ORIGINAL ARTICLE

THE PREDICTIVE POWER OF SIMPLE SYSTEMIC INFLAMMATORY PARAMETERS FOR IN–HOSPITAL MORTALITY IN ELDERLY PATIENTS

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Abstract

Introduction: We evaluated the predictive power of systemic inflammatory parameters, including the neutrophil/lymphocyte ratio, C-reactive protein/albumin ratio, monocyte/eosinophil ratio, and platelet/lymphocyte ratio, for all-cause in-hospital mortality in elderly.

Materials and Method: This single–center and retrospective study enrolled 46,563 patients aged ≥65 years who presented to the emergency department due to various complaints from June 2019 to June 2022. We evaluated the demographics, clinical characteristics, laboratory data, and clinical outcomes of the patients.

Results: A total of 3,385 hospitalized patients, 1,808 males and 1,577 females, were included in the study. The average age was 76.25±7.35 years. The overall mortality rate was 11.73%. Nonsurvivors had significantly elevated neutrophil/lymphocyte, C-reactive protein/albumin, monocyte/eosinophil, and platelet/lymphocyte ratios compared to survivors (p=0.0001 for all comparisons). Elevated neutrophil/lymphocyte and C-reactive protein/albumin ratios were determined as independent predictors of mortality. A neutrophil/lymphocyte ratio ≥9.41 had 46.97% sensitivity and 79.99% specificity for predicting mortality. While the positive predictive value was 23.7%, the negative predictive value was 91.9%. Additionally, a C-reactive protein/albumin ratio ≥13.18 was identified as the cut-off for mortality, with 57.07% sensitivity and 69.91% specificity. Its positive and negative predictive values were 20.1% and 92.5%, respectively.

Conclusion: Mean serum neutrophil/lymphocyte and C-reactive protein/albumin ratios on hospital admission were associated with all-cause mortality in hospitalized patients aged ≥65 years. However, their sensitivity and positive predictive value were relatively low. Nevertheless, negative predictive value for both were significantly high. This implies that these parameters could be used to determine the elderly at a lower risk of mortality.

Keywords: Aged; Biomarkers; Decision Making; Mortality.

INTRODUCTION

The global population is gradually aging. Aged patients visit the emergency department (ED) more frequently than young people do (1). The elderly typically presents to the ED with atypical complaints and findings. Due to comorbidities and polydrug use, the diagnosis and treatment of these individuals may be delayed (1, 2). Furthermore, older patients are at high risk of recurrent ED visits, hospitalization, morbidity, and mortality (3). Although numerous risk scores have been developed to identify at-risk individuals, none offer highly accurate predictions.

Infective parameters, such as neutrophil/lymphocyte ratio (NLR), C-reactive protein/albumin (CRP/Alb) ratio, monocyte/eosinophil ratio (MER), and platelet/lymphocyte ratio (PLR), are simple, rapidly accessible, and widely available markers of inflammatory status. NLR has been linked to the prognosis of infectious disorders, such as sepsis and bacteremia (4). NLR has also been associated with the clinical outcomes of noncommunicable diseases, such as acute myocardial infarction and stroke (5, 6). In a study of 5,166 elderly patients, CRP/Alb ratio was indicative of all-cause in-hospital mortality (7). Chen et al. reported that a low MER is linked to mortality and a poor prognosis in cases of acute ischemic stroke (8). Age-related chronic inflammation is a risk factor for morbidity and mortality in the elderly (9). Infective parameters, such as NLR, PLR, MER, and CRP/Alb ratios, may be predictive of mortality and morbidity in the elderly.

We investigated the predictive power of NLR, PLR, MER, and CRP/Alb serum administration at admission with respect to all-cause in-hospital mortality in elderly patients presenting to the ED.

MATERIALS AND METHOD

Ethics committee approval and patient consent

This study was conducted in accordance with the 1989 Declaration of Helsinki and was approved by the institutional review board of Haseki Research and Training Hospital, Istanbul, Türkiye (approval no. 2022/198). The institutional review board did not request patient consent to access medical records since there were no potentially identifiable markers or patient identifiers.

