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SARCOPENIA, AND CHRONIC PAIN IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME

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Abstract

Introduction: We aimed to investigate whether the rate of sarcopenia is higher in patients with pseudoexfoliation syndrome and if an association exists between pseudoexfoliation syndrome, sarcopenia parameters, and chronic musculoskeletal pain.

Materials and Method: A total of 96 enrolled patients were divided into two equal groups: "pseudoexfoliation syndrome group" and "no pseudoexfoliation syndrome group". The variables were demographic characteristics, sarcopenia parameters (SARC-F, hand-grip strength, chair-rise test, gait speed), and pain parameters (having any chronic musculoskeletal pain, pain regions, and Visual Analog Scale-pain).

Results: Comparison of sarcopenia and pain parameters between the two groups showed that SARC-F (all groups:p<0.001, 65-74 years:p<0,001, 75-84 years:p=0,015), chair rise test (all groups:p<0.001, 65-74 years:p=0,002, 75-84 years:p=0,003), and Visual Analog Scale-pain (all groups:p<0.001, 65-74 years:p=0,007, 75-84 years:p=0,003) scores were statistically significantly higher, while the gait speed (all groups:p<0.001, 65-74 years:p=0,004, 75-84 years:p=0,007) score was significantly lower in "pseudoexfoliation syndrome group" than in "no pseudoexfoliation syndrome group". 60.4% of patients with pseudoexfoliation syndrome had probable sarcopenia, and 83% had chronic musculoskeletal pain. A comparison of the two groups showed that the rate of sarcopenia (all groups:p<0.001, 65-74 years:p<0,001, 75-84 years: p=0,014) and the rate of having chronic musculoskeletal pain (all groups, 75-84 years: p=0.002) was significantly higher in patients with pseudoexfoliation syndrome.

Conclusion: Our study results showed that most patients with pseudoexfoliation syndrome had chronic musculoskeletal pain and probable sarcopenia. Although pseudoexfoliation syndrome and sarcopenia are problems of aging, further research is needed to explain the pathogenetic mechanisms underlying the high rate of sarcopenia and chronic pain in patients with pseudoexfoliation syndrome. ClinicalTrials.gov Identifier: NCT06121154

Keywords: Chronic Pain; Exfoliation Syndrome; Sarcopenia.

INTRODUCTION

Sarcopenia is defined as decreased muscle mass, muscle strength, and muscle function, which leads to lower physical performance, disability, and a reduced quality of life. The European Working Group on Sarcopenia in Older People (EWGSOP) produced a consensus paper, EWGSOP2 (1). In that consensus, muscle strength was the key parameter of sarcopenia; following SARC-F, low muscle strength was enough to screen for causes and start clinical intervention (2). The prevalence of sarcopenia reported in a study in Turkey was 5.2% (3). The prevalence of sarcopenia and chronic musculoskeletal pain problems increases with age. Bakılan et al. (4) reported a noteworthy correlation between sarcopenia and chronic musculoskeletal pain.

Pseudoexfoliation syndrome (PEX) is an age-related, genetic, and systemic disease characterized by abnormal extracellular fibrillar material accumulation in many ocular and extraocular tissues (5). In a biomicroscopic examination, PEX can be easily diagnosed by observing anterior segment changes characterized by white deposits on the pupillary border and anterior lens (6). PEX has been reported to have a high frequency in Scandinavian countries, Türkiye, Greece, and Saudi Arabia. Yildirim et al. (7) reported the frequency of PEX as 5% in people >40 years old in the Central Anatolia region. In addition to the ocular tissues, exfoliating material has been shown to accumulate in the connective tissue layers of the skin and visceral organs, the periphery of blood vessels, and both the smooth muscle layers of the visceral organs. Previous studies have demonstrated the accumulation of cross-linked polyethylene (PEX) materials within the striated muscle layers of visceral organs and cardiac muscles, leading to impaired systolic function of the heart (8,9). On the other hand, sarcopenia affects the striated muscles and decreases muscle mass and function. Sarcopenia and PEX are aging disorders affecting striated muscles and connective tissues. Although the relationship between PEX and systemic diseases such as coronary artery disease, stroke, and sensorineural hearing loss has been extensively researched in the literature (6,10), to the best of our knowledge, the relationship between PEX and sarcopenia has not been investigated. Other studies investigating musculoskeletal system problems associated with PEX are also limited. In a study, sensorial nerve latency was reported to be longer, and sensorial nerve conduction amplitude and velocity were reported to be lower in patients with PEX. The sensory nerves also play a role in the pain mechanism (11). The other study reported the relationship between PEX and calcium channels (12). These calcium channel problems were also detected in chronic pain conditions such as migraine (13). Only one study was found concerning the relationship between PEX and chronic musculoskeletal pain. Ucar et al. (14) reported a possible relationship between osteoarthritis and PEX. Patients with PEX had higher knee pain scores and this finding has been reported to be associated with disturbance of connective tissue metabolism. To the best of our knowledge, despite the existence of such common mechanisms in PEX and pain, no study examining the relationship between PEX and chronic musculoskeletal pain, except for knee pain, has been identified in the literature.

