

ORIGINAL ARTICLE

Medicine Science 2022;11(2):645-50

Association of sarcopenia with geriatric syndromes and neutrophil / lymphocyte ratio

ID Veysel Suzan, ID Bahar Bektan Kanat, ID Hakan Yavuzer

*Cerrahpaşa Faculty of Medicine, Division of Geriatric, Department of Internal Medicine, Istanbul, Turkey*Received 23 December 2021; Accepted 06 March 2022
Available online 09.03.2022 with doi: 10.5455/medscience.2021.12.394Copyright©Author(s) - Available online at www.medicinescience.org
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Abstract

We aimed to search the relationship of sarcopenia with chronic diseases, geriatric syndromes and neutrophil/lymphocyte ratio (NLR). Our study included 258 patients who were admitted to Cerrahpaşa Medical Faculty geriatrics outpatient clinic for the first time between March 2018 and February 2019, and underwent comprehensive geriatric evaluation. Patients under 65 years of age, with active infection, terminal illness, diagnosis of malignancy, presence of trauma and infection in the last month were excluded from the study. Sarcopenia was present in 77 (30%) of the 258 participants involved in the study. Frequency of diabetes mellitus, dementia, delirium, polypharmacy and malnutrition was statistically significantly higher in patients with sarcopenia compared to patients without sarcopenia ($p=0.020$, $p=0.024$, $p=0.016$, $p=0.018$ and $p<0.001$, respectively). In multivariate logistic regression analysis, only malnutrition was found to be independently associated with sarcopenia [odds ratio (OR) 5.455 (95% confidence interval (CI) 2.981–9.984, $p<0.001$]. Patients with sarcopenia had statistically significantly higher NLR, sedimentation and C-reactive protein (CRP) values than patients without sarcopenia ($p=0.030$, $p=0.002$ and $p=0.015$, respectively). Area under the ROC curve (AUC) of NLR was found to be 0.60 [odds ratio (OR) 1.214 (95% confidence interval (CI) 1.016–1.451, $p=0.033$]. The significant relationship between sarcopenia and malnutrition revealed that these two geriatric syndromes should be evaluated together. In addition, increased CRP, sedimentation and NLR in sarcopenia support the idea of mild chronic inflammation in sarcopenia. More comprehensive studies are required to evaluate the usability of NLR in screening for sarcopenia.

Keywords: Sarcopenia, malnutrition, geriatric syndrome, neutrophil/lymphocyte ratio

Introduction

A syndrome is defined as a set of signs and symptoms leading to a particular disorder. Geriatric syndromes are considered to be clinical conditions with common risk factors in older adults [1]. Although geriatric syndromes seem like mixed pictures, they have common features. In geriatric syndromes, multiple organ systems are affected and there are multiple risk factors. Geriatric syndromes, such as malnutrition, cognitive impairment, delirium, depression, sleep problems, urinary incontinence, sarcopenia and polypharmacy causes increased mortality, morbidity and health care costs [2].

Sarcopenia is an important geriatric syndrome that has been studied more in recent years. If not treated; sarcopenia causes deterioration in basic and instrumental activities of daily living, falls, cognitive impairment and an increase in hospitalizations. Sarcopenia is an important geriatric syndrome that is associated with a decrease in both muscle quality and quantity, and is often overlooked and undertreated. For all these reasons, the European Working Group on Sarcopenia in Older People (EWGSOP2) was gathered in 2018 to determine universal diagnostic criteria, measurements and treatment recommendations. In this consensus, it was emphasized that muscle strength was stronger in predicting negative outcomes than muscle mass, and it was recommended to evaluate first muscle strength in the diagnosis of sarcopenia. When low muscle mass is added to low muscle strength, the diagnosis of sarcopenia is confirmed. It was stated that physical performance is important in showing severity rather than diagnosis. In EWGSOP2, sarcopenia was classified as primary and secondary. While the common causes of secondary sarcopenia were shown as malnutrition, inactivity and diseases, sarcopenia due to aging without accompanying

*Corresponding Author: Veysel Suzan, Cerrahpaşa Faculty of Medicine, Division of Geriatric, Department of Internal Medicine, Istanbul, Turkey
E-mail: veysel.suzan@hotmail.com

causes of secondary sarcopenia was called primary sarcopenia [3].