Study design and setting

This single-center, retrospective, and observational study enrolled 46,563 consecutive patients aged ≥ 65 years who presented to the ED from June 2019 to June 2022. Data on patients aged ≥ 65 years who visited the ED with any medical problem were collected from the hospital's automated records and archives. We assessed the patients' demographic information (age and sex), initial complaints and diagnoses, comorbidities, vital signs, laboratory parameters (leukocyte, neutrophil, lymphocyte, eosinophil, monocyte, and platelet counts and CRP and albumin levels), clinical outcomes (discharge, hospitalization, intensive care unit admission, and mortality), and Glasgow Coma Scale (GCS) and quick Sequential Organ Failure Assessment (Q-SOFA) scores. The patients were divided into survivors and nonsurvivors, and the serum systemic inflammatory markers of the two groups at admission were compared to identify factors associated with mortality.

Outcome definition

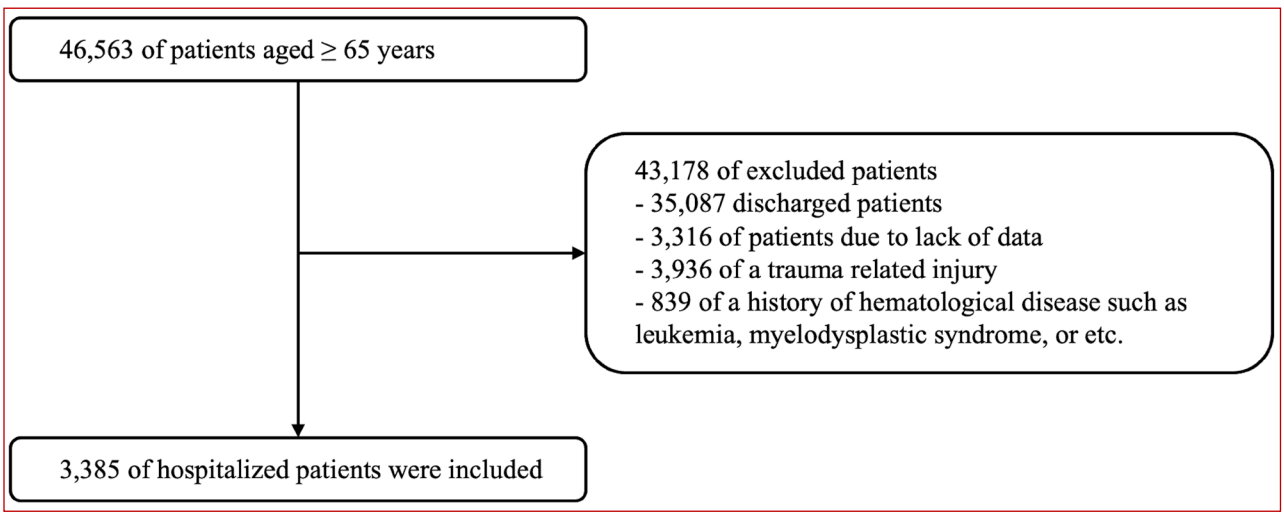
We evaluated the abilities of the NLR, PLR, MER, and CRP/Alb values to predict all-cause in-hospital mortality in elderly patients.

Study population and sampling

To reduce selection bias, all patients who met the eligibility criteria during the study period were included. We enrolled 46,563 consecutive adult patients aged ≥ 65 years who visited the ED with any medical problem. Of these individuals, 35,087 discharged patients were excluded. A further 3,316

were excluded because their data could not be accessed. A total of 3,936 patients were excluded because of trauma-related injuries and 839 patients because of a history of hematological diseases, such as leukemia or myelodysplastic syndrome. Ultimately, 3,385 patients were analyzed (Figure 1).

Figure 1. Flowchart.



Statistical analysis

Data analysis was conducted using SPSS software (version 15.0 for Windows; SPSS Inc., Chicago, IL). Categorical variables (sex and age) are expressed as numbers (n) and percentages (%). Numerical data are expressed as means, standard deviations, median, and interquartile range (IQR). Intergroup comparisons (survivors vs. non–survivors) were conducted by chi–squared and Student's independent t–tests for normally distributed variables (e.g., sex and age) and Mann–Whitney U–test for non–normally distributed variables (e.g., leukocyte, neutrophil, lymphocyte, and thrombocyte counts). Logistic Regression analysis was conducted to determine the factors associated with mortality. Receiver operating characteristic analysis was performed to determine the NLR, PLR, MER, and CRP/Alb cut–off values. The alpha significance level was set at $p < 0.05$.

