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Original Research

Red cell distribution width to albumin ratio and neutrophil to lymphocyte ratio as prognostic markers in elderly emergency department patients

Red cell distribution width /albumin in geriatric patient

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Abstract

Aim: The aim of this study was to evaluate Red Cell Distribution Width/Albumin (RAR) and Neutrophil/Lymphocyte Ratio (NLR) in the follow-up and treatment processes of geriatric emergency department patients.

Material and Methods: We retrospectively collected demographic, complaint, comorbidity, vital signs, and laboratory test data of elderly patients who presented to our emergency department over a 6-month period. Next, we investigated the relationship of RAR and NLR with hospitalization, discharge, and mortality.

Results: This study included 1625 patients 606 (37.3%) were hospitalized, whereas 35 (2.2%) died. RAR was significantly different among the discharged, hospitalized, and dead patients (all $p < 0.001$). NLR was a significant predictor of discharge ($p < 0.001$) but not of hospitalization or mortality ($p > 0.05$). In hospitalized patients, the areas under the receiver operating curves for RAR and NLR were 0.662 and 0.655, respectively, with the optimal cutoffs at 3.64 and 3.75, respectively (both $p < 0.001$). Our univariate logistic regression analysis results indicated that RAR and NLR are effective predictors of both hospitalization and mortality (both $p < 0.001$).

Discussion: RAR strongly predicts hospitalization, discharge, and mortality in elderly emergency department patients, whereas NLR appears to predict discharge alone.

Keywords

Albumin, Geriatrics, Neutrophil-To-Lymphocyte Ratio, Red Cell Distribution Width (Mesh Database)

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Introduction

Population aging—an issue in both developed and developing countries—has led to an increase in the prevalence of chronic health issues [1]. Consequently, the need for and frequency of use of emergency services are increasing among elderly individuals. This situation is predicted to considerably affect emergency departments (EDs) over the next three decades. In Turkey, life expectancy is increasing every year; according to 2020 Turkish Statistical Institute data, the average life expectancy in Turkey was 78.6 years in 2017—comparable to the average life expectancy in 28 European countries (including Turkey; 80.9 years) (This information is available at: http: www.data.tuik.gov.tr). Moreover, the proportion of the population aged ≥65 years in Turkey is expected to increase from 8.5% in 2017 to 11% in 2025 (This information is available at: http: www.data.tuik.gov.tr). Similarly, in the United States, one in five individuals is expected to be aged >65 years by 2030 considerably (This information is available at: https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf). Currently, 10%–15% of the ED population is composed of elderly individuals, who use EDs more than younger adults. Therefore, as the aging population increases, the number of ED visits is expected to increase considerably (This information is available at: https://www.census.gov/content/dam/Census/library/publications/2015/demo/p25-1143.pdf).

Red cell distribution width (RDW) is a quantitative expression of anisocytosis, which is calculated as the standard deviation of red blood cell volume divided by mean red blood cell volume (MCV). RDW, a common hematologic parameter, is part of the standard complete blood count in hospitalized patients. Recent studies have demonstrated that, in patients with varied clinical conditions (e.g., cardiovascular disease, stroke, septic shock, and community-acquired pneumonia), a high RDW is associated with an increased mortality risk [2- 4]. RDW is a strong predictor of mortality in middle-aged and older adults; it is also recognized as an age-related prognostic biomarker in adults aged ≥45 years [5].

Serum albumin is an acute-phase protein that is used as a nutritional marker. Because its levels decrease in an inflammatory state, serum albumin is considered a negative acute-phase protein. As such, in hospitalized elderly patients, serum albumin levels are inversely correlated with morbidity and mortality [6]. Moreover, high albumin levels have been correlated with a short-term improvement in the functional status of hospitalized patients [7].

The RDW-to-albumin ratio (RAR) is a newer biomarker that has been used to evaluate the prognoses of patients with stroke [8], heart failure [9], and acute myocardial infarction (MI) [10]. In this study, we evaluated the role of RAR and the neutrophil-to-lymphocyte ratio (NLR) in assessing the outcome of elderly patients in the ED in terms of hospitalization, discharge, and mortality.

Material and Methods

Study Population

This was a single-center, retrospective, observational study. We included patients aged ≥65 years who presented to the ED of a tertiary education and research hospital over 6 months (July 1 to December 31, 2022). We included only patients with a complete blood count (CBC) and serum albumin data. However, we excluded patients who left the ED voluntarily, had no patient admission information, had hematologic malignancy, and presented with trauma.