Many factors play a role in the pathogenesis of sarcopenia and one of them is chronic inflammation. There are studies in the literature showing that inflammatory cytokines are increased in sarcopenia [4,5]. There are studies in which inflammatory measurements such as neutrophil and neutrophil lymphocyte ratio (NLR) are associated with different diseases, just as in sarcopenia. Tan et al. evaluated the preoperative blood of patients who were operated with the diagnosis of chronic otitis media and found statistically significantly higher neutrophil values in patients with cholesteatoma compared to patients without cholesteatoma [6]. Azab et al. investigated NLR to predict mortality in 316 patients with breast cancer and found $NLR > 3.3$ as an independent factor for mortality [7]. Tamhane et al. also showed that NLR at admission to hospital independently predicted 6-month mortality in acute coronary syndrome [8]. As can be seen from these studies, complete blood count, which is simple, easily accessible and inexpensive, gives us information about inflammation.

Geriatric syndromes have common risk factors and are related to each other in a cause-effect relationship. It is important to know the changes that develop in organs and systems with aging in order to predict which syndrome may develop in which patient and to develop individual-based prevention-treatment options. In this study, we analyzed the relationship of sarcopenia with chronic diseases and geriatric syndromes. In addition, we aimed to investigate the usability of NLR in screening for sarcopenia.

Materials and Methods

Study population and design

Our study included patients who applied to the geriatrics outpatient clinic for the first time in a one-year period between March 1, 2018 and February 28, 2019. In the exclusion criteria of our study; There were patients under 65 years of age, with active infection, terminal disease, diagnosis of malignancy and active rheumatological disease, as well as patients with hip or spine prosthesis (due to the inability of the Bioelectrical impedance analysis (BIA) device to measure correctly). Approval was obtained from the ethics committee of Cerrahpaşa Faculty of Medicine (Date 09.09.2020-Number 117344).

Evaluation of geriatric syndromes

All prescription or non-prescription drugs, complementary and alternative products, and synthetic nutritional supplements were noted. The use of 5 or more drugs per day was defined as polypharmacy [9].

We used the MNA (Mini Nutritional Assessment) test for the diagnosis of malnutrition. This test was developed in the 1990s and has been validated for use in hospitals, clinics and nursing homes in the geriatric population aged 65 and over. Since its validation, it has become the most widely used test in malnutrition for the elderly. In the first part of the MNA form, there were 6 questions evaluating food consumption, weight loss, mobility, stress or acute illness, presence of neuropsychological problems and BMI. In the second part of the MNA form, questions about dietary habits, medical history, drug use, subjective evaluation of health were

asked and anthropometric measurements were recorded. A score of < 24 out of a total of 30 points indicates that the patient is at risk for malnutrition [10].

The patient's sleep-wake circadian rhythm was questioned in detail by interviewing the patient and his relatives. Insomnia was evaluated by asking the patients whether they had any difficulties in falling asleep and/or maintaining sleep [11].

The new definition of the International Continence Society (ICS) in 2002 brought a more practical approach to urinary incontinence. Accordingly, "any involuntary urinary incontinence, regardless of the amount, is defined as urinary incontinence" [12].

In our study, this criterion was accepted for urinary incontinence. The diagnostic criteria for delirium, one of the geriatric syndromes, were accepted as 'admission to the hospital with delirium in the last year and/or hospitalization or intensive care unit admission with the diagnosis of delirium'.

