ORIGINAL ARTICLE

CLINICAL SIGNIFICANCE OF ALBUMIN/GLOBULIN RATIO FOR SURVIVAL PREDICTION IN ISCHEMIC STROKE PATIENTS IN INTENSIVE CARE

Yoğun Bakımdaki İskemik İnme Hastalarında Sağ Kalım Tahmini İçin Albumin/Globulin Oranının Klinik Önemi

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ABSTRACT

Objective: Decreased level of serum albumin is shown to be associated with an increased risk of mortality after stroke. However, the significance of the albumin/globulin ratio (AGR) as a paraclinical marker in determination of the prognosis of stroke is unclear. In this study, we aimed to examine the potential utility of AGR in determination of the need of intensive care unit monitorization and prognosis of patients with acute stroke.

Material and Methods: Sequential samples of all the patients with acute ischemic stroke (AIS) who were hospitalized between 2018 and 2022 in the mentioned centers were analyzed in this research. The data regarding the demographic features, stroke subtypes, and laboratory findings including hemogram, and biochemistry were recorded. AGR, serum osmolality, and colloid osmotic pressure (COP) were also measured. The survival curves of the patients were constructed using the Kaplan-Meier methods and log-rank tests. Estimates of survival changes were made by applying the Cox regression analysis.

Results: Ultimately, the data of 328 patients were analyzed. Thirty nine (30.2%) had passed away before discharge. There were significant differences between the deceased patients and patients surviving in terms of stroke classification, serum albumin, AGR, CRP, COP, and white blood cell count ($p < 0.05$). Serum AGR of 94 patients who were intensive care unit patients showed a statistical difference compared to albumin ($p < 0.05$). The Cox's regression analyses showed that low AGR moderately predicted the mortality of patients.

Conclusion: We found that the AGR provided important data regarding the necessity of critical care monitorization and prognosis of patients with AIS. Our findings support the potential utility of AGR as a simple, and useful paralinical laboratory marker in patients with AIS.

Keywords: *Albumin/Globulin Ratio; Intensive Care Follow-Up; Stroke; Outcome; Surveillance*

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ÖZET

Amaç: Düşük serum albümin düzeyinin inme sonrası yüksek mortalite riski ile ilişkili olduğu gösterilmiştir. Ancak, albümin/globulin oranının (AGO) inme prognozunun belirlenmesinde paraklinik bir belirteç olarak önemi belirsizdir. Bu çalışmada, AGO'nun akut inme hastalarının yoğun bakım ünitesi monitorizasyonuna ve prognozuna olan ihtiyacının belirlenmesindeki potansiyel faydasını incelemeyi amaçladık.

Gereç ve Yöntemler: Bu araştırmada, 2018 ile 2022 yılları arasında adı geçen merkezlerde hastaneye yatırılan akut iskemik inme (Aİİ) tanısı almış tüm hastaların ardışık örnekleri analiz edildi. Demografik özellikler, inme alt tipleri ve hemogram ve biyokimya dahil laboratuvar bulgularına ilişkin veriler kaydedildi. AGO, serum ozmolalitesi ve kolloid ozmotik basınç (KOB) da hesaplandı. Hastaların sağkalım eğrileri Kaplan-Meier yöntemleri ve log-rank testleri kullanılarak oluşturuldu. Sağkalım değişikliklerinin tahminleri Cox regresyon analizi uygulanarak yapıldı.

Bulgular: Sonuç olarak 328 hastanın verileri analiz edildi. Otuz dokuz (%30,2) hasta taburcu olmadan önce hayatını kaybetmişti. Ölen hastalar ile hayatta kalan hastalar arasında inme sınıflandırması, serum albumin, AGO, CRP, KOB ve beyaz kan hücresi sayısı açısından anlamlı farklar vardı ($p < 0,05$). Yoğun bakım ünitesi hastası olan 94 hastanın serum AGO 'su albumine göre istatistiksel olarak farklılık gösterdi ($p < 0,05$). Cox'un regresyon analizleri düşük AGO'nun hastaların mortalitesini orta düzeyde öngördüğünü gösterdi.

Sonuç: AGO'nun Aİİ' li hastaların kritik bakım monitörizasyonunun gerekliliği ve prognozu ile ilgili önemli veriler sağladığını bulduk. Bulgularımız AGO'nun Aİİ' li hastalarda basit ve kullanışlı bir paralinik laboratuvar belirteci olarak potansiyel faydasını desteklemektedir.