RESULTS

This study involved 3,385 hospitalized patients, comprising 1,808 males (53.41%) and 1,577 females (46.59%), with an average age of 76.25 ± 7.35 years. The overall mortality rate was 11.73% (n = 397). Table 1 lists the patients' demographic and clinical characteristics. The sex and age of the survivors and nonsurvivors differed significantly ($p = 0.025$ and $p = 0.0001$, respectively). The nonsurvivors had a significantly higher Q-SOFA score and a lower GCS score than the survivors ($p = 0.0001$ for both comparisons). Moreover, the nonsurvivors had significantly elevated NLR, MER, PLR, and CRP/Alb values compared with the survivors ($p = 0.0001$ for all comparisons).

Multivariate logistic regression analysis identified increased age (odds ratio [OR]: 1.05, 95% confidence interval [CI]: 1.03–1.07; $p = 0.0001$), male gender (OR: 1.52, 95% CI: 1.14–2.01; $p = 0.009$), higher Q-SOFA (OR: 4.72, 95% CI: 3.68–6.03; $p = 0.0001$) score, and

Table 1. Comparison of demographic, clinical and laboratory characteristics in surviving and non–surviving patients.

		Survivors (n = 2,988)	Non–survivors (n = 397)	p*
Characteristic		**n (%)**	**n (%)**	
Sex	Male	1,575 (52.71)	233 (58.69)	0.025
	Female	1,413 (47.29)	164 (41.31)	
		mean ± SD	**mean ± SD**	
Age, years		75.97 ± 7.25	78.29 ± 7.85	0.0001
Lengths of stay		11.56 ± 6.00	8.62 ± 7.10	0.0001
Q-SOFA		0.62 ± 0.90	2.38 ± 0.73	0.0001
GCS		13.46 ± 2.80	7.95 ± 3.48	0.0001
Hemoglobin (g/dL)		13.37 ± 2.62	12.97 ± 2.81	0.004
WBC (10^3/uL)		11.14 ± 5.11	13.71 ± 6.77	0.0001
Neutrophil (10^3/uL)		8.44 ± 4.88	10.92 ± 6.46	0.0001
Lymphocyte (10^3/uL)		1.86 ± 1.25	1.88 ± 1.99	0.736
Thrombocyte (10^3/uL)		244.67 ± 87.12	236.69 ± 97.75	0.091
Monocyte (10^3/uL)		0.68 ± 0.37	0.77 ± 0.54	0.016
Eosinophil (10^3/uL)		0.12 ± 0.16	0.07 ± 0.13	0.0001
CRP (mg/L)		52.15 ± 77.54	99.99 ± 103.91	0.0001
		Median (IQR)	**Median (IQR)**	
NLR		4.41 (2.55–8.38)	8.02 (3.55–16.61)	0.0001
MER		8.60 (3.56–38.05)	44.37 (8.5–144.29)	0.0001
PLR		144.17 (98.47–220.7)	173.24 (98.1–314.95)	0.0001
CRP/Alb		4.16 (1.26–18.31)	17.70 (3.58–56.75)	0.0001

Note: Data are expressed as numbers (n) and percentages (%), means, standard deviations (SD), median, and interquartile range (IQR). *Intergroup comparisons (Survivors vs. non–survivors) were conducted using chi–squared and Student's independent t–tests for normally distributed data (e.g., sex and age) and the Mann–Whitney U test for non–normally distributed data (e.g., leukocyte, hemoglobin neutrophil, lymphocyte, thrombocyte counts, and etc.).

Abbreviations: Q–SOFA, quick Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; WBC, white blood cell; CRP, C–reactive protein; NLR, neutrophil/lymphocyte ratio; MER, monocyte/eosinophil ratio; PLR, platelet/lymphocyte ratio; CRP/Alb, C–reactive protein/albumin ratio.

Table 2. Multivariate logistic regression analysis to determine mortality.

	p	OR	95% CI
Age, years	0.0001	1.05	1.03–1.07
Sex (male)	0.009	1.52	1.14–2.01
Q-SOFA	0.0001	4.72	3.68–6.03
GCS	0.127	0.92	0.88–1.02
NLR	0.003	1.03	1.01–1.05
MER	0.004	1.00	1.00–1.01
PLR	0.241	1.00	0.98–1.01
CRP/Alb	0.0001	1.02	1.01–1.03

Abbreviations: OR, odds ratio; CI, confidence interval; Q–SOFA, quick Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; NLR, neutrophil/lymphocyte ratio; MER, monocyte/eosinophil ratio; PLR, platelet/lymphocyte ratio; CRP/Alb, C–reactive protein/albumin ratio.

elevated NLR (OR: 1.03, 95% CI: 1.01–1.05; p = 0.003) and CRP/Alb (OR: 1.02, 95% CI: 1.01–1.03; p = 0.0001) values as independent predictors of mortality in hospitalized patients aged ≥ 65 years admitted to the ED with any medical problem (Table 2).