Patients were evaluated with a comprehensive approach for the diagnosis of osteoporosis. Detailed anamnesis, physical examination, bone density measurement and, if necessary, vertebral imaging were performed for the diagnosis of vertebral fractures. Bone mineral density measurement was performed with dual X-ray absorptiometry (DXA) method and the references of international clinical guidelines for the diagnosis of osteoporosis were used [13].

EWGSOP2 diagnostic criteria were used in the evaluation of sarcopenia [3]. Hand grip dynamometer (Takei® TKK 5401 model) was used for muscle strength measurement and BIA device (Tanita TBF-300 model) was used for muscle mass measurement.

In addition, CRP, sedimentation, neutrophil, lymphocyte, creatinine and hemoglobin values at the time of admission to the outpatient clinic were recorded.

Statistical Analysis

A sample size of 60 patients per group was calculated to provide 80% power to detect the expected difference between the two groups for serum neutrophil/lymphocyte ratio. Chi-square test was applied for categorical variables. Fisher's exact test was performed in cases that did not meet the chi-square criteria. Student's t-test, a parametric test was used for normally distributed continuous variables; and Mann Whitney-U test, a non-parametric test was used for continuous variables that did not distribute normally. The relationship between sarcopenia and geriatric syndromes were analyzed by univariate logistic regression (LR) method. Stepwise multivariate LR method was applied to the significant values after univariate LR analysis. Receiver operating characteristic (ROC) analysis was performed to determine the importance of NLR in the diagnosis of sarcopenia. SPSS-22 statistical program was used for the analysis and $p < 0.05$ was considered statistically significant.

Results

In our study 258 (183 women) patients were included. When we examined the frequency of geriatric syndromes, polypharmacy was seen in 65%, malnutrition 42%, osteoporosis 30%, depression

27%, dementia 17%, incontinence 16%, insomnia 7% and delirium 6%.

Sarcopenia was present in 77 (30%) of the 258 patients included in our study. Fifty-four (70%) of the patients with sarcopenia and 129 (71%) of the patients without sarcopenia were women. In terms of age, the mean of patients with sarcopenia (78.42 ± 7.61) was statistically significantly higher than the mean of patients without sarcopenia (75.67 ± 7.98) ($p=0.011$). Frequency of diabetes mellitus, dementia, delirium, polypharmacy, and malnutrition in patients with sarcopenia was statistically significantly higher than in patients without sarcopenia ($p=0.020$, $p=0.024$, $p=0.016$, $p=0.018$, and $p<0.001$, respectively). Detailed analysis is given in Table 1.

Table 1. Demographic data, chronic diseases and geriatric syndromes of patients with/without sarcopenia

	Sarcopenia	No sarcopenia	p
Number of patients	77	181	
Female (n, %)	54 (%70)	129 (%71)	0.853
Age*	78.42 ± 7.61	75.67 ± 7.98	0.011
Body mass index*	28.39 ± 6.78	28.74 ± 5.23	0.298
Number of drugs*	7.68 ± 4.08	5.95 ± 3.61	0.001
Hypertension (n, %)	57 (%74)	136 (%75)	0.851
Diabetes mellitus (n, %)	41 (%53)	68 (%37)	0.020
Atrial fibrillation (n, %)	13 (%17)	17 (%9)	0.086
Heart failure (n, %)	7 (%9)	15 (%8)	0.833
Chronic renal disease (n, %)	7 (%9)	8 (%4)	0.142
Chronic Obstructive Pulmonary Disease (n, %)	10 (%13)	14 (%8)	0.184
Osteoporosis (n, %)	24 (%31)	54 (%30)	0.831
Parkinson disease (n, %)	7 (%9)	13 (%7)	0.600
Dementia (n, %)	19 (%25)	24 (%13)	0.024
Depression (n, %)	24 (%31)	46 (%25)	0.342
Urinary incontinence (n, %)	14 (%18)	28 (%15)	0.589
Vertigo (n, %)	5 (%7)	19 (%10)	0.311
Delirium (n, %)	9 (%12)	6 (%3)	0.016
Insomnia (n, %)	6 (%8)	11 (%6)	0.611
Polipharmacy (n, %)	59 (%77)	111 (%61)	0.018
Malnutrition (n, %)	55 (%71)	53 (%29)	<0.001