Anahtar Kelimeler: *Albümin/Globulin Oranı; Yoğun Bakım Takibi; İnme; Sonuç; Sürveyans*

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INTRODUCTION

Stroke is the foremost cause of mortality and disability in the middle age and elderly population (1). Acute ischemic stroke (AIS) is defined as neurological dysfunction due to an abrupt interruption of constant blood flow to a part of the brain (2). According to the Trial Org 10172 in Acute Stroke Treatment (TOAST) classification, ischemic strokes are divided into categories such as cardioembolic, small vessel obstruction, large artery atherosclerosis, and uncertain etiology each of which has different causes and pathophysiology (3).

Serum albumin is a multi-functional protein that is synthesized only in the liver. It regulates osmotic pressure by acting as a conductor, and it has antioxidant, antiapoptotic, and anti-inflammatory properties (4). Serum albumin is generally used to reflect the level of nutrition condition, whereas serum globulin is used to evaluate the severity of chronic inflammation. Both albumin and globulin concentrations are affected by various factors such as the volume status of body fluid just like most parameters (5). On the other hand, AGR which is calculated according to the formula of AGR = serum Albumin / (serum Protein-serum Albumin), combines albumin and globulin and is established as a suitable marker to determine serum protein abnormalities (6,7). Various recent studies remarked on that AGR may be used as a simple and valuable indicator for the evaluation of prognosis in various diseases including cancer, cardiac failure, inflammatory diseases, and cognitive deterioration (7-11). It has been estimated that low AGR (< 1.45) after AIS significantly increases the risk of recurrence of stroke, myocardial infarction, or vascular diseases in long-term periods (6).

The stroke should be regarded as a priority for public health and therefore, determining the prognostic factors that may contribute to the clinical management of patients during hospitalization is important for long-term survival. At this point, we sought to investigate the potential relationship between the AGR at the admission of stroke subjects and prognosis of these patients including mortality and need of intensive care monitorization.

MATERIAL AND METHODS

This study was a cross-sectional analysis of the files of hospitalized patients. The study was carried out as multi-centered and 328 patients with AIS in the intensive care unit and general ward in our city, a province in the middle region of the country, were included in the study. The patients included were those who had been hospitalized between February 2018 and April 2022 in the mentioned centers. The diagnosis and treatment plan of AIS is based on the current directives of the American Stroke Association (12).

Patients with major cardiac, renal, hepatic, and endocrinological disorders; skeletal disorders, malign tumors, last surgery, and especially recent acute infections were excluded. After excluding 60 patients due to the above-mentioned criteria, 328 patients aged above 18 years were included in the study. Neuroimages, anamnesis, laboratory tests, cardiac echoes, treatments in intensive care and general wards where the patients were hospitalized and monitored with carotid-vertebral artery doppler ultrasonography/ angiography of 149 female and 179 male patients included in the study were examined one-by-one. After an in-depth examination of the data of each patient, ischemic stroke etiological classification was categorized as large-artery atherosclerosis (LAS), cardioembolism (CES), and small-vessel occlusion (3). The vascular risk groups of the patients were formed as high blood pressure, dyslipidemia, diabetes, coronary artery disease, and previous stroke-temporary ischemic attack history. The information and data about the patients were obtained from the generated electronic data set and by reviewing the medical charts when necessary.

All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved with an institutional review of the tertiary research and application hospital (2017-KAEK-189_2020.03.09_05).

Blood samples from all patients were taken during the acute phase, within hours of the onset of stroke. Serum albumin (sAlb), protein concentrations and other laboratory examinations (blood urea nitrogen (BUN),

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serum creatinine, aspartate aminotransferase (AspAT), alanine aminotransferase (AlAT), serum sodium-potassium, hemoglobin, white blood cells (WBC), platelet, C-reactive protein (CRP)) were determined using a fully-automatic biochemical analyzer.

Serum globulin (sGlb) was calculated as the difference between serum protein and serum albumin. AGR was calculated as sAlb and sGlb ratio. The patients were divided into three AGR groups based on the similar sizes of hazard for mortality: low AGR group, AGR ≤ 1.0; moderate AGR group, 1.1 < AGR < 1.3; high AGR group, AGR ≥ 1.3. Serum osmolality was calculated as sodium, blood urea nitrogen and glucose (serum osmolality [mOsm / kg] = Osm = 2*Na + BUN / 2.8 + glucose / 18) while COP was calculated using the Hoefs formula (calculated COP = Salb [1.058sGlb + 0.163sAlb + 3.11]) (13, 14).