An NLR ≥ 9.41 had 46.97% sensitivity and 79.99% specificity for predicting mortality, with an area under the curve (AUC) of 0.651 (95% CI: 0.635–0.667). While the positive predictive value (PPV) was 23.7%, the negative predictive value (NPV) was 91.9%. In addition, a CRP/Alb ≥ 13.18 was identified as the cutoff for mortality, with 57.07% sensitivity and 69.91% specificity (AUC: 0.769, 95% CI: 0.741–0.796). Its PPV and NPV were 20.1% and 92.5%, respectively (Table 3 and Figure 2).

Table 3. Systemic inflammatory parameters for determining mortality in elderly.

Criterion	AUC	SE	95% CI	Sensitivity	Specificity	PPV	NPV	LR (+)
NLR ≥ 9.41	0.651	0.016	0.635-0.667	46.97	79.99	23.7	91.9	2.35
MER ≥ 31.11	0.689	0.015	0.673-0.704	57.32	73.09	22.0	92.8	2.13
PLR ≥ 199.71	0.564	0.016	0.547-0.581	44.19	71.65	17.1	90.6	1.56
CRP/Alb ≥ 13.18	0.668	0.016	0.652-0.684	57.07	69.91	20.1	92.5	1.90

Abbreviations: AUC, Area under the curve; SE, Standard error; CI, Confidence interval; PPV, Positive predictive value; NPV, Negative predictive value; LR (+), Likelihood Ratio; NLR, neutrophil/lymphocyte ratio; MER, monocyte/eosinophil ratio; PLR, platelet/lymphocyte ratio; CRP/Alb, C–reactive protein/albumin ratio.

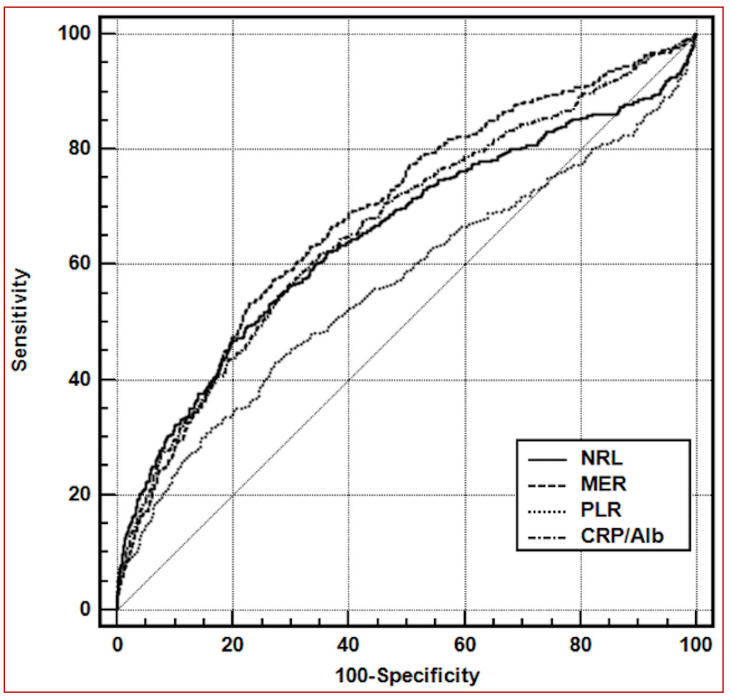


Figure 2. Specificity and sensitivity of the serum systemic inflammatory parameters including NLR, PLR, MER, and CRP/Alb values, for determining the mortality in hospitalized patients aged 65 and older using ROC curves.

Abbreviation: NLR, neutrophil/lymphocyte ratio; MER, monocyte/eosinophil ratio; PLR, platelet/lymphocyte ratio; CRP/Alb, C–reactive protein/albumin ratio.

DISCUSSION

Our findings demonstrate the possibility of using NLR, PLR, MER, and CRP/Alb to predict all-cause in-hospital mortality in elderly patients admitted to the ED.