* Mean±standard deviation

Diabetes mellitus, dementia, delirium, polypharmacy and malnutrition were statistically significant in the univariate logistic regression analysis used to investigate the relationship between sarcopenia and diseases and syndromes. In the multivariate logistic regression analysis of these five diseases or syndromes, malnutrition was independently associated with sarcopenia [odds ratio (OR) 5.455 (95%) confidence interval (CI) 2.981–9.984, $p<0.001$] (Table 2).

NLR, sedimentation and CRP values of patients with sarcopenia were statistically significantly higher than patients without sarcopenia ($p=0.030$, $p=0.002$ and $p=0.015$, respectively) (Table 3). AUC of NLR was 0.60 [odds ratio (OR) 1.214 (95%) confidence interval (CI) 1.016–1.451, $p=0.033$]. When the cut-off value of NLR was taken as 2.43, the sensitivity was 63.6% and the specificity was 51.4%. It is shown in Figure 1.

Table 2. Univariate and stepwise multivariate LR analysis of sarcopenia with chronic disease and geriatric syndromes

	Univariate LR		Stepwise Multivariate LR	
	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
Diabetes mellitus	1.893 (1.104-3.246)	0.020		
Dementia	2.143 (1.093-4.200)	0.026		
Delirium	3.860 (1.324-11.257)	0.013		
Polipharmacy	2.067 (1.127-3.792)	0.019		
Malnutrition	5.991 (3.323-10.799)	<0.001	5.455 (2.981-9.984)	<0.001

LR, Logistic Regression; CI, Confidence interval Statistically significant P values are indicated as bold

Table 3. Comparison of laboratory values of patients with/without sarcopenia

	Sarcopenia	No sarcopenia	p
Neutrophil / Lymphocyte Ratio*	3.09 ± 1.52	2.66 ± 1.42	0.030
C-reactive Protein (CRP)** (mg/L)	4 (1.9-11.5)	2.6 (1-6)	0.002
Sedimentation** (mm/hour)	22 (12-35)	18 (8-26)	0.015
Creatinine* (mg/dL)	0.90 ± 0.30	0.95 ± 0.36	0.275
Hemoglobin* (g/dL)	12.19 ± 1.36	12.54 ± 2.00	0.159

* Mean±standard deviation (SD) ** Median (interquartile intervals)

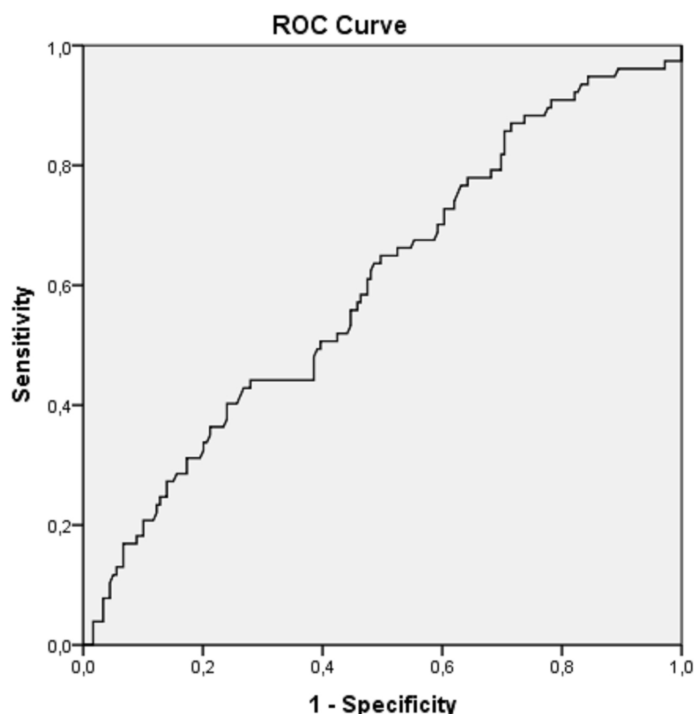


Figure 1. AUC of the neutrophil/lymphocyte ratio in the diagnosis of sarcopenia is 0.60