Study Protocol

Patient age, sex, comorbidity, systolic and diastolic blood pressure, temperature, pulse rate, and fingertip oxygen saturation data were collected from the included patients' medical records. We specifically included neutrophil and lymphocyte counts, RDW, and serum albumin data from their first ED laboratory test, before treatment was initiated. The patients were classified according to their ED outcomes: discharge, hospitalization, or mortality. ED results, mortality in the ED at follow-up, hospitalization, and discharge were recorded. We calculated NLR by dividing neutrophil count (×103 μL) by the lymphocyte count (×103 μL) and RAR by dividing RDW (%) by serum albumin level (g/dL). Sensitivity and specificity for hospitalized, discharged, and dead patients were calculated according to their cutoff RARs and NLRs. Demographic, complaint, comorbidity, vital signs, laboratory tests, and NLR and RAR data of the patients were statistically analyzed according to ED outcome groups.

Statistical Analysis

Here, continuous data are presented as means and standard deviations or medians and interquartile ranges (IQRs), whereas categorical data are presented as numbers and percentages. We used the Kolmogorov–Smirnov test to examine the conformity of the data to normal distribution. We applied Kruskal–Wallis analysis of variance to compare continuous data between discharged, hospitalized, and deceased ED patients, followed by the Kruskal–Wallis multiple comparison test to analyze the origin of between-group differences. The chi-square and Fisher exact tests were used for group comparisons of nominal variables through cross-tabulation. The diagnostic performance of RAR and NLR was evaluated based on the areas under the receiver operating characteristic (ROC) curves (AUCs), with the Youden index used to estimate the optimal cutoff points. The diagnostic accuracy of RAR and NLR values was evaluated using the following accuracy measures: sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Risk factors for hospitalization and mortality were analyzed by univariate and multivariate logistic regression analyses. In the multivariate logistic regression analysis, variables considered risk factors were first included in the univariate logistic regression, and significant variables were then included in the multivariate analysis. The goodness of fit of the model was assessed using the Hosmer-Lemeshow goodness of fit. We used SPSS for Windows 20.0 (SPSS, Chicago, IL, USA) for all statistical analyses and considered $p < 0.05$ to indicate statistical significance.

Ethical Approval

The present study was conducted in accordance with the principles of the Declaration of Helsinki. The Ethics Committee of Ankara Training and Research Hospital approved the study (Date: 2023-04-26, No: E.23/1263).

Results

Over our 6-month study period, 1956 patients aged ≥65 years presented to the ED; all of them underwent testing for CBC and serum albumin. However, we excluded 299 patients because they had missing data and 32 patients because they had hematologic diseases or were receiving active chemotherapy treatment. Finally, 1625 patients were included in the final analysis; their mean age was 77.04 ± 7.90 years, and 54.9% of them were female. Hypertension (70.33%) was the most common comorbidity; furthermore, of all patients, 60.6% were discharged, 37.3% were hospitalized, and 2.2% died. The patients' characteristics are presented in Table 1.

The median (IQR) RAR was 3.67 (0.14–33.26); it demonstrated significant differences between discharged, hospitalized, and dead patients (all $p < 0.001$). In particular, RAR was higher than in discharged patients than in both hospitalized and deceased patients; additionally, it was higher in hospitalized patients than in dead patients. The median (IQR) NLR was 4 (0.1–176.0); moreover, it was lower in discharged patients [3.3 (2.1–6.07)] than in both hospitalized [5.6 (3.0–11.4)] and deceased [6.0 (1.8–11.2)] patients. The NLRs of hospitalized and dead patients demonstrated no significant differences ($p > 0.05$; Table 2).

Table 1. General characteristics of the patients

n=1625	Mean ± SD Median (IQR)
Age (year)	77.04±7.90
	77 (61-97); (70-83)
	n (%)
Gender**	
Female	892 (54.9 %)
Male	733(45.1%)
ComorbiditesComorbidities**	
Hypertension	1143 (70.3%)
Diabetes Mellitus	600 (36.9%)
Coronary Artery Disease	667 (41%)
COPD	254 (15.6%)
Cerebrovascular Disease	238 (14.6%)
CKD/F	136 (8.4%)
Neoplasm	121 (7.4%)
Vital signs*	
SBP (mmHg)	130 (110-155)
DBP(mmHg)	74 (60-82)
Heart rate (/min)	82 (69-98)
Fever (OC)	36.4 (36-36.7)
Breath rate (/min)	18 (16-22)
GCS	15 (14- 15)
Laboratory markers*	
RDW (%)	14. 5 (13.3-16.0)
Albumin (g/dl)	4 (3.6-4.3)
RAR	3.67 (3.22-4.49)
NLR	4 (2.3-8.0)
Lactate (mmol/L)	2.1 (1.50-3.0)
Emergency outcome**	
Discharge	984 (60.6%)
Hospitalization	606 (37.3 %)
Ex	35 (2.2%)

