

Research Article

Relationship Between Neutrophil-Lymphocyte Ratio (NLR) and CRP-Albumin Ratio (CAR) with Mortality in Geriatric Patients Admitted from the Emergency Department

 Ali İhsan Kilci,¹  Yunus Emre Çıkrıkçı,²  Müberra Çakıcı Tosun,³  Hakan Hakkoymaz,¹  Murat Tepe,¹
 Muhammed Semih Gedik¹

¹Department of Emergency Medicine, Kahramanmaraş Sutcu Imam University, Kahramanmaraş, Türkiye

²Department of Emergency Medicine, Goksun State Hospital, Kahramanmaraş, Türkiye

³Department of Emergency Medicine, Kayseri Provincial Health Directorate, Kayseri, Türkiye

Abstract

Objectives: This study aims to compare C-reactive protein/albumin ratio (CAR) and neutrophil/lymphocyte ratio (NLR) in predicting mortality in emergency department patients aged 65+.

Methods: This prospective study examined patients aged 65+ presenting to the emergency department from September-December 2021. Neutrophil, lymphocyte, C-reactive protein, and albumin measurements were obtained to calculate CAR and NLR and investigate their relationship with mortality.

Results: Of 609 patients studied, 282 (46.3%) were admitted to inpatient units and 327 (53.7%) to intensive care. 510 patients (83.7%) were discharged, while 99 (16.3%) died within 4 weeks. Median CAR was significantly higher in deceased patients (3.23) compared to survivors (0.48). Similarly, median NLR was significantly higher in deceased patients (9.55) versus survivors (5.64).

Conclusion: Both CAR and NLR effectively predict mortality in elderly emergency patients, with CAR demonstrating superior effectiveness as a biomarker for determining mortality risk compared to NLR. These findings suggest that CAR could be a valuable tool for risk stratification in the emergency care of elderly patients.

Keywords: Emergency Department, CRP/Albumin Ratio, Neutrophil/Lymphocyte Ratio

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There are various studies in our country comparing emergency department admissions by age groups. In these studies, it has been stated that the emergency department admission rates for patients aged 65 and over are similar and approximately 10%.^[1] It is known that geriatric patients have higher hospitalization rates compared to younger patients when presenting to the

emergency department.^[2] A study conducted in the USA in 2006 found that the hospitalization rate for elderly patients presenting to the emergency department was approximately 40%.^[3] Similarly, a study conducted in our country determined the hospitalization rate from the emergency department for elderly patients to be 53.3%.^[4]

Address for correspondence: Ali İhsan Kilci, MD. Department of Emergency Medicine, Kahramanmaraş Sutcu Imam University, Kahramanmaraş, Türkiye

Phone: +90 554 694 15 44 **E-mail:** alihsankilci@gmail.com

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Lymphopenia generally indicates inadequacy of cellular immunity, while neutrophilia is an important indicator of systemic inflammatory response. The ratio of these two parameters can be used to evaluate the severity of systemic inflammation and the adequacy of cellular immune response. C-reactive protein (CRP) is a positive acute phase reactant synthesized by the liver that rises within hours in the presence of inflammation. In contrast, albumin is also synthesized by the liver but is known as a negative acute phase reactant whose serum levels decrease in inflammatory conditions.^[5] CRP and albumin levels have been widely used as markers of oxidative stress and inflammation in many diseases in recent years. The CRP/albumin ratio (CAR), initially used in clinical evaluations of sepsis patients, is now considered an important biomarker in determining the severity and prognosis of various diseases.^[6] Neutrophil/lymphocyte ratio (NLR) has been associated with the prognosis of infection-related diseases such as sepsis, bacteremia, and appendicitis, and is evaluated as a prognostic biomarker in patients with sepsis. High NLR values have been shown to be associated with poor prognosis in patients with sepsis.^[7] It has also been reported to be connected to the outcomes of mortal and non-infectious diseases such as acute myocardial infarction, stroke, acute pulmonary embolism, and malignancies.^[8-11]

Changes in CRP and albumin levels in malignant diseases and infectious and inflammatory processes suggest that these parameters may be an important prognostic marker for the course of diseases.^[12] There are studies showing that CRP/albumin ratio and neutrophil/lymphocyte ratio are effective in predicting in-hospital mortality in geriatric patients presenting to the emergency department.^[3]

This study aims to compare the CRP/albumin and neutrophil/lymphocyte ratios measured in the emergency department of patients aged 65 and over who were admitted to the hospital from the emergency department, after excluding trauma patients, COVID-19 patients, and patients with hematological pathologies, and to evaluate the effectiveness of these parameters in predicting prognosis.