Discussion

The concept of sarcopenia was first mentioned about 30 years ago [14]. Sarcopenia was included as an separate diagnosis in the ICD-10 coding system in 2016 [15]. Since sarcopenia is associated with many adverse health outcomes such as functional decline, frailty, hospitalization, morbidity and mortality, sarcopenia is getting more and more attention by researchers [3]. Studies searching the relationship between sarcopenia and geriatric syndromes are limited. Therefore, this study aimed to investigate the associations that need attention by revealing the relationship between sarcopenia and geriatric syndromes and NLR.

When we evaluated the prevalence of geriatric syndromes in our study, polypharmacy came first (65%) and was consistent with the literature [16]. In the dementia study, which included 3.4 million people in the USA, the frequency was found to be 14% and was similar to our study (17%) [17]. The frequency of depression ranged from 7 to 49% in the literature, and it was seen at a rate of 27% in our study [18]. The incidence of sarcopenia in our study (30%) was also consistent with the literature [19].

In the literature, there are studies examining the relationship between sarcopenia and only one of the geriatric syndromes. In a study examining the frequency of sarcopenia according to the stages of Alzheimer's disease, it was observed that the prevalence of sarcopenia increased in parallel with the stage of the disease [20]. In a study including twelve geriatric centers, it was shown that the frequency of delirium is higher in patients with sarcopenia [21]. Anagnostis et al. analyzed 15 studies evaluating diabetes mellitus and sarcopenia, and found a significant relationship between them. In this study, diabetes mellitus patients had lower muscle strength and lower physical performance than euglycemic patients, while muscle mass was similar [22]. To investigate the relationship

between sarcopenia and polypharmacy, Pana et al. reviewed the literature between March and May 2021, without time limit, including 22 studies and found a correlation between sarcopenia and polypharmacy in community-dwelling patients [23]. Erdogan et al. detected urinary incontinence at a rate of 48% in 802 female patients over 60 years of age and examined its relationship with sarcopenia. As a result of this study, they found that sarcopenia is an independent risk factor for urinary incontinence. [24]. A systematic review and meta-analysis of the relationship between sarcopenia and depression included 15 studies, and as a result, sarcopenia was found to be independently associated with depression [25]. In a study examining the relationship between sarcopenia and insomnia in geriatric patients, 1592 patients were included, and sarcopenia was found in 238 of them. Sleep problems were observed in 70% of patients with sarcopenia, and sarcopenia was found to be associated with insomnia [26]. Vetrano et al. found a correlation between the severity of Parkinson's disease and sarcopenia in a cross-sectional study involving 210 patients. [27].

In our study, the relationship between sarcopenia and many geriatric syndromes and chronic diseases was examined, and the significant ones were analyzed by multivariate regression analysis. As a result of multivariate regression analysis, a significant independent relationship was detected only in malnutrition. In a study examining the relationship between malnutrition and sarcopenia, including 336 patients, the risk of developing sarcopenia was approximately 4-fold higher at four-year follow-up in patients with malnutrition than in those without malnutrition [28]. In another study that included 506 patients hospitalized in a geriatric clinic, a significant correlation was found between malnutrition and sarcopenia [29]. Both malnutrition and risk of malnutrition are common in geriatric patients, resulting in poor functional performance, increased morbidity and mortality. Malnutrition and sarcopenia have common pathophysiological features, and mild inflammatory state is thought to be one of them [30].

