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Factors affecting the outcome of older adults followed in the intensive care unit according to age stages

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Abstract

Background/Aim: Increased frailty with age along with an increase in comorbidities heighten mortality in intensive care units. According to the World Health Organization, old age is divided into three stages: 65–74 years, 75–84 years, and 85 years and older. The lengthened human lifespan leads to a growth in the number of elderly patients in intensive care units, and the need to know the factors associated with prognosis in the three stages of old age. We aimed to define factors affecting mortality in these three stages of aging and the factors that can help predict prognoses.
Methods: In this retrospective cohort, data of patients over the age of 65 who were admitted to the intensive care unit of Bolu Izzet Baysal State Hospital between January 2016 and December 2020 were recorded using the hospital's automation system. Demographic data, blood tests, diagnoses and inflammatory biomarkers, such as RDW, NLR, and CAR were recorded. The data were analyzed using SPSS, and $P<0.05$ was considered significant.
Results: In this study, 46.2% of the 1566 patients died. The most common diagnosis for admission to the intensive care unit was sepsis, and the most common comorbidity was hypertension. While neurological impairment ($P<0.001$), malignancy ($P=0.006$), and cardiac disease ($P=0.004$) were associated with mortality in all three stages of old age, chronic obstructive pulmonary disease was associated with mortality in the 85 years and older age group ($P=0.011$) and diabetes in those aged 65–74 years and 75–84 years. The APACHE II score ($P<0.001$) and red cell distribution width ($P<0.001$) were highly effective in predicting prognoses in all three stages of old age.
Conclusion: In examining the factors associated with mortality in older age intensive care unit patients, we found that the APACHE II score and red cell distribution width were effective in establishing prognoses for all age groups.

Keywords: geriatrics, intensive care units, mortality, APACHE II, red cell distribution width

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Ethics Committee Approval
The study was approved by Bolu Abant İzzet Baysal University Clinical Researches Ethics Committee (November 23, 2021; 2021/252). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Introduction

Much of the population in intensive care units (ICU) comprises patients of advanced age. Today, patients over the age of 65 are considered older age, and with the recommendation of the World Health Organization, can be divided into three age groups: 65–74,75–84, and 85 years and older. In general, ICUs have high mortality rates. Even if age alone is not a factor, concomitant diseases and age-related systemic disorders can affect mortality [1].

Laboratory follow-ups are carried out daily in critically ill patients to determine the effects of systemic disorders on the body. Scoring systems based on the results of laboratory tests and clinical examinations are used for patient follow-up. The Acute Physiology and Chronic Health Evaluation (APACHE) II is one of the most frequently used scoring systems [2]. With improvements and modifications over the years, it has become a useful and accurate predictor of mortality. There are biomarkers and components of blood tests that are not included in this scoring system but have been proven to play a role in mortality in studies conducted over time. Hospitalization diagnoses, comorbidities, neutrophil count, lymphocyte count, platelet (PLT) count, creatinine level, neutrophil-lymphocyte ratio (NLR), C-Reactive Protein (CRP) albumin ratio (CAR), and red blood cell distribution width (RDW) are among these components [3,4]. Their use became widespread during COVID-19 pandemic [5].

We aimed to determine the conditions affecting mortality and predicting prognosis according to the stages of old age in patients over 65 years of age admitted to the ICU.

Materials and methods

Patient selection

The data of the ICU patients aged 65 years and above were collected after obtaining ethical approval from the Bolu Abant Izzet Baysal University Clinical Research Ethics Committee, dated November 23, 2021 with decision number 2021/252. Based on the classification approved by the WHO, the study population was divided into three subgroups: those aged 65–74, 75–84, and 85 years and older [6]. Inclusion criteria were defined as age >65 years. Exclusion criteria were defined as being under 65 years of age, missing information on patient data, and being diagnosed with COVID-19.

Data collection

This was a retrospective cohort study. Patient data from the hospital database were retrospectively reviewed. The patient’s sex, age, diagnosis of intensive care unit admission, ICU length of stay (LoS), current comorbidities, and status of receiving inotropic therapy and renal replacement therapy were examined and recorded. Leukocyte, lymphocyte, PLT, creatinine, RDW, NLR, and CAR levels were recorded. The APACHE II scoring system was used and recorded in the patients' ICU follow-ups.

Statistical analysis

Descriptive statistics are presented as frequency, percentage, mean, standard deviation, median, minimum, maximum, and 25%–75% percentile (Q1–Q3) values. The assumption of normality was checked by examining the histogram, q-q plot, skewness, and kurtosis values using the Shapiro–Wilk test. As the data were not normally distributed, the Mann–Whitney U test was used to analyze the difference between the numerical data of the groups. In examining the relationships between categorical data, the Pearson chi-square test was used when the expected small cell ratio less than 5 was less than 20%, and Fisher's exact test was used when the expected value was greater than 20%. Multivariate binary logistic regression analysis was performed to identify independent risk factors affecting survival. Statistical significance was set at *P*-value <0.05. SPSS software (version 23.0) was used for comparisons, while Medcalc was used for ROC analyses.

