Investigation of the Relationship of CRP/Albumin Ratio with Clinical Parameters, Prognosis and Physiotherapy in Amyotrophic Lateral Sclerosis CRP/Albumin Ratio in Amyotrophic Lateral Sclerosis

Gülseren DEMİR KARAKILIÇ[*], Güven ARSLAN[**]

Abstract

Aim: The aim of this study was to investigate relationship of baseline CRP/albumin ratio (CAR) value with clinical parameters, post treatment functional capacity and physiotherapy effectiveness in patients with Amyotrophic Lateral Sclerosis (ALS).

Method: Ethical approval was obtained for this study on June 16, 2023, with number E. Kurul-2023-21/751. This retrospective study was undertaken between January 2021 and January 2024. Forty-five patients were included in the study based on their blood test results, ALSFRS-R scores, and disease-related clinical findings accessed through electronic patient records. Forty-five healthy people of similar age and gender who attended check-up clinic without any complaints were included in study as a control group.

Results: A total of 90 people, 45 patients with ALS and 45 healthy people as control group were included in study. The female/male ratio and mean age of both groups were similar and there was no statistical difference. The mean CAR of patients with ALS was 1.92±0.14, while mean CAR of control group 0.82±0,15 and there was no significant difference in mean CAR between the groups (p: 0.2). White Blood Cell (WBC) and Neutrophil were significantly higher in ALS group according to control group (p:0.017, p:0.038). CAR was not found to correlate with clinical parameters of ALS and number of physiotherapy sessions received. Functional ambulation Scale scores were found to be higher as number of physical therapy sessions increased.

Conclusion: This study is first to evaluate CAR in patients with ALS. CAR measured at time of diagnosis of ALS disease was not significantly higher than control group, and we could not find a relationship between CAR and post treatment functional scores. However, CAR may be an important parameter, especially in evaluating malnutrition and chronic inflammation when disease progresses and complications develop.

Keywords: Amyotrophic Lateral Sclerosis, CRP/Albumin ratio, Amyotrophic Lateral Sclerosis Functional Rating Scale, physiotherapy effectiveness.

Amyotrofik Lateral Sklerozda CRP/Albumin Oranının Klinik Parametreler, Prognoz ve Fizyoterapi ile İlişkisinin Araştırılması: Amyotrofik Lateral Sklerozda CRP/Albumin Oranı

Öz

Amaç: Bu çalışmanın amacı, Amyotrofik Lateral Sklerozlu (ALS) hastalarda başlangıç CRP/albümin oranı (CAR) değerinin klinik parametreler, tedavi sonrası fonksiyonel kapasite ve fizyoterapi etkinliği ile ilişkisini araştırmaktır.

Yöntem: Bu çalışma için 16 Haziran 2023 tarihinde E. Kurul-2023-21/751 numarasıyla etik onay alındı. Bu retrospektif çalışma Ocak 2021 ile Ocak 2024 tarihleri arasında gerçekleştirildi. ALS tanısı almış 57 hasta

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ETHICAL STATEMENT: This retrospective study was undertaken between January 2021 and January 2024. Acibadem Mehmet Ali Aydinlar University Medical Research Evaluation Committee approval was obtained before starting the study on 11.01.2024 (approval no: 2023-21/751).

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arasından kan testi sonuçları, Revize Amyotrofik Lateral Skleroz Fonksiyonel Değerlendirme Ölçeği (ALSFRS-R) skor kayıtları ve hastalıkla ilişkili klinik bulguları elektronik hasta raporu aracılığıyla erişilen 45 hasta çalışmaya dahil edildi. Herhangi bir şikayeti olmadan Check-up polikliniğine başvuran benzer yaş ve cinsiyetteki 45 sağlıklı kişi kontrol grubu olarak çalışmaya dahil edildi.