Methods

Ethical approval for this study was obtained from Kahramanmaraş Sütçü İmam University Non-Interventional Clinical Research Ethics Committee with the decision dated 23.11.2021 and numbered 01. All patients planned to be included in the study and their legal guardians were informed about the study; informed consent was obtained from the legal guardian for patients who did not have the capacity to authorize medical procedures.

Patients aged 65 and over who presented to the emergency department between September 1, 2021, and December 31, 2021, and who were decided to be hospitalized after necessary examinations, consultations, and evaluations were included in the study. Of the 932 patients initially considered, 323 were excluded due to refusal to participate or hematological pathologies; thus, a total of 609 patients were evaluated. Trauma patients, hematological disease patients, and COVID-19 patients were excluded from the study due to possible changes in lymphoid and myeloid cell series in trauma patients, significant increases or decreases in various blood parameters in hematological diseases, and the possibility of lymphopenia in COVID-19 patients.

An evaluation form created for patients who agreed to participate in the study was filled out by the examining physician. The collected data were analyzed by the researchers. Demographic and clinical information was obtained from patients included in the study. Age, gender, and chief complaints at emergency department presentation were recorded. Additionally, systolic blood pressure, heart rate, body temperature, fingertip oxygen saturation, and Glasgow Coma Scale measurements were taken. Patients' comorbid diseases such as diabetes mellitus, hypertension, chronic kidney failure, coronary artery disease, congestive heart failure, asthma-COPD, and malignancy were questioned. Hemogram, CRP, and albumin levels were studied from blood samples.

The neutrophil/lymphocyte ratio (NLR) and CRP/albumin ratio (CAR) values were compared between inpatient units and intensive care units during the hospitalization process, and the prognostic value of these parameters was evaluated. Mortality and discharge status were followed for up to 4 weeks after admission in hospitalized patients. ROC analysis was performed for NLR and CAR values of hospitalized patients, and the statistical significance of the determined cut-off values was examined in terms of mortality differences between groups.

Statistical analysis of the data was performed using SPSS 25.0 (SPSS Inc., Chicago, IL) package program. Categorical variables were expressed as numbers and percentages, while continuous variables were expressed as median (minimum-maximum) values. The Shapiro-Wilk test was used to evaluate the normality of distribution for variables. The Mann-Whitney U test was used for quantitative variables between two groups, and the Kruskal-Wallis test for more than two groups. Dunnett's T3 test was applied for post-hoc analysis of quantitative variables. Relationships between categorical variables were analyzed using the Chi-square test or Fisher's ex-

act Chi-square test. ROC curve analysis was performed to determine the prognostic power of CAR and NLR for in-hospital mortality in patients included in the study, and a threshold value was calculated at the highest sensitivity and specificity level. A multivariate model was constructed using logistic regression analysis to identify factors associated with mortality. A p -value <0.05 was considered statistically significant.

Results

During the study period, it was determined that of the 2,186 patients who presented to the yellow and red areas of the emergency department or were followed up in these areas after being evaluated in the green area and subsequently hospitalized, 1,255 (57%) were under 65 years of age, and 932 (43%) were 65 years and over. Of the 609 patients who agreed to participate in the study, 301 were male (49.4%), 308 were female (50.6%), and the average age was 77. When examining the distribution by age groups, there were 254 patients (41.7%) in the 65-74 age range, 258 patients (42.4%) in the 75-84 age range, and 97 patients (15.9%) aged 85 and over. Among the reasons for presenting to the emergency department, the most frequently reported complaints were: weakness (20.5%, $n=125$), dyspnea (19.4%, $n=118$), abdominal pain (12.8%, $n=78$), nausea-vomiting (12.5%, $n=76$), chest pain (5.4%, $n=33$), poor oral intake (5.3%, $n=32$), and fever (2.5%, $n=15$). In initial measurements in the emergency department, 86 patients (14.1%) were hypotensive (systolic blood pressure <100 mmHg), 386 (63.4%) were normotensive (100-140 mmHg), and 137 (22.5%) were hypertensive (≥ 140 mmHg). Additionally, 566 patients had normal body temperature ($<38^{\circ}\text{C}$), while 43 patients had fever ($>38^{\circ}\text{C}$). When evaluating the Glasgow Coma Scale (GCS), 497 patients (81.6%) had a GCS of 12 and above, while 112 patients (18.4%) had a GCS below 12. In comparisons between hypotensive and normotensive patients, both CAR and NLR values were observed to increase in hypotensive patients. However, the increase in CAR value was found to be statistically more significant than NLR ($p<0.001$).