*Data are presented as median (25%–75%), **Data are presented as n (%)
COPD, chronıc obstructıve pulmonary dısease; CKD/, chronic kidney disease, failure; SBP, systolic blood pressure; DBP, Diastolic blood pressure; GCS, Glasgow coma scale; RDW, Red blood cell distribution width; RAR, Red blood cell distribution width albumin ratio; NLR, neutrophil lymphocyte ratio

For RAR, the AUC was 0.662 in hospitalized patients ($p < 0.001$); furthermore, at a cutoff of 3.64, the PPV, NPV, sensitivity, and specificity were 49.2%, 73.1%, 64.8%, and 58.8%, respectively. It was 0.825 in deceased patients ($p < 0.001$); additionally, at a cutoff of 4.01, the PPV, NPV, sensitivity, and specificity were 9.1%, 98.9%, 77.1%, and 72.6%, respectively (Fig. 1). For NLR, the AUC was 0.655 in hospitalized patients ($p < 0.001$); moreover, at a cutoff of 3.75, the PPV, NPV, sensitivity, and specificity were 49.3%, 74.1%, 67.7%, and 57.1%, respectively. It was 0.614 in deceased patients ($p < 0.05$); at a cutoff of 5.05, the PPV, NPV, sensitivity, and specificity were 6.7%, 98.1%, 62.8%, and 68.7%, respectively (Fig. 1).

Our univariate logistic regression analysis demonstrated that the hospitalization risk was elevated in ED patients with high serum albumin and lactate levels, RDW, RAR (>3.64), and NLR (>3.75; $p < 0.001$). When the significant parameters in this univariate analysis were included in our multivariate analysis, an increase in lactate levels by 1 mmol/L led to an increase in hospitalization by 1.229 fold, whereas an NLR of >3.75 led to an increase in hospitalization by 1.782 fold (Table 3). Moreover, another univariate logistic regression analysis indicated that serum lactate and albumin levels, RAR, and NLR were associated with an increased mortality risk (all $p < 0.001$). When the significant parameters in this univariate analysis were included in our multivariate analysis, an increase in lactate levels by 1 mmol/L led to an increase in mortality by 1.445-fold (Table 3).

Discussion

In this study, RAR and NLR were both associated with increased all-cause hospitalization and death in elderly ED patients; in particular, RAR predicted mortality more effectively than NLR.

In a study by Ayrancı et al. that included 784 elderly patients, the median patient age was 75 years, and the most common comorbidity was hypertension (54.5%); furthermore, the ED mortality and hospitalization rates were 0.8% and 49.8%, respectively [11]. Our mortality (2.2%) and hospitalization (37.3%) rates were higher than those reported by Ayrancı et al. This may be due to the differences in the locations of the study hospitals and our patients' inability to receive adequate care services due to difficulties in accessing social support.

Studies have demonstrated that a high RDW is associated with increased mortality in many clinical conditions. A high RDW may result from malnutrition and erythrocyte fragmentation [12]. Specifically, a high RDW and impaired intravascular hemodynamics are associated with vascular pathologies [12]. A

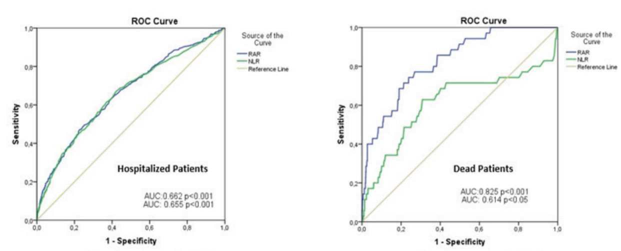

Figure 1. ROC analysis with RAR and NLR in hospitalized and dead patients

recent study included a large group of elderly patients admitted to a hospital for identical reasons; the authors reported that patients with a high RDW at admission stay in the hospital 1.5–2 times longer than patients with a low RDW at admission [13]. Alakare et al. also demonstrated that an increased RDW is associated with increased mortality in elderly patients [14]. Similarly, our results indicated that patients with a high RDW have high hospitalization and mortality risks and that a high RDW predicts hospitalization.