Bulgular: Çalışmaya 45 ALS tanılı hasta ve 45 sağlıklı kişi kontrol grubu olmak üzere toplam 90 kişi dahil edildi. Her iki grubun kadın/erkek oranı ve yaş ortalamaları benzerdi ve istatistiksel olarak fark yoktu. ALS'li hastaların ortalama CAR'ı 1,92±0,14 iken, kontrol grubunun ortalama CAR'ı 0,82±0,15 idi ve ortalama CAR açısından gruplar arasında anlamlı bir fark yoktu (p: 0,2). Beyaz Küre Hücresi (WBC) ve Nötrofil, ALS grubunda kontrol grubuna göre anlamlı olarak daha yüksekti (p:0,017, p:0,038). CAR'ın ALS'nin klinik parametreleri ve alınan fizyoterapi seansı sayısı ile ilişkili olmadığı bulundu. Fonksiyonel ambulasyon Ölçeği puanlarının, fizyoterapi seansı sayısı arttıkça daha yüksek olduğu bulundu.

Sonuç: Bu çalışma, ALS'li hastalarda CAR'ı değerlendirmek için ilk çalışmadır. ALS hastalığının tanısı sırasında ölçülen CAR, kontrol grubundan anlamlı olarak daha yüksek değildi ve CAR ile tedavi sonrası fonksiyonel puanlar arasında bir ilişki bulamadık. Ancak, CAR, özellikle hastalık ilerlediğinde ve komplikasyonlar geliştiğinde yetersiz beslenmeyi ve kronik inflamasyonu değerlendirmede önemli bir parametre olabilir.

Anahtar Sözcükler: Amyotrofik Lateral Skleroz, CRP/Albümin oranı, Amyotrofik Lateral Skleroz Fonksiyonel Derecelendirme Ölçeği, fizyoterapi etkinliği.

Introduction

Amyotrophic Lateral Sclerosis (ALS), one of the rare neurological diseases in the world, is a progressive neurodegenerative disease that affects the upper motor and lower motor neurons in the brain and spinal cord, causing loss of muscle control[1]. The incidence of ALS is estimated to be 2-3 per 100,000 people in European countries and 0.7-0.8 per 100,000 people in Asian countries[2]. ALS is a disease that begins in adulthood, is usually seen between the ages of 51-66, and is more common in men[3]. Although many theories have been proposed for the etiology of ALS, including oxidative stress, mitochondrial dysfunction (loss of function), protein aggregation, autophagy, and glutamate excitotoxicity, the underlying mechanisms have still not been elucidated[4]. While 90-95% of ALS cases are sporadic, 5-10% are seen in the familial form of ALS[5]. ALS classification based on clinical type is divided into two groups: extremity-onset and bulbar-onset. While weakness in the fingers, difficulty in writing and holding objects, weakness in the lower extremities, balance problems, and difficulty in walking are observed in limb-onset ALS; speech and swallowing difficulties are observed in bulbar-onset ALS. Bulbar-onset ALS is rare and the survival time of patients with bulbar onset is shorter than patients with extremity onset[6].

The diagnosis of ALS disease is primarily based on symptoms and neurological examination findings. EMG/electrophysiology has a privileged place as the basic examination method in diagnosis[7]. Upper motor neuron involvement must also be demonstrated clinically in order to diagnose ALS, in addition to detecting widespread lower motor neuron degeneration by clinical and/or electrophysiological methods[8]. ALS is a progressive and fatal disease, and there is no full treatment available today. Medical treatment can only slow down the progression of the disease in the treatment of ALS, and so symptomatic treatment becomes important. The main goal of treatment is to increase survival, quality of life, and physical functionality[9]. Studies suggest stretching for shortened muscles, strengthening exercises to maintain joint movement, and balance

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exercises to prevent the risk of falling, although there is no specific rehabilitation protocol in the treatment of ALS[10,11]. The patient's functional status is one of the most important indicators of quality of life and survival, and revealing the patient's functional status with scoring systems such as The Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) and Functional Ambulation Scale (FAS**)** is important for prognosis[12].

C-reactive protein (CRP) is a positive acute-phase protein synthesized by the liver and adipose tissue, and it is one of the most widely used biomarkers to indicate systemic inflammation[13,14]. While CRP increases as a positive acute-phase reactant in the presence of inflammation, albumin decreases as a negative acute-phase reactant. CRP/albumin ratio (CAR) effectively indicates both malnutrition and inflammation and is a useful biochemical parameter in predicting prognosis in seriously ill patients[15,16]. CAR has been used, especially in recent years, to predict the prognosis of progressive neurodegenerative diseases[17-19].