When evaluating the hospital units where patients were admitted, it was determined that 282 patients (46.3%) were admitted to relevant clinical services, and 327 patients (53.7%) were admitted to intensive care units. In terms of admission diagnoses, central causes were most common (25.3%, $n=154$), followed by abdominal pathologies (22%, $n=134$), pulmonary diseases (16.4%, $n=100$), infectious causes (10.7%, $n=65$), cardiac pathologies (10.2%, $n=62$), and other diseases (15.4%, $n=94$). While 510 (83.7%) of the 609 patients included in the study were discharged within the four-week follow-up period, 99

(16.3%) of the patients admitted for treatment died within the same four-week period. The median CAR value of patients who developed mortality (3.23) was found to be statistically significantly higher compared to patients who did not develop mortality (0.485) ($p<0.001$). Similarly, the median NLR value of patients who developed mortality (9.54) was found to be significantly higher compared to those who did not develop mortality (5.64) ($p<0.001$). The median CRP value of patients who developed mortality (97.1) was found to be significantly higher compared to patients who did not develop mortality (18.6) ($p<0.001$). When evaluating albumin levels, the mean value in discharged patients was measured as 35.59, while it was determined to be 30.11 in patients with a mortal course. The median albumin value of patients who developed mortality (30.3) was found to be significantly lower compared to those who did not develop mortality (35.9) ($p<0.001$). The statistical data related to in-hospital mortality are presented in detail in Table 1.

In analyses based on admission locations, the median NLR value in patients admitted to inpatient units ($n=282$) was 5.23 (0.84-72.3), while the median NLR value in patients admitted to intensive care ($n=327$) was 6.84 (0.1-105.2). The median CAR value was measured as 0.475 (0.03-17.99) in patients admitted to inpatient units and 0.82 (0.03-37.35) in patients admitted to intensive care. These findings indicate that CAR ($p<0.001$) is more effective than NLR ($p=0.18$) in predicting intensive care admission in comparisons based on admission locations.

When evaluating patients' comorbid diseases, hypertension was most commonly observed (65.8%, $n=401$), followed by diabetes mellitus (35%, $n=213$), coronary artery disease (29.7%, $n=181$), asthma-COPD (19.5%, $n=119$), congestive heart failure (13.3%, $n=81$), chronic kidney failure (11%, $n=67$), and malignancies (8.4%, $n=51$). In the additional chronic diseases group, Alzheimer's disease, dementia, and osteoporosis were most common. In patients with a history of diabetes ($n=213$), the mean NLR was measured as mean 9.25 and the CAR as 2.37, while in patients without a diabetes diagnosis ($n=396$), the mean NLR was 9.46 and the mean CAR was 2.08. The increase in

Table 1. Statistical data obtained according to in-hospital mortality status

	Exitus (n=99) Median (min-max)	Discharged (n=510) Median (min-max)	p
CAR	3.23 (0.08-37.35)	0.48 (0.03-17.99)	<0.001
NLR	9.54 (0.5-105.2)	5.64 (0.1-72.3)	<0.001
CRP (mg/dL)	97.1 (2.57-960)	18.6 (1-554)	<0.001
Albumin (g/L)	30.3 (13.9-47.6)	35.9 (2.5-47.3)	<0.001

