Research Article

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Does a Relationship Exist Between Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Sarcopenia in Alzheimer's Disease?

Nilgun Cinar*, Sevki Sahin, Miruna Florentina Ates and Sibel Karsidag

Faculty of Medicine, Department of Neurology, Maltepe University, Istanbul, Turkey

***Corresponding author**
Nilgun CINAR, Associate Prof. M.D. Faculty of Medicine, Department of Neurology, Maltepe University, Istanbul, Turkey, Tel: 00(90)5325480636; E- Mail: cinarnilgun@gmail.com

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Abstract

Aim: *The prevalence of sarcopenia is higher in Alzheimer's disease (AD) when compared with subjects with normal cognition. Easy-to-use screening tools can make it easier to reach the diagnosis. We aimed to evaluate inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in AD cases with or without sarpcopenia.*

Materials and Methods: *Seventy-four possible AD cases who were resident in nursing home were included in to cross-sectional study. Body mass index (BMI), fat mass index (FMI), muscle mass index (MMI), and fat free mass index (FFMI) were assessed with electronic body composition analyzer. Short physical performance battery (SPPB), mini-nutritional assessment (MNA) and hand grip strength test were used for mobile patients. Calf circumference and mid-arm circumference were used for immobile patients. A diagnosis of sarcopenia was established according to the 'European Working Group on Sarcopenia in Older People' criterias. NLR and PLR were calculated as the ratio of the neutrophil count to lymphocyte count, and platelet count to lymphocyte count, respectively. Findings of AD cases with and without sarcopenia were compared according to NLR and PLR ratios.*

Results: *The sarcopenia rate was found to be 48%. Significantly higher NLR and PLR values were found in sarcopenic group. NLR were found to be negatively correlated with FFMI, while PLR were found negativeliy correlated with both FFMI and MNA.*

Conclusion: *It was found that NLR and especially PLR values are significantly related to sarcopenia in AD. Evaluation of NLR and PLR may be useful for sarcopenia screening.*

Keywords: Malnutrition, Sarcopenia, Alzheimer's, Inflammation, Screening Test.

Introduction

Alzheimer's disease (AD) is the most common type of dementia. Nutritional support is an important issue in AD to prevent malnutrition and to improve daily living activities [1]. Sarcopenia is characterised by a progressive loss of skeletal muscle mass and muscle function. Previous studies showed that the prevalence of sarcopenia was increased in patients with AD compared with that in subjects with normal cognition [2]. In AD patients, sarcopenia increased disability, loss of independence, and hospitalisation and therefore it can negatively affect daily living activities [3].

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are useful and inexpensive markers of systemic inflammation, and high levels of NLR and PLR are important in assessing inflammation in sarcopenic patients [4]. Inflammation can be closely associated with sarcopenia. So the importance of feeding and the reduction of sarcopenia will be effective in reducing the risk of chronic inflammation in Alzheimer's patients [4]. The aim of this study was to evaluate the contribution of NLR and PLR to sarcopenia in Alzheimer's patients.

Material and Methods

Patient Selection

Seventy-four AD subjects who were diagnosed according to National Institute of Neurological and Communicative Disorders and Stroke - Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) were our focus group [5]. AD cases who had similar care standards and residing in the same nursing home were included in the study. Subjects who had score between II-III (moderate-severe cases) according to Clinical Dementia Rating (CDR) scale and eligible to complete the body composition measurement or anthropometrical measurements were enrolled in the study [6]. They were excluded if they had any current infectious disease, or

had end-stage organ diseases. The Local Ethics Committee approved the study protocol and all subjects or their legal representatives gave written informed consent before participating in the study.

Calculation of Body Composition

TANITA© SC-330 (Tanita Corp., Tokyo, Japan) analyzer was used for assessment of body composition. The results are included in the fat mass index (FMI) and fat free mass index (FFMI). The FMI was calculated as the FM (kg) divided by the height (m) squared. The FMI is accepted to be abnormal if less than 2 for men and 3,5 for women. The FFMI was calculated as the fat free mass (FFM) (kg) divided by the height (m) squared. The FFMI is accepted to be abnormal if less than 19 for men and 17 for women. Body mass index (BMI, kg/m^2) was calculated as weight (kg) divided by height squared (m^2) [7-9].

Physical Performance

The SPPB (short physical performance battery) is a scale ranging from 0 to 12 points and it is used to evaluate balance, gait, strength and endurance by examining an individual's ability to stand with the feet together side-by-side, and in semi-tandem and tandem positions, the time needed to walk 10 meters, and the time needed to rise from a chair. An increasing risk of disability has been accepted with scores ≤8. A handgrip test was used to test immobile patients by dynomemetre for muscle strength. Abnormal handgrip test values were accepted as being < 30 kg for men, and < 20 kg for women [10].

Anthropometric Measurements

Anthropometric analyses were performed on the immobile patients by measuring calf circumferences. A calf circumference <31 cm has been accepted as signifying muscle mass loss. A mid-arm circumference < 22 cm for women, and <23 cm for men has been accepted as signifying muscle mass loss [11].