Pseudoexfoliation syndrome, sarcopenia, and chronic pain are all aging disorders affecting connective tissue and striated muscles, PEX may contribute to sarcopenia and chronic musculoskeletal pain through common pathways. The first aim of this study was to investigate whether the rate of sarcopenia was higher in patients with PEX. The second aim was to investigate any association between PEX, sarcopenia parameters (SARC-F, chair rise test, grip strength, gait speed), and chronic musculoskeletal pain.

MATERIALS AND METHOD

This case-control study involved 96 patients who were admitted to the Department of Physical Medicine and Rehabilitation Outpatient Clinic at

Eskişehir Osmangazi University Hospital, between March and August 2023. The inclusion criteria were being ≥60 years old and undergoing a detailed complete ophthalmic examination by an experienced physician within one month at the Department of Ophthalmology in the same hospital.

The exclusion criteria were having ophthalmic diseases that cause vision loss and reduce quality of life and mobility, including smoking, acute/subacute pain, amputation, infection, active arthritis, active cancer, having any prosthesis or surgery in the lower extremities and lower back, neurological disorders, malabsorption, weight loss, uncontrolled major systemic diseases, impaired cognitive function, and being immobilized.

The detailed complete ophthalmic examination included evaluations of refraction, visual acuity, intraocular pressure (Goldmann applanation tonometry), and anterior and posterior segment examinations.

The criteria to diagnose PEX were, after pupillary dilatation, white fluffy dandruff-like material on ≥1 anterior segment structures, including the pupillary margin, the anterior lens capsule, or the angle in the biomicroscopic examination. The patients were categorized into two groups according to their PEX-positive (n = 48) or PEX-negative (n = 48) status (7).

All patients were questioned on their age, gender, weight, height, drug usage, cane usage, educational/employment status, family type, and systemic diseases.

A physiatrist carried out a detailed musculoskeletal examination. Chronic musculoskeletal pain was accepted as persistent pain for >3 months, and the pain regions (upper extremity/cervical region, lower extremity/lumbar region, and the whole body) were recorded. The Visual Analog Scale (VAS) was used to measure general body pain severity, with assessments ranging from "zero" (indicating no pain) to "ten" (worst conceivable pain) (15).

The SARC-F is recommended in the EWGSOP2 to determine sarcopenia patients in usual geriatric practice. The SARC-F has five questions evaluating strength, assistance in ambulation, chair rise, climbing stairs, and falls. The cut-off point for predicting sarcopenia is a score of 4; "4 and more" means there is a risk of sarcopenia. Low gait speed is characterized by walking slower than 0.8 meters per second. Low muscle strength was evaluated with the "chair rise test" and the "grip strength". The EWGSOP2 recommends using the chair rise test to assess the strength of leg muscles. This test measures the time taken to rise from the sitting position without using the upper extremities five times, and the strength of the muscles is defined as "low" when the time taken is more than fifteen seconds (1). Grip strength was assessed using a hand-held dynamometer (Baseline, White Plains, New York, USA), and the cut-off thresholds were 32 kg for males and 22 kg for females. "Probable sarcopenia" was defined according to the EWGSOP2 algorithm as having a "4 and more" score in SARC-F with low muscle strength (1).

The Physical Activity Scale for the Elderly (PASE) is a questionnaire, comprising 12 questions concerning the frequency and duration of various activities conducted during the preceding week. These activities encompass leisure pursuits, household chores, and occupational tasks. The questionnaire employs diverse scoring methods: leisure and strengthening activities are graded based on frequency (ranging from "never" to "often") and duration (categorized into different time intervals), while household and work-related activities are simply marked as "yes" or "no." In the case of work-related activities, the duration was quantified in hours per week, regardless of whether the work was paid or unpaid. The final PASE score is calculated by assigning empirically derived weights to each activity and summing up the scores obtained from all activities (16).