CAR ($p=0.343$) in diabetic patients was found to be more significant than in NLR ($p=0.815$), and this increase was thought to be associated with the increased frequency of hypoalbuminemia due to proteinuria seen in diabetic patients. In patients with a history of malignancy, both CAR ($p<0.001$) and NLR levels ($p<0.001$) were identified as being associated with mortality. In patients without a history of malignancy, CAR was observed to have a stronger relationship with mortality compared to NLR. Additionally, it was determined that CAR was more significantly associated with mortality than NLR in CKD (chronic kidney disease) patients. In asthma patients, despite NLR being routinely elevated, it could not be associated with mortality ($p=0.558$), however, the relationship of CAR with mortality was found to be more significant compared to NLR in asthma patients ($p<0.001$) (Table 2).

According to the results of the ROC analysis, NLR demonstrated limited discriminative ability in predicting mortality (AUC=0.625; 95% CI: 0.563–0.686; $p<0.001$), the cutoff value for NLR was determined to be 7.63 with a sensitivity of 62.6% and a specificity of 62.9%. In contrast, CAR emerged as a stronger predictor (AUC=0.787; 95% CI: 0.740–0.835; $p<0.001$), the cutoff value was determined to be 1.78, achieving 78.5% sensitivity and 72.4% specificity (Table 3).

The ROC analysis for NLR is shown in Figure 1.

The ROC analysis for CAR is shown in Figure 2.

In the multivariate logistic regression model assessing factors associated with mortality, age, gender, and NLR were not statistically significant predictors. However, CAR levels were significantly associated with mortality (OR=1.244; 95% CI: 1.146–1.351; $p<0.001$). Additionally, admission to the intensive care unit (OR=2.553; 95% CI: 1.178–5.529; $p=0.017$) and low GCS scores (≤ 12) (OR=15.492; 95% CI: 8.054–29.800; $p<0.001$) were identified as strong predictors of mortality. When compared with low blood pressure

Table 3. ROC analysis results for CAR and NLR

Risk Factor	AUC (95%)	Cutt off	p	Sensitivity %	Spesifity %
NLR	0.625 (0.563-0.686)	7.63	0.000	62.60%	62.90%
CAR	0.787 (0.740-0.835)	1.78	0.000	78.50%	72.40%

as the reference, both normal blood pressure (OR=0.421; $p=0.017$) and high blood pressure (OR=0.172; $p<0.001$) were associated with a reduced risk of mortality. Furthermore, the presence of congestive heart failure was determined to be an independent risk factor that significantly increased mortality (OR=2.341; 95% CI: 1.074–5.101; $p=0.032$) (Table 4).

Discussion

In this study, the relationship between neutrophil/lymphocyte ratio (NLR), CRP/albumin ratio (CAR), and in-hospital mortality was investigated in patients aged 65 and over who were admitted to the hospital from the emergency department. Our findings show that both NLR and CAR values were significantly higher in patients with high mortality. These results suggest that these two biomarkers, which reflect the severity of the inflammatory response, may be important in determining prognosis in geriatric patients.

Previous studies have shown that NLR can be used as a prognostic marker in sepsis, acute coronary syndrome, pulmonary embolism, malignancies, and other systemic inflammatory diseases.^[13,14] Similarly, CAR has been reported to be an important prognostic indicator in infectious diseases and critical patient management.^[6-15] Our study demonstrates that these biomarkers also have prognostic value in elderly patients who have admission indications in the emergency department.

Table 2. CAR and NLR median values (min/max) of patients with a history of malignancy, chronic renal failure (CRF) and asthma and the p values of these values related to mortality are presented below

Patient History	CAR in Exitus Median (min-max)	CAR in Discharged Median (min-max)	NLR in Exitus Median (min-max)	NLR in Discharged Median (min-max)	CAR p	NLR p
Malignancy						
Yes	5.42 (0.08-23.8)	1.06 (0.04-17.9)	13.33 (2.57-29.9)	4.72(0.6- 40.6)	<0.001	<0.001
No	3.12 (0.08-37.3)	0.47 (0.03-15.9)	8.73 (0.5-105)	5.70 (0.1-72.3)	<0.001	0.006
CRF						
Yes	4.82 (0.23-17.1)	0.65 (0.06-12.6)	9.66 (0.5-30.1)	6.49 (0.6-47.7)	<0.001	0.306
No	3.12 (0.08-37.3)	0.46 (0.03-17.9)	9.44 (1.08-105.2)	5.54 (0.1-72.3)	<0.001	<0.001
Asthma-COPD						
Yes	2.78 (0.08-37.3)	0.77 (0.06-13.3)	9.54 (1.19-31.58)	6.76 (0.73-72.3)	<0.001	0.558
No	3.29 (0.08-23.8)	0.44 (0.03-17.9)	9.50 (0.5-105.2)	5.44 (0.1-55.1)	<0.001	<0.001