Malnutrition is often associated with decreased muscle mass, deterioration in muscle functions, anemia, hypoalbuminemia, immune dysfunction, decreased cognitive functions, increased risk of falling, the need for mechanical ventilation, prolonged hospitalization, and mortality[20]. Malnutrition is common in ALS due to decreased swallowing and nutritional functions and prolonged stays in hospitals and intensive care units due to complications. Albumin, an objective indicator of malnutrition, was found to be low in patients with ALS in previous studies and was considered a poor prognosis indicator[13,21-24]. CRP, an objective indicator of inflammation, has been found to be high in ALS patients in previous studies and has been shown to be associated with poor prognosis[24-26].

There is no study in the literature examining the relationship between CRP, CAR or inflammatory parameters and physiotherapy in ALS. The literature mostly evaluates the effect of physiotherapy on ALS. Forty-eight patients with ALS were given controlled and moderate-intensity aerobic exercise in addition to standard treatment, ROM and strengthening exercises; no difference was found between the groups[10]. 18 patients with ALS were given moderate-intensity graded aerobic exercise; there was no significant change in ALSFRS-R scores in the treatment group compared to the control group[27].

Although CRP and albumin are frequently studied in patients with ALS, CAR has not been studied in patients with ALS in the literature, and the relationship of inflammatory parameters with physiotherapy in patients with ALS has not been evaluated. In this study, we aimed to investigate the relationship of initial CAR value with clinical parameters and physiotherapy in patients with ALS.

Material and Methods

Study Design

This retrospective study was undertaken between January 2021 and January 2024. Acibadem Mehmet Ali Aydinlar University Medical Research Evaluation Committee approval was obtained before starting the study on 11.01.2024 (approval no: 2023-21/751). Provincial Health Directorate's Scientific Research Commission and adhered to the principles of the Helsinki Declaration.

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Patients

It was planned to screen all patients diagnosed with ALS in the records, including all records examined in our hospital in the last 3 years since ALS is a very rare disease, although a G-power power analysis application was used to calculate the sample size. Before starting work, Power analysis was done with G-power version 3.1.9.4 and it was calculated that a total of 52 patients would need to be included in the study for an effect size of 0.518, a margin of error of 0.05 and a power of 95% according to the CAR parameter[17]. Patients diagnosed with ALS at Neurology, and the Physical Medicine and Rehabilitation outpatient clinic between January 2021 and January 2024 were scanned. Considering the patients' comorbidities, patients with conditions that could affect CAD at the time of initial diagnosis (e.g., history of infectious disease in the last month, active infection and antibiotic-antiviral use, rheumatological disease diagnoses) were not included in the study. Forty-five patients were included in the study based on their blood test results, ALSFRS-R scores, and disease-related clinical findings accessed through electronic patient records. Forty-five healthy people of similar age and gender who attended the check-up clinic without any complaints were included in the study as a control group.

Demographic information such as age and gender of the patient and control groups at the time of initial diagnosis; clinical information the patient group; such as ALS initial symptom of age of ALS onset, disease duration, family history, comorbidities, FAS scores, ALSFRS-R scores, whether or not they received physiotherapy, physiotherapy sessions applied, and mortality rates were recorded. Patient and control groups' biochemical parameters such as creatinine, albumin, CRP, Erythrocyte Sedimentation Rate (ESR), White Blood Cell (WBC), hemoglobin (HGB), platelet (PLT), neutrophil (NEU), lymphocyte (LYMP), monocyte (MONO), and CAR levels; were recorded at the time of first admission to the hospital.

The physiotherapy program was applied 3 days a week, for an average of 45 minutes, for 8-10 weeks, in the form of joint range of motion, strengthening and stretching exercises, balance and walking training.

Outcome Measures

Functional Ambulation Scale (FAS): was used to determine the ambulation levels of the patients. Ambulation level was evaluated in 6 categories, including FAS 0-5 before and after treatment. As scores increase in FAS, ambulation improves; while the patient cannot ambulate in stage 0, he can ambulate independently in stage 5[28]. The evaluation of the FAS was obtained retrospectively from the patient's electronic patient card, using patient evaluation data from the last Neurology, and the Physical Medicine and Rehabilitation outpatient clinic follow-up.

The Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) is a scale consisting of 12 parameters such as speech, salivation, swallowing, handwriting, feeding, dressing and self-care, turning and covering in bed, walking, climbing stairs, dyspnea, orthopnea and respiratory failure and it is evaluated with a total of 48 points. Each question is evaluated between 0 and 4 points. The functionally normal patient is evaluated with four points. Zero points are given to the

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worst functional state while scores decrease from four to below due to functional deterioration Turkish validity and reliability study was conducted by Koç et al in 2016[29]. The evaluation of the ALSFRS-R was obtained retrospectively from the patient's electronic patient card, using patient evaluation data from the last Neurology, and the Physical Medicine and Rehabilitation outpatient clinic follow-up.

Statistical Analysis

All analyses were carried out with SPSS 26.0 (IBM, USA). The findings of the study are expressed as frequency and percentages. Normality analysis was carried out using the Kolmogorov-Smirnov test. The variables that were not normally distributed are presented as the median and interquartile range (IQR) with 25–75 percentiles. Descriptive statistics mean and standard deviation (mean (SD)) were used for normally distributed variables; mean and minimum-maximum values were used for non-normally distributed variables. Categorical variables were compared using the Chi-Square test. Continuous repeated measurements were compared using the paired samples t-test and the Wilcoxon signed-ranks test. Fischer exact, Pearson Chi-Square, and Yate's continuity correction test were applied. Pearson correlation analysis between CAR, ALSFRS-R, FAS and clinical factors was done. Finally, a ROC curve analysis to find cut-off values for CAR was applied.

Results

A total of 90 people, 45 patients with ALS and 45 healthy people as the control group were included in the study. Clinical findings of patients with ALS are listed in Table 1.

Table 1. Clinical characteristics of the patients with ALS

		n(%)
ALS onset symptom	Walking disorder	29(64.4)
	Speech disorder	7(15.6)
	Loss of fine motor skills in hands	5(11.1)
	Fasciculations	4(8.9)
ALS onset age (Mean±SD)	50.36±8.54	
ALS duration (Mean Years)	4.89	
Family history	Yes	3(6.7)
	No	42(93.3)
Comorbidity	No	12(26.7)
	Hypertension	15(33.3)
	Coronary artery disease	10(22.2)
	Diabetes Mellitus	5(11.1)
	Hypothyroidism	2(4.4)
	Hypertension+Diabetes Mellitus	1(2.2)
Physiotherapy treatment	Yes	16(35.6)
	No	29(64.4)
Number of Physiotherapy Sessions Received (Mean)	24	
	FAS score 0	24(53.3)

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FAS score	FAS score 1	5(11.1)
	FAS score 2	1(2.2)
	FAS score 3	6(13.3)
	FAS score 4	9(20)
ALSFRS-R score (Mean)	13.22	
Death	Yes	15(33.3)
	No	30(66.7)

ALS: Amyotrophic Lateral Sclerosis, N: Number, SD: Standard deviation, FAS: Functional ambulation scale, ALSFRS: Amyotrophic Lateral Sclerosis Functional Rating Scale

Ten (22.2%) of the patients with ALS were female; 12 (22.2%) of the control group were female and the gender ratio was the same between groups. There was no significant difference in mean age between the groups (p: 0.97). Albumin and CAR values showed normal distribution based on Skewness and Kurtosis tests[30,31]. The mean CAR of patients with ALS was 1.92±0.14, while the mean CAR of control group 0.82±0,15 and there was no significant difference in mean CAR between the groups (p: 0.2). There was a statistical difference between the ALS and control groups only in the number of WBC and NEU; WBC and NEU were significantly higher in the ALS group compared to the control group (p:0.01, p:0.03) (Table 2).