Inflammatory cytokines are known to accelerate muscle loss, stimulate protein catabolism and suppress muscle synthesis. However, the exact relationship between inflammatory parameters and sarcopenia is not fully understood. Bian et al found increased IL-6 and TNF- α in patients with sarcopenia compared to those without sarcopenia [31]. In another study, patients with chronic renal failure were divided into groups with and without sarcopenia, and no significant difference in IL-6 levels was found between the two groups [32]. On the contrary, in a systematic review and meta-analysis of 11249 patients (3,072 sarcopenic) from 17 studies, in which Bano et al. evaluated the relationship between inflammation and sarcopenia, CRP was found to be significantly higher in patients with sarcopenia than in patients without sarcopenia; there was no significant difference in terms of IL-6 and TNF- α levels [33]. In our study, increased CRP, sedimentation and NLR in sarcopenia support the idea of mild chronic inflammation in sarcopenia.

NLR has been associated with many diseases, especially malignancies. It is an advantage that NLR is an accessible marker that is widely used in routine studies in clinics. In a meta-analysis on prognosis in head and neck cancers, it was shown that those with higher NLR have a worse prognosis because of the higher probability of metastasis [34]. In another meta-analysis, it was emphasized that an increase in NLR in patients with acute ST-elevation myocardial

infarction adversely affected the length of stay and prognosis [35]. Borges et al designed a cross-sectional study including 123 patients with cancer and found that NLR was linked with an increased risk of sarcopenia in hospitalized cancer patients [36].

Limitations

One of the limitations of the study is its cross-sectional retrospective nature. Another limitation is that other inflammatory biomarkers (IL-1, IL-6, TNF- α) that we can compare with NLR were not evaluated in our study.

Conclusion

Our study is important because we investigated the relationship of sarcopenia with many chronic diseases and geriatric syndromes. Malnutrition was the only geriatric syndrome associated with sarcopenia as a result of multivariate regression analysis. Therefore, it is important to screen for sarcopenia and malnutrition in all geriatric patients and to treat them if detected. The fact that NLR, sedimentation and CRP were higher in patients with sarcopenia in our study supports the idea of mild inflammation in sarcopenia. In addition, our study will guide new studies investigating the use of NLR in screening sarcopenia, as a prognostic criterion or as a marker of response to treatment.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Approval was obtained from the ethics committee of Cerrahpaşa Faculty of Medicine (Date 09.09.2020-Number 117344).