Statistical Analysis

Main descriptive statistics were presented as number (percentage) for categorical variables, as mean, standard deviation (SD) for continuous variables of normal distribution, and as median, (interquartile range, IQR) for non-normal distribution. The presence of normal distribution was examined with the Kolmogorov-Smirnov test. The study also used a t-test for the difference between means, a Mann-Whitney U test for the difference between medians, and a $\chi 2$ test to compare the rates. The comparisons of survival by time in terms of general mortality and AIS-induced mortality were analyzed with the Kaplan-Meier method, and their significance was determined using the long rank, berslow and tarone-ware tests.

The adjusted mortality model was formed using the data with a significant difference and no multiple linear connections for the bad surveillance. AGR classification (categorical variable), age, sex, AspAT, TOAST classification, CRP, comorbid diseases, and serum osmolality were calculated using Cox regression analysis based on their power over exitus and main causes in etiology. A significant difference between all results was defined as P < 0.05. The data were analyzed using SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) for windows.

RESULTS

The study included 328 patients diagnosed with AIS [149 females (45.4%), 179 males (54.6%)]. Among the patients, 234 were hospitalized and monitored in the neurology general ward whereas 94 had been monitored in intensive. Thirty-nine of the patients who had been monitored in the intensive care unit deceased during the hospitazation whereas 289 patients were discharged. The baseline demographics, clinical and laboratory data of the patients are presented in Tables I and II. The data regarding the comorbidities and AGR subgroups are presented in Table III. The mean age of the patients was 71.99 ± 11.44 years. The mean AGR value was 1.97 ± 12, the median was 1.30, and the minimum and maximum values varied between 0.42 and 220.5.

As seen in Table I, there was a difference between the patients who had passed away and who survived, in terms of age, AspAT, albumin, globulin, AGR, CRP, WBC, COP values, and stroke subgroup ($p < 0.05$). In terms of stroke subgroup, cardioembolic stroke was the most prevelant subgroup [21 (53.8%)] among the patients who died whereas small-vessel occlusion was the most common one [133 (46%)] among the patients who were discharged.

As seen in Table II, a significant difference was found between the patients hospitalized in intensive care and general wards in terms of age, fasting glucose, BUN, AspAT, protein, globulin, AGR, and CRP values ($p< 0.05$). Besides; the AGR differed between groups ($p< 0.05$), however, there was no difference in albumin values ($p = 0.710$).

Nineteen (48.7%) patients who died and 47 (16.3%) patients who were discharged had low AGR (Table III). One hundred thirty-one (56%) patients who were monitored in intensive care and 40 (42.6%) patients who were monitored inwards were found to have high AGR. The results of the Kaplan Meier analysis showed that 19 (48.71%) patients with low AGR values, 9 (23.07%) patients with high AGR values, and 11 (28.20%) patients with moderate AGR values were associated with decreasing mortality in the following days in terms of survival ($p < 0.001$) (Figure 1). According to the Cox regression model established in Table IV; age, AspAT enzyme, serum osmolality, and AGR were found to be associated with the exitus

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Table 1. Baseline characteristics stratified by outcome.