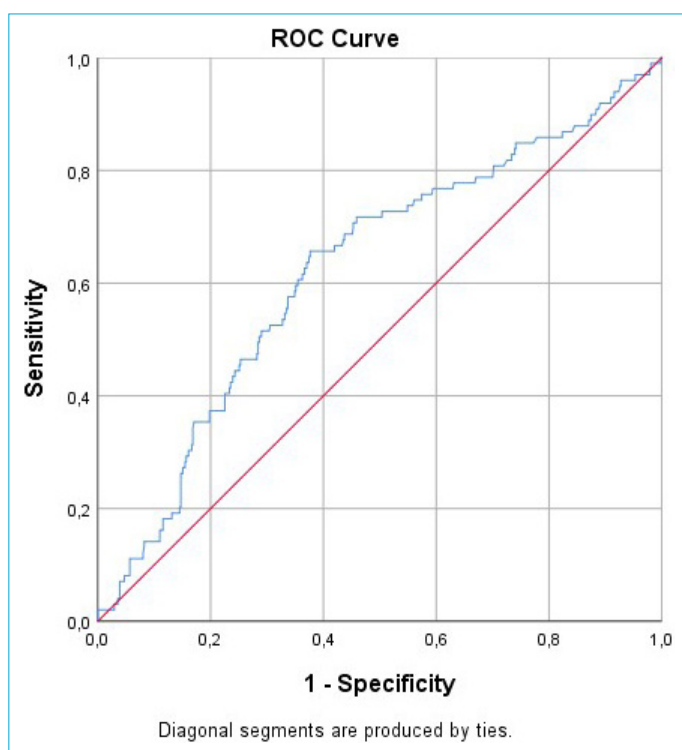


Figure 1. NLR - ROC Analysis.

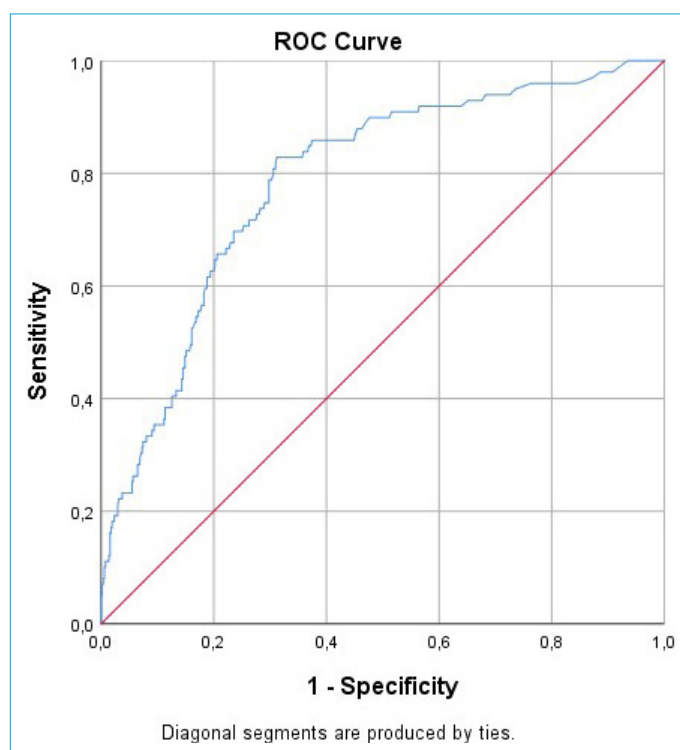


Figure 2. CAR – ROC Analysis.