Results

In this study, 723 (46.2%) of the 1566 patients died. The mean age of the patients was 78.96 years. Overall, 50.8% of the patients were male. Among the patients, 32.6% were aged 65–74, 38% were 75–84, and 29.4% were 85 years and older. On the basis of the patients' ICU admission diagnoses, the majority were diagnosed with sepsis, pneumonia, and stroke. The most common comorbidities were hypertension (HT) 26.9% and chronic obstructive pulmonary disease (COPD) 23.8% (Table 1).

Table 1: Demographic and clinical characteristics of the study groups

	Total patients (n=1566)
Age (years), Age groups, n (%)	78.9 (65–100)
65–74 years	510 (32.6)
75–84 years	595 (38)
85 years and older	461 (29.4)
Mortality, n (%)	723 (46.2)
Sex, n (%)	
Female	795 (50.8)
Male	771 (49.2)
Diagnosis, n (%)	
Sepsis	633 (40.4)
Pneumonia	287 (18.3)
Stroke	230 (14.7)
Acute kidney injury	85 (5.4)
Pulmonary thromboembolism	74 (4.7)
Intoxication	15 (1)
Urinary tract infection	23 (1.5)
Other	197 (12.6)
Comorbid diseases, n (%)	
Hypertension	422 (26.9)
Diabetes mellitus	289 (18.5)
COPD	373 (23.8)
Malignity	254 (16.2)
Neurologic disorders	287 (18.3)
Cardiac disease	272 (17.4)

COPD: chronic obstructive pulmonary disease

The difference between discharge and exitus status in each of the age groups by numerical variables is presented in Table 2. Age was found to be statistically significant only in the 75–84 years age group (*P*=0.007). No significant differences were observed between the other groups. LoS was higher among patients who died for all age groups (*P*<0.001). The RDW (*P*<0.001), leukocyte count (*P*=0.001), NLR (*P*<0.001), CAR (*P*<0.001), creatinine (*P*<0.001), and APACHE II scores (*P*<0.001) were also higher for those who died in all age groups. Lymphocyte (*P*<0.001) and PLT counts (P<001 in 65-74, *P*=0.026 in >75) were lower among patients who died in all age groups (Table 2).

The analysis of discharged and deceased patients in the three age groups using categorical variables is shown in Table 3. While the rate of diabetes mellitus (DM) was higher in those who died in the 65–74 (*P*=0.05) and 75–84 (*P*=0.02) years age groups than in those who were discharged, this difference was

Table 2: Comparison of old age groups according to mortality predictors

Variables		65–74 years			75–84 years			85 years and older		
		n	m	*P*-value	n	m	*P*-value	n	m	*P*-value
Age(year)	Survived	306	69.4	0.292	346	79.47	0.007	191	88.9	0.647
	Died	204	69.7		249	78.91		270	89.13	
LoS(day)	Survived	306	8.5	<0.001	346	9.82	<0.001	191	9.24	<0.001
	Died	204	12.8		249	14.3		270	15.03	
RDW	Survived	306	15.6	<0.001	346	15.83	<0.001	191	15.91	<0.001
	Died	204	18.3		249	1775		270	17.67	
Leukocyte (10^3/µL)	Survived	306	11.6	<0.001	346	11.74	<0.001	191	10.52	<0.001
	Died	204	14.8		249	14.31		270	13.23	
Lymphocyte (10^3/µL)	Survived	306	1.2	<0.001	346	1.16	0.003	191	1.39	<0.001
	Died	204	0.96		249	0.97		270	0.93	
Platelet (10^3/µL)	Survived	306	228	<0.001	346	220.03	0.292	191	216.19	0.026
	Died	204	200		249	208.91		270	197.63	
NLR	Survived	306	12.88	<0.001	346	13.31	<0.001	191	11.46	<0.001
	Died	204	22.42		249	20.09		270	20.3	
CAR	Survived	306	21.29	<0.001	346	25.7	<0.001	191	26.17	<0.001
	Died	204	38.22		249	28.22		270	38.89	
Creatinine (mg/dL)	Survived	306	1.53	<0.001	346	1.58	<0.001	191	1.52	0.007
	Died	204	2.16		249	1.91		270	1.77	
APACHE ll	Survived	306	17.73	<0.001	346	19.45	<0.001	191	21.93	<0.001
	Died	204	26.73		249	28.22		270	28.49	

APACHE: Acute Physiology and Chronic Health Evaluation, CAR: CRP to albumin ratio, NLR: neutrophil to lymphocyte ratio, RDW: red cell distribution width, LoS: Length of Stay

Table 3: Patient characteristics affecting mortality according to older age groups