	Deceased patients (N = 39)	Living patients (N = 289)	P
Age (years)	80 (73-85)	72 (64-79)	< 0.001
Sex (Female) (n) (%)	20 (51.3)	129 (44.6)	0.541*
(Male) (n) (%)	19 (48.7)	160 (55.4)	
TOAST classification (%)			
Cardioembolism	21 (53.8)	91 (31.5)	0.003**
Large-artery atherosclerosis	9 (23.1)	60 (20.8)	
Small-vessel occlusion	8 (20.5)	133 (46)	
Undetermined etiology	1 (2.6)	5 (1.7)	
Serum glucose (mg/dL)	132.80 (107-179)	118 (100-149.60)	0.082
Blood urea nitrogen (mg/dL)	18.80 (17-37.5)	21 (18.17-31)	0.251
Creatinine (mg/dL)	0.95 (0.81-1.19)	0.92 (0.75-1.10)	0.297
AspAT (U/L)	23 (18-29.5)	18 (14.05-23.56)	0.001
AlAT (U/L)	16 (11-23)	14.60 (11-21.65)	0.329
Serum protein (mg/dL)	6.72 (6.50-6.95)	6.72 (6.39-7.10)	0.505
Albumin (mg/dL)	3.40 (2.88-4.00)	3.86 (3.52-4.10)	< 0.001
Globuline (mg/dL)	3.19 (2.86-3.72)	2.90 (2.68-3.20)	0.001
AGR	1.15 (0.78-1.29)	1.32 (1.15-1.48)	< 0.001
CRP (mg/L)	13.51 (4.63-28.5)	3.55 (1.87-11.48)	< 0.001
Serum sodium (mEg/L)	139 (137-141)	138.63 (137-140)	0.228
Serum potassium (mEg/L)	3.99 (3.75-4.55)	4.20 (3.90-4.55)	0.200
Hemoglobin (g/dL)	13.54 ± 1.77	13.06 ± 1.97	0.122[a]
WBC (10^3/uL)	10.67 (8.89-14.20)	8.30 (6.93-10.23)	< 0.001
Platelet (10^3/uL)	232 (172-349)	227 (179.5-269.5)	0.744
Serum osmolality (mOsm/kg)	294.25 (289.45-303.76)	293.04 (289.15-298.69)	0.251
cCOP (mmHg)	24.35 (19.55-26.85)	26.11 (23.60-28.37)	0.004

AGR: Albumin-to-globulin ratio; AspAT: Aspartate aminotransferase; AlAT: Alanine aminotransferase cCOP: Calculated colloid osmotic pressure, CRP: C-reactive protein, WBC: White blood cell. * Yates correction,** Fisher's exact test. a Student's t test, others: Mann-Whitney U test, p < 0.05 statistical significant.

(p < 0.05, all). Hazard ratio (HR) and 95% confidence interval (CI) was shown for the risk of study outcomes associated with the AGR.

As seen in Table V, the most common subtype was cardioembolic stroke in the low AGR. The following subtypes in the low AGR group, was the large artery stroke [16 (24.2%)] and the small vessel disease group [17 (25.8%)]. The rates of other stroke subtypes according to the distinct AGR levels are presented in the same table (p = 0.018).

DISCUSSION

In this study, we found that low serum AGR was associated with poor survival in patients with AIS. Additionally, the importance of AGR evaluation within the first 24 hours especially in patients who were hospitalized in intensive care was revealed. AGR as well as albumin is important for patients who survived and died, and it was found that AGR showed more significance in patients who were hospitalized in the intensive care unit than albumin. We did not find differences in serum albumin level between the patients who were monitorized in intensive care and those in neurology. In terms of the type of hospitazation and survival rates, the low AGR value was found to be significantly correlated with a poor course. In addition,

Table 2. Basic features of the patients according to the units.

	General Ward (N = 234)	Intensive Care Unit (N = 94)	P
Age (years)	73 (64-79)	75 (68-84)	0.005
Sex (Female) (n) (%)	101 (43.2%)	48 (51.1%)	0.194*
(Male) (n) (%)	133 (56.8%)	46(48.9%)	
TOAST classification (%)			
Cardioembolism	68 (29.1%)	44 (46.8%)	< 0.001**
Large-artery atherosclerosis	37 (15.8%)	32 (34%)	
Small-vessel occlusion	124 (53%)	17 (18.1%)	
Stroke of undetermined etiology	5 (2.1%)	1 (1.1%)	
Fasting glucose (mg/dL)	115 (98.75-148.42)	129 (105.75-159.12)	0.012
Blood urea nitrogen (mg/dL)	22 (18.17-34)	18.17 (17-25.37)	0.035
Creatinine (mg/dL)	0.92 (0.76-1.09)	0.94 (0.75-1.16)	0.529
AspAT (U/L)	18 (14-23.3)	21 (16.52-26.10)	0.009
AlAT (U/L)	14.10 (10.77-21.25)	16 (11-22.92)	0.175
Serum protein (mg/dL)	6.72 (6.35-7)	6.79 (6.60-7.36)	0.035
Albumin (mg/dL)	3.86 (3.5-4.10)	3.82 (3.30-4.20)	0.710
Globuline (mg/dL)	2.86 (2.64-3.20)	3.03 (2.79-3.44)	0.004
AGR	1.31 (1.15-1.48)	1.26 (1.02-1.43)	0.030
CRP (mg/L)	3.18 (1.49-9.14)	10.89 (3.37-21.67)	< 0.001
Serum sodium (mEg/L)	138.63 (137-140)	138.63 (136-140)	0.845
Serum potassium (mEg/L)	4.2 (3.90-4.51)	4.17 (3.80-4.60)	0.489
Hemoglobin (g/dL)	13.57 ± 1.78	13.26 ± 1.85	0.151[a]
WBC (10^3/uL)	8.28 (6.86-10.09)	9.31 (7.72-13.10)	< 0.001
Platelet (10^3/uL)	221 (176-262.25)	236 (179.25-314)	0.127
Serum osmolality (mOsm/kg)	293.40 (290-299)	292 (288-297)	0.076
cCOP (mmHg)	26.05 (23.45-27.83)	26.31 (22.14-29.28)	0.498