Elderly patients frequently present to the ED with unusual symptoms, comorbidities, drug use, and delayed diagnosis (1, 2). Emergency physicians need fast, simple, low-cost, repeatable, and widely available markers of medical conditions in the elderly. Ratio indices are increasingly used to predict the clinical outcomes of patients who present to the ED. For example, NLR, PLR, MER, and CRP/Alb are easily calculated and predictive of clinical outcomes (4–11). The key finding of this study was that NLR and CRP/Alb values were independent predictors of mortality in hospitalized patients aged ≥ 65 years; however, their sensitivity and PPV values were relatively low.

NLR has been linked to the clinical outcomes of various diseases and may be a prognostic indicator of infectious disorders (4–6, 10, 11). NLR was independently associated with 28-day mortality in patients with severe sepsis and septic shock (10). In addition, NLR was associated with a high mortality rate in acute myocardial infarction cases (5). In a study with 5,056 patients, NLR was related to poor outcomes in unspecified critical illnesses (11). Similarly, our study demonstrated that NLR at ED admission was independently predictive of all–cause mortality in patients aged ≥ 65 years. The mechanism underlying the relationship between NLR and noncommunicable disease mortality is unclear. Song et al. hypothesized that NLR is associated with mortality because it represents an imbalance in the inflammatory response triggered by acute illness (9). Chronic inflammation, which has been linked to aging, is another possibility (12). Although NLR was found to be associated with mortality in the hospitalized elderly in our study, its sensitivity and PPV were relatively low. In a study by Song et al., an NLR > 6 demonstrated a sensitivity of 62.86% and a specificity of 69.93% for predicting mortality (9). Reflecting our findings, the sensitivity and specificity of NLR in their study were not sufficient for clinical decision-making.

PLR and MER values are associated with prognosis and clinical outcomes in various clinical conditions (8, 13–15). In a study involving 280 patients with acute ischemic stroke, a high MER was related to poor clinical outcomes and mortality (8). MER has been correlated with short- and long-term mortality in ST-elevation myocardial infarction (13). In addition, an elevated MER predicts long-term mortality in pulmonary embolism patients (14). Moreover, mortal patients with acute exacerbation of chronic obstructive pulmonary disease had elevated NLR and PLR values (15). Similarly, in our study, nonsurvivors had significantly elevated MER and PLR values compared with survivors, suggesting that these markers may be useful for predicting clinical outcomes. However, multivariate logistic regression analysis indicated that neither PLR nor MER can reliably and independently predict mortality in hospitalized elderly patients.

An elevated level of CRP, an acute-phase reactant, has been linked to the prognosis of ischemic diseases, infections, and malignancies (16). Serum albumin level is a sensitive indicator of nutritional status. Hypoalbuminemia is associated with increased hospital mortality among older patients (17). CRP and albumin are prognostic markers in various clinical scenarios, but their combination can provide inflammatory and nutritional information. Among 811 elderly patients, CRP/Alb ratio was found to be predictive of all-cause mortality (7). Kaplan et al. (18), Sogut et al. (19), and Bai et al. (20) reported that CRP/Alb value is a significant predictor of a poor clinical outcome in patients with acute pancreatitis, acute coronary syndrome, and neurocritical illness, respectively. In our study, a mean CRP/Alb ≥ 13.18 was identified as the cutoff for predicting mortality, with 57.07% sensitivity and 69.91% specificity among patients aged ≥ 65 years admitted to the ED with any medical condition.

The strength of our study is the large sample size (46,563 patients). However, this study also has several limitations. This was a retrospective observational study conducted at a single center, which increases the possibility of undiscovered confounding factors and restricts the generalizability of the findings. In addition, the primary outcome was all-cause in-hospital mortality. Despite the large sample size, there were only 397 mortalities, and we could not analyze the causes of mortality. These issues should be considered in future studies.

CONCLUSIONS

Our study identified elevated NLR and CRP/Alb values as potential systemic inflammatory parameters for predicting in-hospital mortality in patients aged ≥ 65 years. However, the PPV for both NLR and CRP/Alb was found to be low, suggesting that these parameters may not be strong indicators of mortality. Moreover, the sensitivity and specificity values for both parameters were not reliable enough for use in clinical decision-making. Nevertheless, the NPVs for NLR and CRP/Alb were significantly high. This implies that NLR values < 9.41 and CRP/Alb values < 13.18 might be safely used by clinicians to identify elderly patients at a lower risk of in-hospital mortality.

Statement of Ethics: This study was approved by the Institutional Review Board of Haseki Research and Training Hospital, Istanbul, Turkey (approval no. 2022/198).

Conflict of interest statement: The authors declare no competing interests.

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Data Availability Statement: The data underlying this study are available from the corresponding author upon reasonable request.

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