Nutritional Assessment

A mini nutritional assessment (MNA) form was used to identify nutritional status. The MNA consists of 4 groups of questions and measurements: basic anthropometrical measurement (BMI, arm, hip circumference, loss of body mass), total condition evaluation (mobility, self-sufficiency, chronic defects, presence of acute disease, psychological condition and polypharmasia), eating habits (food and liquid consumption and the ability to eat), and judging the condition of nutrition and health. The range of minumum and maximum score of the MNA is 0-29. A normal MNA and a good state of nutrition is represented by a score above 24, a score in the range of 17–23.5 represents a risk of malnutrition and a score under 17 confirms malnutrition [12].

NLR and PLR Calculation

A complate blood count sample was drawn from each participants. NLR and PLR was calculated as the ratio of the neutrophil cell count to lymphocyte cell count, and platelet cell count to lymphocyte cell count respectively, as previously described [13].

Diagnosis of Sarcopenia

A diagnosis of sarcopenia was described according to the the European Working Group on Sarcopenia in Older People (EWGSOP) criteria [3]. The diagnosis was established by an algorithm (Figure 1).

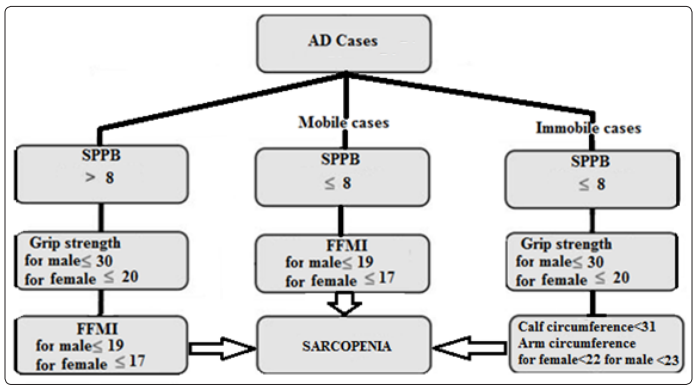

Figure 1: Diagnostic algorithm for sarcopenia used in this study. (Modified from European Working Group on Sarcopenia in Older People (EWGSOP) criteria) [3].

Statistical analysis

The SPSS (Statistical Package for the Social Sciences) v16 software was used for our calculations. Descriptive statistics were used to determine the frequency of other findings and sarcopenia. The results were shown as mean ± standard deviation (SD). For the comparison of means of continous variables between two groups (Sarcopenia + and sarcopenia – group) was applied to an independent sample Student's *t*- test or Mann-Whitney U tests. Categorical variables were assessed by a Chi-squared test. A logistic regression analysis was performed to analyze interactions between FFMI and MNA, age, NLR, PLR, and SSPB. The level of significance was $p < 0.05$.

Results

A total of 74 cases (Female/male: 49/25, mean age±SD: 78 ±11 years) were enrolled in the study. The mean duration of nursing home stay was 1.8±0.9 years. A sarcopenia rate of 48 % was found. The data of physical function, body composition, nutritional status, NLR and PLR values of the study group are presented in Table 1.

Table 1: Characteristics of the participants [n = 74] (SPBB: short physical performance battery, BMI: body mass index, FFMI: fat free mass index, MNA: mini nutritional assessment, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio)

Parameter	Value
SPBB	4.2±4
BMI [kg/m^2]	25±5
FFMI	17±2
Immobility[%]	53
MNA [%]	-Malnutrution 22
	-Risk of malnutrition 54
	-Normal 24
NLR	2,7±1,6
PLR	149±75

NLR, PLR and malnutrition ratios were found to be higher in sarcopenia plus cases. Table 2 shows the differences between sarcopenia (+) and sarcopenia (-) cases.

Table 2: Nutritional Status, Body Composition, Physical Function, Neutrophil and Platelet- to-lymphocyte ratio of Sarcopenia (+) and Sarcopenia (-) Patients (SPBB: short physical performance battery, PLR: platelet-to-lymphocyte ratio, NLR: neutrophil-to-lymphocyte ratio, MNA: Mini nutritional assessment, CRP: C reactive protein, FFMI: fat free mass index)

	SARCOPENIA + [n:36]	SARCOPENIA - [n: 38]	p
Age, years, mean [SD]	80±9	77±12	0,2
Female/male [n]	27/9	22/16	0,09
Immobility [%]	56	50	0,4
SPBB	3±3	5±5	0.03*
Duration of nursing home stay [years]	1.7±0.7	1.9±1	0.2
MNA [%]	Malnutrition 36	Malnutrition 8	0,006*
	Risk of malnutrition 50	Risk of malnutrition 58	
	Normal 14	Normal 34	
MNA [Mean±SD]	17±5	21±3	0,0001*
NLR	3,2±1.9	2,3±1,1	0,02*
PLR	180±77	131±69	0,04*
CRP	1,9±4	3,6±6	0,5
FFMI	16,2±1	19,8±1,5	0,0001*
Fat index	5±3	8±3	0,004*
Calf circumference [cm]	26±3	36±4	0,0001*
Mid arm circumference [cm]	24±3	29±5	0,001*
Muscle strength	13±6	20±10	0,005*

NLR were found negatively to be correlated with FFMI, while PLR were found to be negatively correlated with both FFMI and MNA (Table 3).