Table 2. Laboratory test results of the patients and the control group

		ALS (N:45)	**Control (N:45)**	**Reference Values**	**p**	Skewness Curtosis
Gender (n/%)	Female	10(22.2)	10(22.2)		1	
	Male	35(77.8)	10(22.2)			
Age (Mean±SD)		55.24±5.67	55.29±5.61		0.97	1.78 3.90
Cretatinine mg/dL (Mean)		0.56	0.58	0.70-1.20 mg/dL	0.72	0.86 3.58
ALB g/dL (Mean± SD)		3.86± 0.65	4.03± 0.45	3.50-5.20 g/dL	0.13	-0.80 1.42
CRP mg/dL (Mean)		5.63	2.75	<5 mg/dL	0.17	0.89 0.13
ESR mm/H (Mean)		27.56	26.36	<20 mm/H	0.86	0.69 1.53
WBC x10^3/uL (Mean)		10.22	8	4.10-10.60 x10^3/uL	**0.01**	2.70 10.55
HGB g/dL (Mean)		13.38	12.97	13.50-16.20 g/dL	0.32	-0.78 1.90
PLT x10^3/uL (Mean)		277.33	286.58	150-439 x10^3/uL	0.62	0.48 -0.17

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NEU x10^3/uL (Mean)	4.53	5.54	1.90-7.10 x10^3/uL	**0.03**	3.04 12.48
LYMP x10^3/uL (Mean)	1.71	1.85	1.30-3.76 x10^3/uL	0.38	1.10 4.10
MONO x10^3/uL (Mean)	0.88	0.93	0.35-1.01 x10^3/uL	0.86	3.33 9.71
CRP/ALB ratio (Mean± SD	1.92±0.14	0.82±0.15		0.20	1.12 0.27
ALSFRS-R (Mean± SD	14.23± 2.30	-		-	0.63 -0.19

ALS: Amyotrophic Lateral Sclerosis, CRP: C Reactive Protein ESR: Erythrocyte Sedimentation Rate, WBC: White Blood Cell, HGB: Hemoglobulin, PLT: Platelet, NEU: Neutrophil, LYMP: Lymphocyte, MONO: Monocyte, CAR: CRP/albümin ratio

Correlation Analysis

CAR was not found to correlate with the clinical parameters of ALS. As expected, ALSFRS scores and FAS scores were strongly correlated. FAS scores and the number of physiotherapy sessions were found to be associated, and FAS scores were found to be higher as physical therapy sessions increased. The duration of ALS disease increased as the age at onset of ALS decreased (Table 3).

Table 3. Correlation of CAR, ALSFRS-R and FAS with each other and other clinical parameters in patients with ALS

	n=45	**CAR**	**ALSFRS-R**	**FAS**	**ALS Duration**	**ALS Onset Age**	**Physio Sessions Received**
CAR	Pearson Correlation	1	0.10	0.20	-0.07	-0.01	-0.12
	Significance		0.50	0.17	0.64	0.92	0.43
ALSFRS-R	Pearson Correlation	0.10	1	**0.88**	0.03	-0.23	0.23
	Significance	0.50		**0.00**	0.80	0.12	0.11
FAS	Pearson Correlation	0.20	**0.88**	1	0.03	-0.21	**0.33**
	Significance	0.17	**0.00**		0.80	0.16	**0.02**
ALS Duration	Pearson Correlation	-0.07	0.03	0.03	1	**-0.75**	-0,13
	Significance	0.64	0.80	0.80		**0.00**	0.36
ALS Onset Age	Pearson Correlation	-0.01	-0.23	-0.21	**-0.75**	1	0.15
	Significance	0.92	0.12	0.16	**0.00**		0.32
Number of Physiotherapy Sessions Received	Pearson Correlation	-0.12	0.23	**0.33**	-0,13	0.15	1
	Significance	0.43	0.11	**0.02**	0.36	0.32	

CAR: CRP/albumin, ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale, FAS: Functional Ambulation Scale, ALS: Amyotrophic Lateral Sclerosis, N: Number