Written informed consent was obtained from all patients. This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval was granted by the Local Ethics Committee, with the date and number 21/02/23-22.

Statistical Analysis

A total of 96 patients were determined as the required sample size (48 patients allocated to each group) with a sufficient statistical power 0.80 and a moderate effect size (0,52) using G*Power software package (version 3.1.9.4) (Franz Faul, Universität Kiel, Düsseldorf, Germany). Furthermore, the power of our study, calculated based on the SARC-F outcome (alpha = 0.05), was determined to be 0.99. The distribution of each continuous variable was assessed for normality using the Shapiro-Wilk test. Normally distributed variables were compared using the t-test and expressed as mean ± standard deviation (SD). Non-normally distributed variables were compared using the Mann-Whitney U test and presented as median values (25%-75%). Categorical variables were conveyed as frequencies and percentages and were compared using the Chi-square test. A p-value less than 0.05 was considered statistically significant. All analyses were performed using the SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 96 patients (51 female, 45 male) (mean age: 71.18 ± 6.93) were included in the study. The demographic characteristics of the two groups were statistically similar (Table 1).

Table 1. Comparison of demographic characteristics between PEX-positive and PEX-negative patients

		PEX-positive (n=48)	PEX-negative (n=48)	p value
Age (25-75%)		73,0 (66,25-76,0)	69,50 (64,0-73,75)	0,076
Gender (female/male) n (%)		25 (52,1%) / 23 (47,9%)	26 (54,2%) / 22 (45,8%)	0,838
Body Mass Index (mean±SD)		28,86±4,59	27,43±4,14	0,114
Chronic diseases (yes) n (%)		40 (83,3%)	41 (85,4%)	0,416
DM (yes)		19 (39,5%)	23 (47,9%)	0,411
Cardiac Disease (yes)		18 (37,5%)	12 (25,0%)	0,186
COPD (yes)		8 (16,6%)	9 (18,7%)	0,789
Hipertension (yes)		30 (62,5%)	34 (70,8%)	0,386
Employment status n (%)	Working	1 (2,0%)	3 (6,3%)	0,369
	Never worked	17 (35,5%)	21 (43,7%)	
	Retired	30 (62,5%)	24 (50%)	
Educational status n (%)	Lower than high school	32 (66,7%)	38 (79,2%)	0,251
	High school and higher	16 (33,3%)	10 (20,8%)	
Family status n (%)	Alone	7 (14,6%)	11 (22,9%)	0,576
	Nuclear family	34 (70,8%)	31 (64,6%)	
	Extended family	7 (14,6%)	6 (12,5%)	
Cane usage (yes) n (%)		1 (2%)	2 (4,1%)	0,557

(PEX: pseudo-exfoliation syndrome, SD: Standard deviation, DM: Diabetes mellitus, COPD: Chronic obstuctive pulmonary disease, Most of the patients had more than one chronic diseases)

Table 2. Comparison of ophtalmologic characteristics between PEX-positive and PEX-negative patients

		PEX-positive (n=48)	PEX-negative (n=48)	p value
PEX n(%)	Unilateral	38 (79,2%)		
	Bilateral	10 (20,8%)		
Refraction errors (yes) n (%)		25 (89,3%)	28 (58,3%)	0,583
Glaucoma n (%) (yes)		44 (91,7%)	22 (45,9%)	<0,001
Maculopathy n (%) (yes)		17 (35,4%)	16 (33,3%)	0,830
Cataract n (%) (yes)		33 (68,7%)	29 (60,4%)	0,393

(PEX: pseudoexfoliation syndrome)

Table 3. Comparison of pain, sarcopenia parameters and PASE scores between PEX-positive and PEX-negative patients according to age groups