Table 3: Correlation matrix of patient parameters (Correlations greater than an absolute 35 are shown in parenthesis. Parameters which showed significant relationship with NLR and PLR presented in bold (FFMI: fat free mass index, SPBB: short physical performance battery, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MNA: Mini nutritional assessment, BMI: body mass index, FMI: fat mass index)

Variables	(FFMI)	(Age)	(SPBB)	(NLR)	(PLR)	(MNA)	(BMI)	(FMI)
FFMI	1.00							
Age	(- .35)	1.00						
SPBB	(.52)	(- .34)	1.00					
NLR	(- .35)	-.02	-.02	1.00				
PLR	(- .57)	-.12	-.21	(.42)	1.00			
MNA	(.60)	-.12	(.58)	-.16	(- .35)	1.00		
BMI	(.76)	-.18	(.42)	-.34	-.43	(.65)	1.00	
FMI	(.43)	-.03	.26	-.25	-.23	(.52)	(.91)	1.00

Linear regression analyses showed that the factors below had an independent influence on FFMI; MNA and PLR in model two (Table 4) .

Table 4: Linear regression analyses show that MNA (mini nutritional assessment) and PLR (platelet-to-lymphocyte ratio) are independent factors on FFMI (a. dependent variable: FFMI: muscle mass/height²)

		Unstandardized Coefficients		Standardized Coefficients		
Model Nr.		B	Std. Error	Beta	t	Sig.
1	(Constant)	-,237	3,325		,071	,944
	MNA	,787	,141	,804	5,579	,000
2	(Constant)	4,793	3,663		1,308	,209
	MNA	,670	,139	,684	4,834	,000
	PLR	-,014	,006	-,309	-2,181	,044

Discussion

The prevalence of sarcopenia varies in different studies. In a study from Turkey, the prevalence of sarcopenia among elderly males residing in nursing homes was reported to be 85% [14]. Van Kan et al found the prevalence of sarcopenia ranged from 3.3 to 18.8% in elderly women in their study [15]. We found a sarcopenia ratio of 48% in Alzheimer's patients staying in nursing homes. Different ratios of sarcopenia among the studies might be related to the specific sarcopenia criteria being used [16].

The loss of muscle actually associated with aging is most strongly associated with reductions in physical activity. Individuals in the study with Alzheimer's disease had lower levels of physical activity; in addition, behavioral changes associated with dementia may contribute to the loss of lean mass [16]. Our study showed that age has a negative effect on muscle mass and physical performance in our AD population.

Cobo et al. reported that 54.6% of cases had risk of malnutrition, 36.2% were normal, and 9.2% had malnutrition in their study included institutionalized elderly population [16]. We found 54% had a risk of malnutrition, 22% had malnutrition, and 24% were normal according to the MNA scores in our study group.

Alternatively, Alzheimer's disease and sarcopenia may share an underlying mechanism, such as inflammation or changes in the process of building tissue [17,18]. Changes in the infammatory pathways, including elevation in the inflammatory cytokine levels, can cause sarcopenia [13,19]. Inflammatory cytokines induce muscle wasting and alter protein catabolism as well as inhibiting muscle synthesis. High levels of inflammatory cytokines are negatively related to muscle strength and mass [20]. Schaap and colleagues assessed geriatric subjects over a period of 5 years to evaluate the association between the serum levels of inflammatory markers and loss of muscle mass and strength. They observed that higher levels of inflammatory markers were markedly associated with a greater 5-year decline in the thigh muscle area [19,20].

Compared to other inflammation markers NLR and PLR are regarded as an important indicator of systemic inflammation in multiple cases such as cardiovascular disease, diabetes mellitus and autoimmune diseases [13,21]. Also higher NLR with sarcopenia was found to be related to poor prognosis in some cancers [4]. Soto et al reported a relationship between faster clinical progression of AD and severity of sarcopenia in their study [22].

To our knowledge, this is the first study that compares NLR/PLR and sarcopenia. The results of the current study are in agreement with other reports that found both NLR and PLR levels were greater in AD patients with sarcopenia than in those without sarcopenia in nursing home patients. Furthermore, we found that especially PLR was correlated with sarcopenia and its severity. PLR has been shown to be superior to NLR as an inflammatory marker in some studies [23].

In some studies sarcopenia is found to be associated with higher serum CRP levels, but not with higher IL6 or TNF-α which are important proinflammatory cytokines compared to the controls [24]. Controversially, we found no relationship between CRP levels and sarcopenia in our study group.

Conclusion

Sarcopenia may affect the prognosis of AD. Our study is the first report on AD patients to investigate the relationship between inflammation and sarcopenia based on NLR and PLR. We found that NLR and PLR are independently associated with sarcopenia. These are inexpensive and objective parameters that can be determined from routine blood tests. Regular follow-up of NLR and PLR can aid in sarcopenia surveillance and following up the progression of AD. Further research on NLR and PLR could provide greater insights into their association with sarcopenia.

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Conflict of Interest: The authors have no conflicts of interest relevant for this article.

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