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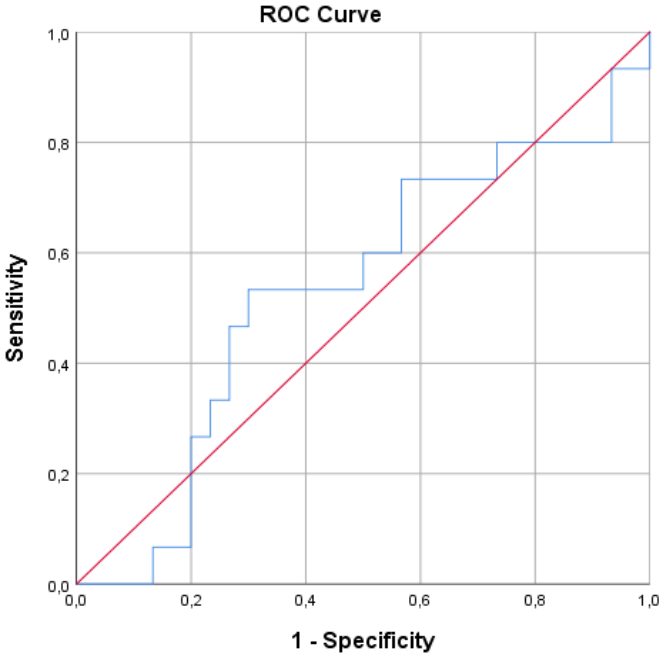
According to the AUC values, the power of the ROC curve analysis was poor. It revealed no statistically significant cut off values for CAR.

Table 4. ROC curve analysis for CAR values against ALSFRS-R and FAS scores

	Area	Std Error	Asymptotic Sig	Confidence Interval	
				Lower Bound	Upper Bound
ALSFRS-R	0.531	0.094	0.736	0.346	0.716
FAS	0.502	0.088	0.982	0.329	0.675

ROC: Receiver Operating Characteristic, CAR: CRP/albumin, ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale, FAS: Functional Ambulation Scale

Figure 1. CAR ROC curve and ALSFRS-R (left), and FAS scores (right)



Discussion

A total of 90 people, 45 patients with ALS and 45 healthy people as the control group were included in the study. The mean CAR of patients with ALS was 1.92±0.14, while the mean CAR of control group 0.82±0,15 and there was no significant difference in mean CAR between the groups (p: 0.2). WBC and NEU were significantly higher in the ALS group compared to the control group. CAR was not found to correlate with the clinical parameters of ALS. FAS scores were found to be higher as the number of received physical therapy sessions increased.

Most of our patients with ALS were male (77.8%), and their mean age was 55.24±5.67, convenient with other studies[1,5,32]. The mean age at onset of ALS was 50.36±8.54 like found in many research[33,34]. The onset symptom of ALS was mostly walking disorder[35,36]. The mean ALS duration was 4.89 years[1,34]. Family history was low like in the other studies in the literature[1,37]. The majority of patients with ALS had no ambulation, and

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those with a FAS score of 0 constituted the majority, similar to the literature[10,28]. The observed mortality rate of 33% was lower than the reported values in other studies, despite a mean disease duration of nearly 5 years[34,35]. This may be attributed to advances in intensive care, palliative care, home care services, and physiotherapy support.

There was no significant difference in mean CRP and albumin between ALS and the control group in our study. Albumin was also evaluated while evaluating 46 studies on lipid profile and iron homeostasis in patients with ALS in a meta-analysis published in 2021; no difference was found in albumin values in patients with ALS compared to control patients, similar to our study[22]. Creatinine and albumin values were compared in 45 patients diagnosed with ALS and 30 healthy controls in a study conducted in Romania in 2024; creatinine and albumin were found to be statistically low in the ALS group[23]. There may have been no statistical difference as the patients had not yet developed complications or malnutrition since we looked at the effect of creatinine and albumin values at the time of initial diagnosis on the functional scales. In a study conducted in Sweden in 2021, similar to our study[25], there was no difference in creatinine and CRP values at the time of initial diagnosis in patients with ALS compared to healthy control patients. Eleven studies were evaluated in a systematic review evaluating the effect of CRP level on the prognosis of ALS in 2022, and CRP levels were generally found to be higher than the control group and were associated with poor ALSFRS-R scores[26]. While CRP level was evaluated during the period when the clinic worsened and complications developed, when ALSFRS-R scores were evaluated in the hospital in most of these studies, CRP at the time of initial diagnosis was evaluated in our study.