			All patients (n=96)			65-74 years (n=46)			75-84 years (n=27)		
			PEX-positive (n=48)	PEX-negative (n=48)	p value	PEX-positive (n=21)	PEX-negative (n=25)	P value	PEX-positive (n=18)	PEX-negative (n=9)	p value
Sarcopenia parameters (mean±SD)	**SARC-F score**		4,29±2,56	1,52±1,84	**<0,001**	3,90±1,92	1,44±1,75	**<0,001**	5,38±3,10	2,44±1,81	**0,015**
	Gait Speed		0,84±0,28	1,05±0,18	**<0,001**	0,87±0,19	1,04±0,17	**0,004**	0,72±0,24	1±0,19	**0,007**
	Grip Strength		23,10±8,41	25,39±6,72	0,144	23,33±8,47	23,68±6,37	0,875	21,16±8,67	24,11±5,92	0,370
	Chair Rise Test		17,71±5,95	12,54±3,15	**<0,001**	15,63±3,70	12,38±2,62	**0,002**	20,82±6,27	15,38±2,15	**0,003**
Pain parameters	**Chronic musculoskeletal pain (yes) n(%)**		40 (83,3%)	26 (54,1%)	**0,002**	17 (80,9%)	15 (60%)	0,124	18(100%)	5 (55,5%)	**0,002**
	Pain Regions n(%)	**Upper extremity and cervical region**	2 (5,0%)	3 (11,5%)	0,582	2 (11,8%)	2 (13,3%)	0,981	0 (0%)	1 (20%)	0,142
		Lower extremity and lumbar region	28 (70%)	16 (61,5%)		10 (58,8%)	9 (60%)		15 (83,3%)	3 (60%)	
		Whole body	10 (25,0%)	7 (27,0%)		5 (29,4)	4 (26,7%)		3 (16,7%)	1 (20%)	
	VAS (25-75%)		5,0 (2,25-6,75)	1,0 (0-3,0)	**<0,001**	5 (1,5-7)	2 (0-3)	**0,007**	5 (3,75-7)	2 (0-3,5)	**0,003**
PASE score (25-75%)			31,5 (28-44,25)	30 (20-50)	0,298	31 (20-35,75)	30 (28-46,50)	0,575	27 (17,5-55)	25 (15-60)	0,909

(PEX: pseudoexfoliation syndrome, VAS: Visual analog scale, PASE: the Physical Activity Scale for the Elderly)

Table 4. The relation between PEX and sarcopenia according to age groups

	All patients (n=96)			65-74 years (n=46)			75-84 years (n=27)		
	PEX-positive (n=48)	PEX-negative (n=48)	P value	PEX-positive (n=21)	PEX-negative (n=25)	P value	PEX-positive (n=18)	PEX-negative (n=9)	P value
No sarcopenia n (%)	19 (39,6%)	42 (87,5%)	**<0,001**	8 (38,1%)	22 (88,0%)	**<0,001**	5 (27,8%)	7 (77,8%)	**0,014**
Sarcopenia n (%)	29 (60,4%)	6 (12,5%)		13 (61,9%)	3 (12,0%)		13 (72,2%)	2 (22,2%)	

(PEX: pseudoexfoliation syndrome)

The ophthalmologic characteristics of the patients are given in Table 2.

The patients were evaluated according to age groups (all patients, 65-74 years, 75-84 years). The PASE scores were similar between PEX-positive and PEX-negative patients in all age groups. The evaluation of all patients showed that 83% of the PEX-positive patients had certain chronic musculoskeletal pain, while this rate was 54% in PEX-negative patients. SARC-F score (all groups: p <0.001, 65-74 years: p<0,001, 75-84 years: p=0,015) chair rise test (all groups: p <0.001, 65-74 years: p=0,002, 75-84 years: p=0,003) and VAS scores (all groups: p <0.001, 65-74 years: p=0,007, 75-84 years: p=0,003) were significantly higher in PEX-positive patients than in PEX-negative patients while gait speed (all groups: p <0.001, 65-74 years: p=0,004, 75-84 years: p=0,007) were significantly lower in PEX-positive patients than in PEX-negative patients. The rate of having chronic musculoskeletal pain (all groups: p=0.002, 75-84 years: p=0,002) were statistically significantly higher in PEX-positive patients than in PEX-negative patients. However, grip strength (p>0,005) and pain regions (p>0,005) were statistically similar between the PEX-positive and PEX-negative in all age groups. (Table 3).

The evaluation of all patients showed that probable sarcopenia was identified in 29 (60.4%) patients in the PEX-positive group and 6 (12.5%) patients in the PEX-negative group. A comparison of the two groups showed that the rate of sarcopenia was significantly higher in the PEX-positive group (all groups: p <0.001, 65-74 years: p<0,001, 75-84 years: p=0,014). In patients aged between 65 and 74 years, 13 (61,9%) of 21 PEX-positive patients had probable sarcopenia while 3 (12%) of 25 PEX-negative patients had probable sarcopenia (p<0.001) Also in patients aged between 75 and 84 years, 13 (72,2%) of 18 PEX-positive patients had probable sarcopenia while 2 (22,2%) of 9 PEX-negative patients had probable sarcopenia. (p=0.014) (Table 4).