In our study, the median CAR value in patients with mortality was 3.23, while in patients without mortality, this value was found to be 0.48, and the difference was statistically significant ($p < 0.001$). Similarly, the median NLR value in patients with mortality was 9.54, while in surviving patients, this value was found to be 5.64 ($p < 0.001$). These findings are parallel to previous studies and reveal that high CAR and NLR values are associated with poor prognosis.^[12,16] In our study, CAR was observed to have a higher sensitivity in predicting mortality compared to NLR. These results are consistent with studies published in recent years, which reported that CAR exhibits high AUC and strong hazard ratios in predicting early mortality, particularly in elderly patients presenting to an emergency department. This finding may explain the prognostic superiority of CAR, as it reflects not only the severity of inflammation but also nutritional/catabolic status.^[17]

While the CAR cut-off value (1.78) and NLR cut-off value (7.63) in our study are close to the ranges reported in the literature, it should be noted that these values may vary in different populations and laboratory units. Some recent studies have reported higher CAR values, primarily because the value used for albumin in calculations is g/dL rather than g/L. Therefore, local validation (local laboratory ranges) should be considered if integration into emergency department protocols is considered.^[12,17]

In our study, the 4-week mortality rate among hospitalized patients was 16.3%, compared with 9.9% in a similar study.

The rate of intensive care unit admissions was also higher in our cohort (53.7%). We consider that the main reason for this difference is that our hospital is a tertiary care center, where a higher proportion of patients—particularly oncological cases—present to the emergency department in a critical condition.^[12]

The results of our study indicate that CAR and NLR may be important biomarkers in determining the prognosis of geriatric patients in the emergency department. CAR, in par-

Table 4. Factors affecting mortality

Parameters	B	Sig.	Exp (B)	95% C.I. for EXP(B)	
				Lower	Upper
Age	.017	.374	1.017	.979	1.057
Gender (Ref- Male)	-.167	.589	.846	.462	1.550
NLR	.010	.424	1.010	.985	1.035
CAR	.219	.000	1.244	1.146	1.351
Hospitality (Ref- Service)	.937	.017	2.553	1.178	5.529
GCS (Ref >12)	2.740	.000	15.492	8.054	29.800
Blood Pressure (Ref-Low)		.001			
Normal	-.865	.017	.421	.207	.855
High	-1.760	.000	.172	.067	.439
Congestive heart failure (Ref- No)	.850	.032	2.341	1.074	5.101
Constant	-4.510	.004	.011		

ticular, was found to be superior in predicting mortality, as in the study by Razai et al.^[6] Evaluation of these biomarkers before making admission decisions for patients in the emergency department can make patient management more effective. Furthermore, considering the significant relationship between CAR and mortality, we believe that determining a standard cut-off value for clinical use may guide the early recognition, intervention, and hospitalization of critically patients.

Limitations of the Study

This study has some limitations. Firstly, as it is a study conducted in a single center, the generalizability of the results is limited. More comprehensive evaluation of the prognostic value of these biomarkers is needed through multi-center studies in broader populations.

Additionally, only certain patient groups were included in the study, and trauma patients, individuals with hematological diseases, and COVID-19 patients were excluded. Excluding COVID-19 patients may have removed an important subgroup where inflammatory markers like CAR and NLR might be particularly relevant. While the study considered comorbidities such as diabetes, chronic kidney disease, and malignancy, other factors such as frailty, nutritional status, and preexisting inflammatory conditions were ignored. A more detailed multivariate analysis incorporating these variables could enhance the robustness of the conclusions.

Conclusion

In our study, CAR and NLR were shown to have a significant relationship with mortality in geriatric patients admitted to the hospital from the emergency department. In particular, CAR was determined to be a stronger marker in mortality prediction. These biomarkers are considered potential indicators that can be used to support admission decisions in the emergency department and determine patient prognosis. Most importantly, it can also guide early interventions. Larger-scale and prospective studies using mortality risk scores established for geriatric emergency patients, such as the Charlson Comorbidity Index or APACHE II, in the future can better define the clinical uses of these biomarkers.

Disclosures

Ethics Committee Approval: Ethical approval for this study was obtained from Kahramanmaraş Sütçü İmam University Non-Interventional Clinical Research Ethics Committee with the decision dated 23.11.2021 and numbered 01.

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