AGR: Albumin-to-globulin ratio; AspAT: Aspartate aminotransferase; AlAT: Alanine aminotransferase CRP: C-reactive protein, WBC: White blood cell, cCOP: Calculated colloid osmotic pressure, * Pearson chi-square, ** Fisher's exact test. a Student's t test, others: Mann-Whitney U test, $p < 0.05$ statistical significant.

Table 3. Comorbidities and AGR according to clinical follow-up and outcome classifications.

	Deceased patients	Living patients	P	General Ward	Intensive Care Unit	P
Hypertension (n) (%)	34 (87.2)	235 (81.3)	0.501*	189 (80.8)	80 (85.1)	0.355*
Diabetes (n)(%)	16 (41)	111 (38.4)	0.889*	86 (36.8)	41 (43.6)	0.248**
Prior stroke or TIA (n) (%)	16 (41)	80 (27.7)	0.126*	60 (25.6)	36 (38.3)	0.023**
CAD (n) (%)	19 (48.7)	87 (30.1)	0.031*	59 (25.2)	47 (50)	< 0.001*
Dyslipidemia (n)(%)	21 (53.8)	132 (45.7)	0.430*	103 (44)	50 (53.2)	0.132*
AGR classification			< 0.001*			0.015*
Low AGR	19 (48.7)	47 (16.3)		38 (16.2)	28 (29.8)	
Moderate AGR	11 (28.2)	80 (27.7)		65 (27.8)	26 (27.7)	
High AGR	9 (23.1)	162 (56.1)		131 (56)	40 (42.6)	

TIA: Transient ischemic attack, CAD: Coronary artery disease, AGR: Albumin-to-globulin ratio. * Yates correction ** Pearson chi-square, $p < 0.05$ statistical significant.

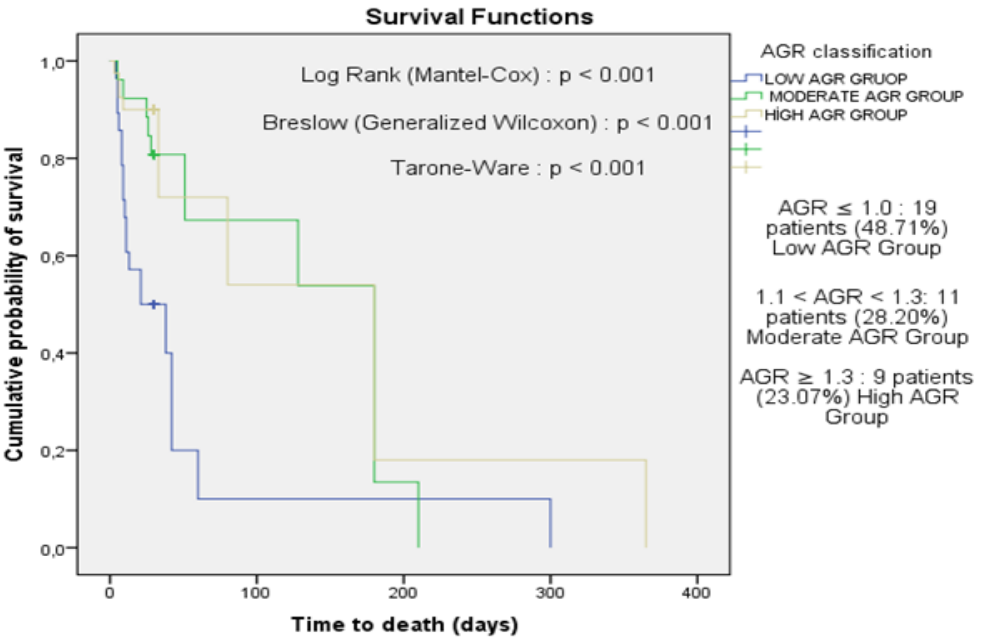

Figure 1. Mortality curve over time based on AGR classification (Kaplan Meier Survival Analysis) (Kaplan Meier Survival Analysis), Survival Time: 60 ± 25.631 days (9.763-110.237), AGR: Albumin-to-globulin ratio.