DISCUSSION

To the best of our knowledge, in the existing literature, there was no study examining the relationship between PEX and either sarcopenia or chronic pain. Our study was conducted in the geriatric population according to age groups and the findings of this study indicated that in the aging population, most patients with PEX had certain chronic musculoskeletal pain and probable sarcopenia.

Our results showed that the VAS-pain scores were higher in patients with PEX in all three age groups. Besides that, only the rate of chronic musculoskeletal pain showed statistically higher rates in PEX-positive patients compared to PEX-negative patients in all group analyses and the 75-84 years age group. However, despite chronic

musculoskeletal pain being present in 80% of PEX-positive patients and 60% of PEX-negative patients in the 65-74 years age group, no statistical difference was observed.

Only one other study was observed evaluating VAS-pain scores in patients with PEX. Ucar et al. (14) reported a probable relationship between osteoarthritis and PEX. Similar to our study, pain scores were evaluated using the VAS, and the VAS values of patients who were PEX-positive were significantly higher than those of patients who were PEX-negative. Thus, these two studies observed a similar result that patients with PEX had higher musculoskeletal pain scores. In the literature, we could not identify any study regarding the relationship between chronic pain and PEX. One possible underlying mechanism may be that PEX affects peripheral nerves, especially sensorial nerve fibers. Coban et al. (11) compared electroneuromyographic findings between patients who were PEX-positive and PEX-negative, and sensorial nerve latency was observed to be longer. In contrast, sensorial nerve conduction amplitude and velocity were lower in patients who were PEX-positive.

Taner et al. (17) reported that PEX is associated with atrial electromechanical delay. Additionally, myocardial systolic velocities were observed to be lower in patients with PEX. The risk of arrhythmia was reported to be higher in PEX and a decreased global arousal threshold may be associated with a decreased arousal threshold of sensory nerves that cause pain.

Aung et al. (12) reported a significant relationship between the *CACNA1A* rs4926244 locus and increased susceptibility to the development of PEX. *CACNA1A* encodes the alpha 1A subunit of the type P/Q voltage-gated calcium channel, which involves multiple processes, such as neurotransmitter release and is widely expressed throughout the central nervous system. In addition, *CACNA1A* mutations are observed in a few patients with craniofacial pain, such as migraine (13). The relationship between calcium channels and pain, decreased thresholds, and sensory nerve fiber involvement in PEX may explain the relationship between PEX and chronic pain. Further studies are needed to explain the exact underlying mechanisms.

Our results showed that 60.4% of all our patients who were PEX-positive had probable sarcopenia, this rate was 61% in patients aged between 65-74 and 72% in patients aged between 75-84. Moreover, their SARC-F scores and chair rise test scores were higher, while gait speed was lower in patients who were PEX-positive than in patients who were PEX-negative. A literature review reveals no study evaluating a relationship between PEX and sarcopenia. Possible mechanisms underlying this association are described below.

In previous studies, PEX material has accumulated in the striated muscle layers of the visceral organs and cardiac muscle (8,9). In addition to the involvement of the cardiac muscle, the systolic function of the heart was observed to be impaired in previous studies (17). Sarcopenia affects the striated muscles and decreases muscle mass and function. The detection of sarcopenia in most patients with PEX here made us contemplate that PEX might affect striated muscles in the musculoskeletal system, including cardiac muscle. Further studies are needed in this area.

Vascular disorders are more common in patients with PEX and those with sarcopenia. Lower basal capillary perfusion in the fingers of patients who were PEX-positive and histological microvascular changes (8) have been reported previously. Earlier studies have reported that sarcopenia is known to aggravate vascular disorders such as atherosclerosis. This association was explained as being due to the alteration of intracellular mechanisms caused by changes in myokine secretion and poor vascular hemostasis (18).