References

1. Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. *Clin Interv Aging*. 2018;13:1899-905.
2. Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *J Am Geriatr Soc*. 2007;55:780-91.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48:16-31.
4. Keller K. Sarcopenia. *Wien Med Wochenschr* 2019;169:157-72.
5. Saini A, Faulkner S, Al-Shanti N, Stewart C. Powerful signals for weak muscles. *Ageing Res Rev*. 2009;8:251-67.
6. Tan M, Toplu Y. Comparison of the hematological parameters of chronic otitis patients with and without cholesteatoma. *Medicine* 2021;10.3:812-5.
7. Azab B, Bhatt VR, Phookan J, et al. Usefulness of the neutrophil-to-lymphocyte ratio in predicting short- and long-term mortality in breast cancer patients. *Ann Surg Oncol*. 2012;19:217-24.
8. Tamhane UU, Aneja S, Montgomery D, et al. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol*. 2008;6:653-7.
9. Ferner RE, Aronson JK. Communicating information about drug safety. *BMJ*. 2006;333:143-5.
10. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999;15:116-22.
11. Buysse DJ. Insomnia. *JAMA*. 2013;309:706-16.
12. Abrams P, Cardozo L, Fall M et al. The standardization of terminology of lower urinary tract function: Report from the standardization subcommittee of the International Continence Society. *Neurourology and Urodyn*. 2002;21:167-78.
13. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int*. 2014;25:2359-81.
14. Cruz-Jentoft AJ, Sayer AA. Sarcopenia published correction appears in *Lancet*. 2019;393:2636-46.
15. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle* 2016;7:512-4.
16. Safran DG, Neuman P, Schoen C, et al. Prescription drug coverage and seniors: findings from a 2003 national survey. *Health Aff* 2005;5:152-66.
17. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. *Neuroepidemiology*. 2007;29:125-32.
18. Djernes JK. Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatr Scand*. 2006;113:372-87.
19. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing*. 2014;43:748-59.
20. Yazar T, Olgun Yazar H. The prevalence of sarcopenia and dynapenia according to stage among Alzheimer-type dementia patients. *Idoggyogy Sz*, 2019;72:171-9.
21. Bellelli G, Zambon A, Volpato S, et al. GLISTEN Group Investigators. The association between delirium and sarcopenia in older adult patients admitted to acute geriatrics units: Results from the GLISTEN multicenter observational study. *Clin Nutr*. 2018;37:1498-504.
22. Anagnostis P, Gkekakos NK, Achilla C, et al. Type 2 Diabetes Mellitus is Associated with Increased Risk of Sarcopenia: A Systematic Review and Meta-analysis. *Calcif tissue Int*, 2020;107:453-63.
23. Pana A, Sourtzi P, Kalokairinou A, Velonaki VS. Sarcopenia and polypharmacy among older adults: A scoping review of the literature. *Arch Gerontol Geriatr*. 2022;98:104520.
24. Erdogan T, Bahat G, Kilic C et al. The relationship between sarcopenia and urinary incontinence. *Eur Geriatr Med*. 2019;10:923-9.
25. Chang K, Hsu T, Wu W, et al. Is sarcopenia associated with depression? A systematic review and meta-analysis of observational studies. *Age Ageing*. 2017;46:738-46.
26. Nagaura Y, Kondo H, Nagayoshi M, Maeda T. Sarcopenia is associated with insomnia in Japanese older adults: a cross-sectional study of data from the Nagasaki Islands study. *BMC Geriatr*. 2020;20:256.
27. Vetrano D, Pisciotto M, Laudisio A et al. Sarcopenia in Parkinson Disease: Comparison of Different Criteria and Association With Disease Severity. *J Am Med Dir Assoc*. 2018;19:523-7.
28. Beaudart C, Sanchez-Rodriguez D, Locquet M, et al. Malnutrition as a Strong Predictor of the Onset of Sarcopenia. *Nutrients*. 2019;11:2883.
29. Verstraeten L, van Wijngaarden JP, Pacifico J, et al. Association between malnutrition and stages of sarcopenia in geriatric rehabilitation inpatients: RESORT. *Clin Nutr*. 2021;40:4090-96.
30. Sieber CC. Malnutrition and sarcopenia. *Aging Clin Exp Res*. 2019;31:793-8.
31. Bian AL, Hu HY, Rong YD, et al. A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF- α . *Eur J Med Res*. 2017;22:5.
32. Margiotta E, Caldiroli L, Callegari ML, et al. Association of Sarcopenia and Gut Microbiota Composition in Older Patients with Advanced Chronic Kidney Disease, Investigation of the Interactions with Uremic Toxins, Inflammation and Oxidative Stress. *Toxins (Basel)*. 2021;13:472.

33. Bano G, Trevisan C, Carraro S, et al. Inflammation and sarcopenia: A systematic review and meta-analysis. *Maturitas*. 2017;96:10-5.
34. Yu Y, Wang H, Yan A, et al. Pretreatment neutrophil to lymphocyte ratio in determining the prognosis of head and neck cancer: a meta-analysis. *BMC Cancer*. 2018;18:383.
35. Zhang S, Diao J, Qi C, et al. Predictive value of neutrophil to lymphocyte ratio in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention: a meta-analysis. *BMC Cardiovasc Disord*. 2018;18:75.
36. Borges TC, Gomes TL, Pichard C, et al. High neutrophil to lymphocytes ratio is associated with sarcopenia risk in hospitalized cancer patients. *Clin Nutr*. 2021;40:202-6.