Table 4. Multivariate survival analysis in Cox's regression model.

Covariate	B	SE	Wald	Sig.	Exp(B)	95.0% CI for Exp(B) Lower- Upper
Age	0.04	0.02	3.93	**0.04**	1.04	1.00-1.09
Sex	0.33	0.38	0.75	0.38	1.39	0.66-2.94
TOAST classification			2.52	0.47		
CES	0.63	1.24	0.26	0.60	1.88	0.16-21.44
LAA	0.07	1.29	0.00	0.95	0.92	0.07-11.60
SVO	0.60	1.32	0.21	0.64	1.83	0.13-24.59
Hypertension	0.36	0.56	0.42	0.51	1.44	0.47-4.36
Diabetes mellitus	0.02	0.42	0.00	0.95	1.02	0.44-2.34
Prior stroke / TIA	0.73	0.47	2.45	0.11	2.08	0.83-5.24
CAD	0.61	0.44	1.93	0.16	0.54	0.22-1.28
Dyslipidemia	0.41	0.43	0.92	0.33	0.66	0.28-1.53
CRP	0.00	0.00	1.72	0.18	1.00	0.99-1.01
AspAT	0.04	0.01	12.72	**<0.01**	1.04	1.01-1.06
Serum osmolality	0.02	0.00	5.64	**0.01**	1.02	1.00-1.03
AGR groups			6.88	**0.03**		
Low AGR	1.04	0.48	4.73	**0.03**	0.35	0.13-0.90
Moderate AGR	1.11	0.49	5.09	**0.02**	0.32	0.12-0.86

CES: Cardioembolism, LAA: Large-artery atherosclerosis, SVO: Small-vessel occlusion, TIA: Transient ischemic attack, CAD: Coronary artery disease, Low AGR Group: AGR ≤ 1.1, Moderate AGR Group: 1.1 < AGR < 1.3, Cox regression analysis, enter method (Omnibus test p = 0.000, chi square = 105.309, -2 log likelihood = 329.654,) AspAT: Aspartate aminotransferase;

Table 5. Chi-square table based on between AGR and TOAST classification.

	AGR Classification		
	Low AGR Group	Moderate AGR Group	High AGR Group
Cardioembolism (N =112)	32	35	45
% Within TOAST	28.6%	31.2%	40.2%
% Within AGR	48.5%	38.5%	26.3%
Large-artery atherosclerosis (N = 69)	16	16	37
% Within TOAST	23.2%	23.2%	53.6%
% Within AGR	24.2%	17.6%	21.6%
Small-vessel occlusion (N = 141)	17	39	85
% Within TOAST	12.1%	27.7%	60.3%
% Within AGR	25.8%	42.9%	49.7%
Undetermined etiology (N = 6)	1	1	4
% Within TOAST	16.7%	16.7%	66.7%
% Within AGR	1.5%	1.1%	2.3%
TOTAL 328	66	91	171
	20.1%	27.7%	52.1%

p = 0 0.018, $\chi 2$ = 15.307 df = 6, TOAST; According to the Trial Org 10172 in Acute Stroke Treatment; AGR; Albumin-to-globulin ratio.

this study evaluates the importance of AGR according to the TOAST classification, which contributes to intensive care hospitalizations.

The first hours after acute stroke are most critical times for adjusment of the effective treatments. Reliable and simple predictive indicators must be determined to prevent the recurrence of stroke (15). Natural healing models should be further examined to evaluate the effectiveness of current healing interventions (16). Albumin is involved in many reactions in the body, but it is a negative phase reactant, and its synthesis decreases in acute and chronic inflammation. Serum albumin is synthesized in the liver and it has antioxidant features such as normal microvascular permeability and coagulation (17). Previous studies showed that plasma protein synthesis is inhibited in malnourished patients (18). Hypoalbuminemia may increase the tendency toward proinflammatory conditions as well as increase morbidity and mortality (5). Serum albumin and globulin are two main compounds of serum total protein and these can be measured easily and inexpensively (19). A decrease in AGR that is calculated with the formula is correlated to a decrease in albumin level and an increase in globulin level.