The skeletal muscle extracellular matrix comprises collagen and other connective tissue proteins, such as elastin. Fibrosis is the key mechanism in sarcopenia pathogenesis, and overexpression of TGF-β1 promotes fibrosis around myofibers and activates myofibroblasts to produce collagen and fibronectin (19). In PEX cases, Mastronikolis et al. (20) reported that overexpression of TGF-β induces the expression of LOXL1 (lysyl oxidase-like 1), belonging to the lysyl oxidase (LOX) family. LOXL1, LOXL2, LOXL3, and LOXL4 are extracellular copper-dependent enzymes that play an important role in cross-linking of the extracellular matrix. LOXL1, which catalyzes the first step in collagen and elastin cross-linking in connective tissues, was identified as a strong genetic risk factor for PEX (20). In addition, a recent study highlighted that treatment with a LOXL2 inhibitor reduced skeletal muscle fibrosis and increased muscle mass and strength in mice (21). TGF-β and LOX family members affect connective tissue in PEX and seem to affect sarcopenia.

From the above data, a relationship between sarcopenia and PEX can be inferred. Both conditions could result from chronic inflammation and an imbalance between oxidants and antioxidants. The pathogenesis of sarcopenia is multifactorial and is usually related to oxidative stress (22), systemic inflammation, endocrine function changes, immobility, mitochondrial dysfunction, and malnutrition (23). Most of these factors do not act in isolation and intersect or overlap in relation to oxidative stress. Sullivan-Gunn et al. (24) reported that hydrogen peroxide, catalase, and glutathione peroxidase play key roles in the onset of sarcopenia in an aging mouse model. Similarly, Yaz et al. (25) reported that serum malondialdehyde levels, superoxide dismutase, catalase enzymic activities, and glutathione levels significantly differ in patients who were PEX-positive compared to those in patients who were PEX-negative.

Both sarcopenia and PEX have similar pathogenetic pathways, including increased oxidative stress and vascular disorders, dysregulation of LOX family members, and altered function of calcium transport.

The main limitation of this study is not adopting a definitive diagnosis of pain conditions, such as disc herniation or osteoarthritis. The other limitations were the small number of patients and not evaluating chronic pain with an objective parameter. A strength of this study is that it excluded patients with ophthalmic diseases that cause vision loss and reduce quality of life and mobility because vision impairment in older adult patients can lead to physical inactivity and inappropriate nutrition. Although PEX and sarcopenia are both prevalent problems in the aging population, additional studies are needed to explain the pathogenetic mechanisms responsible for the elevated occurrence of sarcopenia and chronic pain among PEX patients.

Previous studies primarily focused on visceral organs, the heart, and the central nervous system, however, limited literature focused on the musculoskeletal system. The advantage of our research over other previous studies is that it is the first which evaluate the musculoskeletal system in terms of the relationship between PEX and either sarcopenia or chronic musculoskeletal pain. Most of the patients with PEX had probable sarcopenia and chronic musculoskeletal pain in our study. Based on our findings, it can be concluded that patients with PEX should be evaluated by a physiatrist for chronic pain and sarcopenia. PEX is most commonly diagnosed in the ophthalmology department, and increasing awareness among ophthalmologists about sarcopenia and chronic musculoskeletal pain may lead to early referral for physiatrist consultation, which can significantly improve the quality of life for these patients.