Although CRP and albumin are frequently studied in patients with ALS, CAR has not been studied in patients with ALS in the literature. CAR has been studied in the literature in neurodegenerative diseases such as Parkinson's and multiple sclerosis. CAR was examined in 151 Parkinson's patients and 150 healthy controls in a study conducted in Turkey in 2019, and CAR was found to be significantly higher in the Parkinson's group compared to the control group[38]. CAR was examined in 120 MS patients and 62 healthy controls in a study conducted in Turkey in 2020, and it was found that CAR was significantly higher in the MS group than in the control group; It has been found to be associated with MS subtypes and disease activity[17]. This may be due to the fact that CRP and albumin were evaluated at the time of initial diagnosis, not in the advanced stages of the disease, and that complications or malnutrition had not yet developed during this period. The fact that the inflammatory response and nutritional status had not yet changed significantly in the early stages of the disease may have caused a statistically significant difference not to be observed between the groups. In addition, different inflammatory mechanisms in the pathophysiology of the diseases examined in previous studies may contribute to the significant increase in CAR, unlike ALS. Therefore, additional studies are needed to evaluate how CAR changes in ALS patients in advanced disease stages or in long-term follow-up studies.

We did not find a relationship between CAR and the number of physiotherapy received in our study. In our hospital, patients diagnosed with ALS were referred to the Physical Medicine and Rehabilitation outpatient clinic not when the disease was first diagnosed or in the early stages, but when the disease progressed and walking problems developed

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or when fine dexterity in the hands began to deteriorate. Since we recorded the blood values at the time of the first diagnosis of the disease, we could not access the blood values before and after physiotherapy. Nevertheless, since patients were referred to physiotherapy at an advanced stage or when complications developed, it may indicate that the patient's physiotherapy application indicated a poor prognosis.

We compared the patients who received physiotherapy in our study with previous studies on physiotherapy in ALS since there is no study in the literature examining the relationship between CRP, CAR, or inflammatory parameters and physiotherapy in ALS. In our study, 16 patients with ALS were given standard physiotherapy consisting of joint range of motion, strengthening and stretching exercises, balance, and walking training 3 days a week for an average of 45 minutes for 8–10 weeks. There was no significant improvement in ALSFRS-R scores while there was an improvement in FAS scores at the end of treatment. Forty-eight patients with ALS were divided into two groups in a study conducted in 2018; while group 1 was given controlled and moderate-intensity aerobic exercise in addition to the standard treatment, rum and strengthening exercises, twice a week for 6 months; the second group was given standard treatment for the same period. ALSFRS-R scores increased significantly in both groups, but there was no difference between the groups at the end of treatment[39]. Eighteen patients with ALS were divided into two groups in a study conducted in 2019. Group 1 was subjected to moderate-intensity gradual aerobic exercise, 3 sessions a week for 4 weeks, each lasting 40 minutes; the second group did not receive any treatment. There was no significant change in ALSFRS-R scores in the treatment group compared to the control group at the end of the study[40].

Sixteen patients with ALS were divided into two groups in a study conducted in 2019; while the 1st group was subjected to medium and high intensity aerobic and strength exercises, 3 sessions a week for 12 weeks, each session lasting 50 minutes; the second group received standard care. There was no significant change in ALSFRS-R scores in the treatment group compared to the control group at the end of the study[27]. Ten studies on physiotherapy in patients with ALS implemented in the last 5 years and whose effectiveness was evaluated with ALSFRS-R were examined in a systematic review published in 2021 and it has been reported that physiotherapy generally increases the patient's function and quality of life[10]. The average ALSFRS-R score of patients receiving physical therapy was 32.75 in the review conducted in 2021, while it was 13.22 in our study. The reason for the lack of improvement in ALSFRS-R scores in our study may be that the patients receiving physical therapy had low initial ALSFRS-R scores and consisted of patients with severe disease.

Conclusion

This study is the first to evaluate CAR in patients with ALS. We examined CAR at the time of initial diagnosis and before infections and complications developed, rather than at the advanced stage of the disease, in our study. CAR measured at the time of diagnosis of ALS disease was not significantly higher than the control group, and we could not find a relationship between CAR and post treatment FAS scores. However, CAR may be an important parameter, especially in evaluating malnutrition and chronic inflammation

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when the disease progresses and complications develop. Multicenter studies involving a larger number of patients are needed for this recommendation.

Limitations

The limitations of the study are that it is retrospective and single-center, the number of patients is relatively small since ALS is a rare disease, and the values before and after physiotherapy was not compared.

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