modified D-CCI score. All statistical analyses were performed with a significance level of $p < 0.05$. The sample size was calculated as 301 people with alpha: 0.05 Beta: 0.2 Power: 90% and above in power analysis.

## RESULTS

The study sample comprised 311 individuals aged ≥80 years, including 64 individuals with AMD and 247 individuals without AMD. Thus, the prevalence of AMD in the study population was 20.5%. The characteristics of the study population are presented in Table 1. Comparisons of demographic variables including age, gender, and comorbidity index revealed no remarkable differences between the two groups. However, the prevalence of sarcopenia was higher among the AMD patients (89.1% vs. 52.6%, $p < 0.01$).

**Table 1. Characteristics of the study sample.**

| Variables | Age Related Macular Degeneration (AMD) | | *p* |
|---|---|---|---|
| | **Yes (Nsd:=64)** | **No (n=247)** | |
| Age (years), mean + SD | 85.9±3.8 | 85.8±3.9 | 0.89 |
| Gender | | | |
| Female, n (%) | 34 (53.1) | 156 (63.4) | 0.13 |
| Male, n (%) | 30 (46.9) | 90 (36.6) | |
| Deyo-Charlson comorbidity index (D-CCI), mean + SD | 1.77±0.83 | 1.85±1.02 | 0.56 |
| Sarcopenia, n (%) | 57 (89.1) | 130 (52.6) | 0.01 |

Categorical variables were indicated as number (%) and determined by the Chi-square test.
Numerical variables with normally distrubuted were indicates as mean ± standart deviation and determined by t-test.
Values given in bold indicate statistically significant results ($p < 0.05$).
AMD: Age Related Macular Degeneration, SD: Standard deviations, D-CCI :Deyo-Charlson comorbidity index

**Table 2. Association of sarcopenia with AMD**

| Variables | Unadjusted | | Model | |
|---|---|---|---|---|
| | OR (95% CI) | *p* | OR (95% CI) | *p* |
| Age | 1.01 (0.94-1.08) | 0.89 | - | |
| Gender | 1.53 (0.88-2.67) | 0.13 | - | |
| Deyo-Charlson comorbidity index (D-CCI) | 0.92 (0.69-1.22) | 0.56 | - | |
| Sarcopenia | 7.33 (3.22-16.71) | **0.01** | 7.41 (3.21-17.07) | **0.01** |

**Model:** Adjusted for age, gender and D-CCI.; Values given in bold indicate statistically significant results ($p < 0.05$).
AMD: Age Related Macular Degeneration, D-CCI: Deyo-Charlson comorbidity index

Univariate regression analysis was conducted to determine which independent variables were associated with AMD. The analysis revealed that sarcopenia was significantly associated with AMD, with an odds ratio (OR) of 7.33 (95% confidence interval [CI]: 3.22–16.71, $p < 0.01$). The analysis showed that age, gender, and D-CCI scores were not significantly associated with AMD ($p > 0.05$). These findings are presented in Table 2.

In multivariate regression analysis performed to evaluate the clinical determinants of AMD, a significant association was identified between sarcopenia and AMD (OR: 7.41, CI: 3.21–17.07, $p < 0.01$) (Table 2). The model explained 16.4% of the variance in AMD (Nagelkerke $R^2$), and the omnibus test confirmed the high significance of the model (-2LL = 277.339, $\chi^2 = 33.832$, $p < 0.01$).

## DISCUSSION

Advanced age is the most significant factor contributing to the risk of AMD[14]. Late-onset AMD has been observed in more than 10% of individuals over the age of 80 [15]. Our study has yielded results consistent with those reported in the literature, indicating that approximately 20% of individuals aged 80 and above are affected by AMD. However, the relationship between AMD and sarcopenia has yet to be fully elucidated in the literature. The present study shows that older individuals with AMD are more likely to suffer from sarcopenia compared to those without AMD. Furthermore, the presence of sarcopenia has been shown to cause an approximately 7.5-fold increase in the risk of AMD. The findings of this study constitute a significant and novel contribution to the existing literature on this topic.

The significant relationship between these two diseases, both of which are more common in older individuals, suggests the possibility that sarcopenia and AMD may share common underlying pathological processes[16]. On the other hand, it is difficult to determine whether the AMD observed in individuals with potential sequelae of sarcopenia is due to underlying pathophysiological changes or is a direct effect of muscle loss. Furthermore, it should be emphasized that oxidative stress and inflammation, which are involved in the pathogenesis of both diseases, may also constitute a common underlying pathway.