Increases and decreases in albumin and globulin levels basically change the plasma oncotic pressure. COP which is known as the oncotic pressure that balances the fluid distribution between intravascular and extravascular compartments is regulated by serum protein (essentially sAlb) and the endothelium barrier (20). Changes in COP are correlated to fluid drifts between compartments and this impairs vascular permeability and results in the transition of small-molecular-weight particles such as albumin to the extravascular range. However, globulin has a higher weight than albumin and it may not perform barrier transition (21). Therefore, AGR which reflects the globulin value remaining in the cell is regarded as an indicator that defines different pathophysiological mechanisms from COP, total sPrt or sAlb concentration (11). Globulin is a significant part of non-albumin protein and it consists of numerous proinflammatory proteins such as immunoglobulins, supplements, and C-reactive protein. High globulin levels are thought to indicate inflammation and/or host immunity (22). All these results on nutrition and inflammatory condition led us to conclude that AGR is significant for the AIS population. Although AGR has been investigated since 1917, the number of evidence supporting its prognostic value has recently increased with the majority of studies on patients with cancer, kidney failure, and cardiac patients (5, 11, 23, 24). It was emphasized

that decreased serum albumin concentration in acute stroke patients reflects malnutrition condition during stroke, and its deficiency in total protein concentration indicates changing hepatic synthesis or transvascular albumin loss. It was asserted that a decrease in AGR cannot only be associated with the nutritional condition (25). Beamer et al. emphasized that low AGR in AIS may increase the risk of vascular complications after stroke since it increases plasma viscosity due to globulin and fibrinogen increase (6). Maeda et al. revealed that low serum AGR accompanies cognitive impairment in the population aged between 70 and 80 (7). In our study, it was observed that both those who died and those who were hospitalized in intensive care were older.

Another point emphasized in this study is that cardioembolic stroke among TOAST classification was observed more in patients who were hospitalized in intensive care. That is, the significant effect on the AGR level is due to cardiovascular changes. In addition, the fact that cardioembolic patients are in the majority of the low AGR group shows us the importance of multisystemic evaluation of the causes that may lead to low AGR. With increasing age, the inflammatory process and cardiac insufficiency of patients may play a role in the occurrence of low AGR. According to the Cox regression analysis results of the patients, low AGR was once again shown as one of the indicators of mortality. It is seen that stroke is not a clinical entity on its own according to all these data. Multisystemic findings and comorbid conditions that emerge with increasing age in patients complicate the management of the stroke patient and negatively affect the risk of complication, duration of hospital stay, and treatment success. Compared to the low AGR group, there is a gradually increasing need for intensive care follow-up from the moderate AGR group to the high AGR group. Preventing the increase in plasma viscosity with increasing age should be brought into prominence in terms of preventive medicine and especially the elderly population on which this increase is higher should be motivated.

The present study has some limitations. First, it consisted of a compilation of etiological studies that we routinely performed in the hospital. We could not do extra research because it would require a budget. Secondly, AGR was obtained through a formula. No direct measurements were made. Also, there are no records regarding the nutritional conditions of the patients. The level of the liver reserve can significantly affect the clinical results of patients since albumin is synthesized in the liver, but glutamic-pyruvic transaminase, and glutamic-oxalocetic transaminase tests were not evaluated in this study since the primarily evaluated parameter was liver functions.

Despite these limitations, the researchers verified all ischemic stroke results documented in the medical records with simultaneous radiological studies and etiological scans with simultaneous consultations to ensure the accuracy of patient data in the study.

CONCLUSION

In conclusion, our findings may suggest the low AGR even more than albumin in the first 24 hours of AIS requires intensive care follow-up, and considering the multifactorial relationship of cardioembolic stroke with low AGR, it may be associated with the poor outcome when the correlation between mortality and surveillance. Therefore, patients who come to the general emergency should be examined not only for a stroke but also as a general system. Further studies should be conducted to confirm these findings and whether management changes in the AIS patient group will decrease the stroke load. It is also a matter of curiosity whether therapeutic strategies for patients at high risk of AGR can improve their long-term clinical outcomes and will be important for future studies.

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