REFERENCES

1. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019; 48(1):16-31. (DOI: 10.1093/ageing/afy169)
2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; 39(4):412–23. (DOI: 10.1093/ageing/afq034)
3. Simsek H, Meseri R, Sahin S, et al. Prevalence of sarcopenia and related factors in community-dwelling elderly individuals. Saudi Med J. 2019; 40(6):568-74. (DOI: 10.15537/smj.2019.6.23917)
4. Bakilan F, Ozgen M, Ortanca B, et al. The relationship between chronic musculoskeletal pain, quality of life and sarcopenia. Turk J Geriatr. 2021; 24(1):60-70. (DOI: 10.31086/tjgeri.2021.200)
5. Ritch R, Schlotzer-Schrehardt U. Exfoliation syndrome. Surv Ophthalmol. 2001; 45(4):265– 315. (DOI: 10.1016/s0039-6257(00)00196-x)
6. Wang W, He M, Zhou M, Zhang X. Ocular pseudoexfoliation syndrome and vascular disease: a systematic review and meta-analysis. PLoS One. 2014; 9(3):e92767. (DOI: 10.1371/journal.pone.0092767)
7. Yildirim N, Yasar E, Gursoy H, Colak E. Prevalence of pseudoexfoliation syndrome and its association with ocular and systemic diseases in Eskisehir, Turkey. Int J Ophthalmol. 2017;10(1):128-34. (DOI: 10.18240/ijo.2017.01.21)
8. Schlötzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. Am J Opthalmol. 2006; 141(5):921-37. (DOI: 10.1016/j.ajo.2006.01.047)
9. Naumann GO, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist: intraocular and systemic manifestations. Ophthalmology. 1998; 105(6):951-68. (DOI: 10.1016/S0161-6420(98)96020-1)
10. Samarai V, Samarei R, Haghighi N, Jalili E. Sensory-neural hearing loss in pseudoexfoliation syndrome. Int. J. Ophthalmol. 2012; 5(3):393-96. (DOI: 10.3980/j.issn.2222-3959.2012.03.28)
11. Coban DT, Cakir T, Erol MK, et al. Electroneuromyographic findings in pseudoexfoliation syndrome. Int Ophthalmol. 2018;38(2):705-12. (DOI: 10.1007/s10792-017-0520-8)
12. Aung T, Ozaki M, Mizoguchi T, et al. A common variant mapping to CACNA1A is associated with susceptibility to exfoliation syndrome. Nat Genet. 2015;47(4):387-92. (DOI: 10.1038/ng.3226)
13. Grieco GS, Gagliardi S, Ricca I, et al. New CACNA1A deletions are associated to migraine phenotypes. J Headache Pain. 2018;19(1):75. DOI: (10.1186/s10194-018-0891-x)
14. Ucar M, Sarp U, Kirboga K, Adam M, Arik HO, Gundogdu F. Is there an association between pseudoexfoliation syndrome and knee osteoarthritis? Z Rheumatol. 2015;74(9):819-23. (DOI: 10.1007/s00393-015-1575-4)
15. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. Ann Emerg Med. 2001;38(6):633-8. (DOI: 10.1067/mem.2001.118863)
16. Ayvat E, Kilinc M, Kirdi N. The Turkish version of the Physical Activity Scale for theElderly (PASE): its cultural adaptation, validation, and reliability. Turkish journal of medical sciences 2017;47(3):908-15. (DOI:10.3906/sag-1605-7)
17. Ulus T, Isgandarov K, Moghanchizadeh SH, Bozkurt M, Mutlu F, Yıldırım N. Atrial Conduction Time in Patients with Pseudoexfoliation Syndrome. OJM. 2019;41(1):31-38. (DOI: 10.20515/otd.412143) (in Turkish)
18. Jo D, Yoon G, Kim OY, Song J. A new paradigm in sarcopenia: cognitive impairment caused by imbalanced myokine secretion and vascular dysfunction. Biomed Pharmacother. 2022;147:112636. (DOI: 10.1016/j.biopha.2022.112636)
19. Marty E, Liu Y, Andre S, Or O, Lane J. A review of sarcopenia: enhancing awareness of an increasingly prevalent disease. Bone. 2017;105:276-86. (DOI: 10.1016/j.bone.2017.09.008)
20. 2Mastronikolis S, Pagkalou M, Baroutas G, Kyriakopoulou K, Makri OE, Georgakopoulos CD. Pseudoexfoliation syndrome: The critical role of the extracellular matrix in pathogenesis and treatment. IUBMB Life. 2022;74(10):995-1002. (DOI: 10.1002/iub.2606)
21. Wu Y, Wu Y, Yang Y, et al. Lysyl oxidase-like 2 inhibitor rescues D-galactose-induced skeletal muscle fibrosis. Aging Cell. 2022;21(7):e13659. (DOI: 10.1111/acel.13659)

22. Meng SJ, Yu LJ. Oxidative stress, molecular inflammation and sarcopenia. Int J Mol Sci. 2010;11(4):1509-26. (DOI: 10.3390/ijms11041509)

23. Rolland Y, Czerwinski S, Abellan Van Kan G, et al. Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. J Nutr Health Aging. 2008;12(7):433-50. (DOI: 10.1007/BF02982704)

24. Sullivan-Gunn MJ, Lewandowski PA. Elevated hydrogen peroxide and decreased catalase and glutathione peroxidase protection are associated with aging sarcopenia. BMC Geriatr. 2013;13:104. (DOI: 10.1186/1471-2318-13-104)

25. Yaz YA, Yıldırım N, Yaz Y, Tekin N, Inal M, Sahin FM. Role of oxidative stress in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Turk J Ophthalmol. 2019;49(2):61-7. (DOI: 10.4274/tjo.galenos.2018.10734)