A study on patients aged ≥72 years reported that serum albumin levels decrease with aging [15]. In hospitalized elderly patients, serum albumin levels are inversely correlated with morbidity and mortality [16]. Similarly, higher serum albumin levels were associated with a shorter recovery in functional status in hospitalized patients [7]. These results are corroborated by our current findings: in discharged patients, serum albumin levels were higher than those in hospitalized and deceased patients.

Several studies have demonstrated that NLR is a prognostic

Table 2. Comparison of age, gender, vital signs and laboratory findings of patients who were discharged, hospitalized and died in the emergency department

	Discharge a (n=984)		Hospitalization b (n=606)		EX c (n=35)		p*	Post hoc test
	Mean ± SD Median (IQR)		Mean ± SD Median (IQR)		Mean ± SD Median (IQR)			
	76.39±7.68		78.03±8.07		78.17±9.26			a-b p<0.001
Age (year)	76 (70-82)		78 (72-84)		78 (68-85)		0.0001*	a-c p=0.841
								b-c p=1.000
	139.54±27.60		126.41±34.02		76.23±30.22			a-b p<0.001
SPB	135 (120-160)		123 (100-149)		70 (45-100)		<0.001	a-c p<0.001
								b-c p<0.001
	75.74±14.44		69.40±18.33		45.69±18.74			a-b p<0.001
DBP	75 (67-84)		70 (56.7-80)		40 (32-60)		<0.001	a-c p<0.001
								b-c p<0.001
	82.99±18.55		89.43±24.32		88.69±50.50			a-b p<0.001
Heart rate (/min)	80 (69-92)		87 (72-103)		90 (32-132)		<0.001	a-c p=0.769
								b-c p=1.000
	36.42±0.49		36.64±0.74		36.22±0.79			a-b p<0.001
Fever	36.4 (36-36.5)		36.5 (36-36.8)		36 (36-36.6)		<0.001	a-c p=0.054
								b-c p<0.001
	18.20±3.92		22.93±7.38		23.23±13.24			a-b p<0.001
Breath rate (/min)	18 (16-20)		21 (17-28)		25 (6-34)		<0.001	a-c p<0.001
								b-c p=1.000
	14.90±0.36		13.47±2.52		8.06±4.42			a-b p<0.001
GCS	15 (15-15)		15 (13-15)		8 (3-13)		<0.001	a-c p<0.001
								b-c p<0.001
	14.82±4.66		15.77±3.23		17.05±3.12			a-b p<0.001
RDW	14 (13.2-15.4)		15 (13.9-16.8)		16.2 (14.5-19.8)		<0.001	a-c p<0.001
								b-c p=0.034
	4.01±0.47		3.69±0.66		3.29±0.68			a-b p<0.001
Albumin	4.1 (3.8-4.3)		3.8 (3.3-4.2)		3.3 (3.0-3.8)		<0.001	a-c p<0.001
								b-c p=0.002
	3.77±1.30		4.52±1.84		5.56±2.18			a-b p<0.001
RAR	3.50 (3.14-4.08)		4.03 (3.4-5.03)		4.84 (4.03-6.48)		<0.001	a-c p<0.001
								b-c p=0.002
	5.09±5.50		9.32±12.20		8.51±8.18			a-b p<0.001
NLR	3.3 (2.10-6.07)		5.6 (3.0-11.4)		6.0 (1.8-11.2)		<0.001	a-c p=0.039
								b-c p=1.000
	2.23±1.27		3.20±3.05		10.12±6.20			a-b p<0.001
Lactate	2 (1.4-2.6)		2.4 (1.7-3.4)		9.6 (4.8-14.5)		<0.001	a-c p<0.001
								b-c p<0.001
	n	%	n	%	n	%		
Gender								
Female	563	57.2	308	50.8	21	60.0	0.038**	a-b p=0.013
Male	421	42.8	298	49.2	14	40.0		a-c p=0.743
								b-c p=0.291

* Kruskal-Wallis Analysis of Variance
** Ki kare Test
SBP, systolic blood pressure; DBP, Diastolic blood pressure; GCS, Glasgow coma scale; RDW, Red blood cell distribution width; RAR, Red blood cell distribution width albumin ratio; NLR, neutrophil lymphocyte ratio;

Table 3. Univariate and Multivariate Logistic Regression Analysis of risk factors for hospitalization and death