One possible explanation for the pathological mechanisms of AMD could be the high sensitivity of retinal pigment epithelial (RPE) cells to oxidative stress[17]. The high metabolic activity and resulting high oxygen consumption, the high polyunsaturated fatty acid contents, and significant exposure to light may be the reasons why RPE cells are sensitive to oxidative stress. The primary function of these cells is to clear photoreceptor outer segment remnants by a process called heterophagy[18]. However, the continuous uptake of photoreceptor outer segment remnants by non-dividing senescent RPE cells leads to the accumulation of an undegradable and autofluorescent metabolite called lipofuscin in lysosomes, thus contributing to the development of retinal inflammation together with oxidative stress[19]. Consistent with these observations, inflammatory cytokines were found to promote muscle loss, stimulate protein catabolism, and suppress the synthesis of muscle fibers in sarcopenia[20].

An individual's dietary patterns may have an impact on the risk of AMD. High-fat, high-carbohydrate diets characterized by "fast foods" are risk factors for AMD, whereas fish consumption, consumption of polyunsaturated fatty acids, and consumption of

fruits and vegetables are protective against the disease[21]. Accordingly, mice fed high-fat, high-cholesterol diets with fructose-enriched water showed AMD-like retinal degeneration, including basal deposits, RPE cell loss, and thickening of Bruch's membrane[22]. Nutrition and diet also play major roles in the development of sarcopenia. For example, saturated fat can activate the innate immune system, leading to the production of pro-inflammatory molecules such as IL-6 and TNF-α, which cause insulin resistance over time[23]. Diet-induced inflammation has been implicated in the development of musculoskeletal diseases, including sarcopenia[24]. For this reason, a diet rich in fruits and vegetables is suggested in order to decrease the risk of sarcopenia[25].

Physical inactivity is a common risk factor associated with the development of both AMD and sarcopenia. Knudtson et al. subjectively measured physical activity and the risk of developing AMD over a period of 15 years, and they showed that participation in an active lifestyle was associated with a 70% reduction in the risk of AMD over 15 years as measured by fundus photography[26]. In addition, sarcopenia may develop early in life due to a lack of physical activity or a sedentary lifestyle. Physical activity also prevents the loss of muscle mass in a variety of ways and increases muscle strength[27].

The strengths of the present study are particularly evident in its large sample size of the oldest-old population, comprising adults aged ≥80 years. However, the relatively lower number of participants with AMD (n = 64) may have limited the power of certain subgroup analyses. Furthermore, the study sample was restricted to individuals from a single hospital in Turkey and may not be representative of older adults in other settings. Conversely, the specificity of the analyzed demographic group, comprising the oldest-old adult population, enhances the relevance and applicability of the findings in the context of geriatric research. Further research incorporating more diverse samples from multiple locations or employing more rigorous selection criteria could enhance the robustness and applicability of the present findings. It is important to note that the cross-sectional design employed in this study also imposed limitations on the determination of causality. Furthermore, the diagnostic methods employed to identify sarcopenia, including handgrip strength and sit-to-stand tests, are reliable and represent a valuable assessment approach for the oldest-old population, but they might not fully elucidate the full disease spectrum. A more comprehensive understanding of the impact of sarcopenia on AMD could be gained through broader assessments including invasive procedures such as muscle biopsy. In addition, studies that incorporate the type and duration of AMD and sarcopenia in their statistical analyses would allow a clearer understanding of the relationship between the two diseases. Furthermore, the inclusion of individuals presenting for a multitude of reasons may have introduced selection bias, as potential confounding variables such as nutritional status, lifestyle, physical activity levels, and psychological factors may have been present. Another limitation of our study is that it was anticipated that the number of individuals undergoing cataract surgery would be high because the patients were over 80 years of age. Therefore, whether participants were pseudophakic or not was not evaluated in this study. As a result, the ability to draw definitive conclusions about the directionality of the observed relationship is limited. It is recommended that future investigations examine this relationship using prospective study designs to better elucidate the dynamics at play and provide a more robust understanding of the underlying causal mechanisms.

In conclusion, the presence of sarcopenia in older individuals was found to be associated with an independent increased risk of AMD. Healthcare providers should devote more attention to the screening and management of sarcopenia in the oldest-old population. The results of this study reveal that sarcopenia shows an independent association with the development of AMD in older individuals, highlighting the potential effects of muscle mass loss on metabolic disorders. These findings suggest that sarcopenia may be a critical determinant not only of physical functioning but also of metabolic health. Accordingly, prospective studies should further investigate the causal relationship between sarcopenia and AMD. Furthermore, randomized controlled trials evaluating the effects of targeted interventions for sarcopenia (e.g., resistance exercises, protein-supported nutritional approaches and multidisciplinary follow-up programs) on AMD are expected to make important contributions to the literature. The data to be obtained will form the basis for the development of both preventive and therapeutic strategies in terms of holistic health management of elderly individuals.

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