	Risk Factors for Hospitalization						Risk Factors for Death					
	Univariate			Multivariate			Univariate			Multivariate		
	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value
Age	1.027	1.014-1,040	<0.001				1.030	0.986-1.075	0.183			
Gender (male)	1.294	1.056-1.585	0.013				1.122	0.564-2.232	0.744			
SBP	1.014	1.011-1.018	<0.001	1.008	1.002-1.014	0.008	1.094	1.070-1.117	<0.001			
DBP	1.025	1.018-1.031	<0.001				1.141	1.107-1.177	<0.001			
GCS	4.464	3.571-5.586	<0.001	3.315	2.475-4.445	<0.001	8.064	4.464-14.492	<0.001	3.861	1,658-9,009	0,002
BR	1.165	1.140-1.191	<0.001	1.127	1.098-1.156	<0.001	1.149	1.094-1.207	<0.001	1,189	1,023-1,382	0,024
Albumin	2.762	2.272-3.355	<0.001				7.633	4.366-13.333	<0.001			
RDW-CV	1.107	1.065-1.150	<0.001				1.029	0.998-1.061	0.064			
Lactate	1.332	1.239-1.432	<0.001	1.229	1.129-1.337	<0.001	1.977	1.679-2.329	<0.001	1,445	1,138-1,835	0,003
RAR >3,64	2.638	2.139-3.253	<0.001				8.971	4.971-19.991	<0.001			
NLR >3.75	2.774	2.245-3.429	<0.001	1.782	1.360-2.336	<0.001	3.714	1.847-7.470	<0.001			

OR: Odds Ratio
CI: Confidence Interval
SBP, systolic blood pressure; DBP, Diastolic blood pressure; GCS, Glasgow coma scale; BR, breath rate; RDW, Red blood cell distribution width; RAR, Red blood cell distribution width albumin ratio; NLR, neutrophil lymphocyte ratio

marker of acute coronary syndromes, cerebrovascular events, cancer, and acute infections [17- 20]. In the current study, NLR was significantly lower in the hospitalized and deceased patients than in the discharged patients, regardless of their diagnosis. In a study by Song et al. that included 2777 elderly patients, the AUC for NLR was 0.714 in dead patients [21].

RAR is a novel biomarker previously used to diagnose acute MI, aortic aneurysm, pneumonia, diabetes, and cancer; it is also considered a prognostic indicator [8- 10]. To our knowledge, this is the first study evaluating the use of RAR to predict hospitalization, discharge, and mortality in elderly ED patients. We found that RAR differed between discharged, hospitalized, and deceased ED patients. Moreover, the RARs of the discharged patients were lower than those of both the hospitalized and deceased patients, whereas the RARs of the hospitalized patients were lower than those of the dead patients. Hong Wu et al. reported that in patients with acute MI, 90-day mortality was lower when the RAR was <4.32 ($p < 0.001$) [10]. Another study reported that the RAR was associated with significant 28-day mortality in 234 patients with pneumonia in another univariate [odds ratio (OR) = 1.545, 95% confidence interval (CI) = 1.282–1.862, $p < 0.001$] and multivariate (OR = 1.379, 95% CI = 1.103–1.723, $p < 0.005$) logistic regression analyses [22]. In a study on the role of RAR in predicting mortality in 1480 patients with stroke, a high RAR was significant (all $p < 0.001$) in 30-day, 90-day, and 1-year mortality [8]. Similarly, a population-based, prospective, cohort study investigating the prognostic role of RAR found that higher RAR was associated with an increased risk of death from any disease according to multivariate analysis [23]. Among a total of 50,622 patients from the United States (aged ≥18 years) and 418,950 patients from the United Kingdom (aged ≥37 years), the mean RAR for the first group was 3.15 and for the second group was 2.99 [23]. The reason the mean RAR in that study were lower than in ours may be due to our patient group including an older population. The authors reported that the RAR was statistically significantly higher in predicting mortality for all causes of a total of 7,590 deaths in the first group and 36,973 deaths in the second group, regardless of age. The causes of mortality that RAR predicted with statistical significance were cancer, heart disease, cerebrovascular disease, respiratory disease, diabetes, and other causes [23].

In the current study, NLR and RAR were better at predicting hospitalization and mortality, respectively. This may have been due to the inclusion of all hospitalized patients in one group, without stratifying hospitalized patients based on which department they were admitted (inpatient care or intensive care unit); additionally, the mortality rate among our patients was low.

RAR is thus an accessible biomarker predicting hospitalization in elderly ED patients. However, this finding warrants a larger-scale prospective study.

Limitation

The main limitation of this study is its retrospective, single-center design. Studies predicting mortality after discharge and mortality during hospitalization in elderly patients are warranted.

Conclusion

The current results revealed that high RAR levels predict hospitalization and mortality in elderly ED patients. Therefore, RAR is a simple, accessible prognostic biomarker that could improve the management of elderly ED patients in the future.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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