		65–74 years old			75–84 years old			85 years and older		
Prognosis		**Survived**	**Died**		**Survived**	**Died**		**Survived**	**Died**	
Variables		**n (%)**	**n (%)**	***P*-value**	**n (%)**	**n (%)**	***P*-value**	**n (%)**	**n (%)**	***P*-value**
Sex	Female	136 (44.4)	76 (37.3)	0.107	178 (51.4)	128 (51.4)	0.992	117 (61.3)	160 (59.3)	0.666
	Male	170 (55.6)	128 (62.7)		168 (48.6)	121 (48.6)		74 (38.7)	110 (40.7)	
Diagnosis	Pneumonia	54 (17.6)	36 (17.6)		66 (19.1)	52 (20.9)		34 (17.8)	45 (16.7)	
	Stroke	50 (16.3)	21 (10.3)		57 (16.5)	43 (17.3)		23 (12.0)	36 (13.3)	
	Sepsis	91 (29.7)	104 (51.0)		123 (35.5)	112 (45.0)		72 (37.7)	131 (48.5)	
	Acute kidney injury	19 (6.2)	9 (4.4)		11 (3.2)	9 (3.6)		15 (7.9)	22 (8.1)	
	Pulmonary thrombo-embolism	20 (6.5)	7 (3.4)		23 (6.6)	13 (5.2)		7 (3.7)	4 (1.5)	
	Trauma	10 (3.3)	2 (1.0)		6 (1.7)	0 (0.0)		3 (1.6)	1 (0.4)	
	Intoxication	7 (2.3)	2 (1.0)		3 (0.9)	1 (0.4)		1 (0.5)	1 (0.4)	
	Urinary tract infection	2 (0.7)	2 (1.0)		2 (0.6)	3 (1.2)		7 (3.7)	7 (2.6)	
	Other	53 (17.3)	21 (10.3)		55 (15.9)	16 (6.4)		29 (15.2)	23 (8.5)	
Comorbidity	HT	76 (24.8)	50 (24.5)	0.933	88 (25.4)	81 (32.5)	0.058	51 (26.7)	76 (28.1)	0.732
	DM	48 (15.7)	46 (22.5)	0.05	64 (18.5)	66 (26.5)	0.02	24 (12.6)	41 (15.2)	0.426
	COPD	70 (22.9)	37 (18.1)	0.198	96 (27.7)	82 (32.9)	0.173	47 (24.6)	41 (15.2)	0.011
	Malignancy	39 (12.7)	58 (28.4)	<0.001	45 (13.0)	61 (24.5)	<0.001	12 (6.3)	39 (14.4)	0.006
	Neurologic disorder	29 (9.5)	30 (14.7)	0.07	55 (15.9)	73 (29.3)	<0.001	24 (12.6)	76 (28.1)	<0.001
	Cardiac disease	43 (14.1)	23 (11.3)	0.036	60 (17.3)	64 (25.7)	0.013	26 (13.6)	56 (20.7)	0.004

COPD: chronic obstructive pulmonary disease, HT: hypertension, DM: diabetes mellitus

Table 4: Univariate logistic regression analysis of the variables for the development of mortality

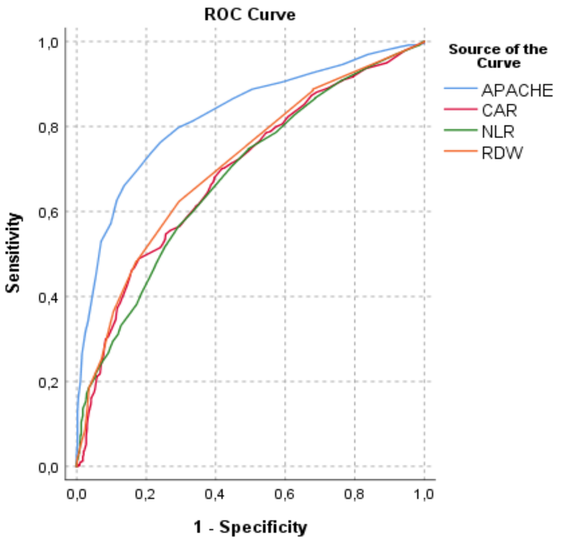
	65–74 years old		75–84 years old		85 years and older	
	OR [95%CI]	***P*-value**	**OR [95%CI]**	***P*-value**	**OR [95%CI]**	***P*-value**
Age	0.975 [0.891–1.067]	0.584	0.842[0.766–0.925]	<0.001	1.009[0.932–1.092]	0.833
RDW	1.298 [1.18–1.428]	<0.001	1.174[1.076–1.281]	<0.001	1.25[1.143–1.368]	<0.001
Leukocyte (10^3/µL)	1.055[1.002–1.11]	0.04	1.007[0.961–1.054]	0.776	1.06[1.001–1.122]	0.04
Lymphocyte(10^3/µL)	0.883[0.574–1.357]	0.57	0.913[0.557–1.495]	0.716	0.74[0.513–1.069]	0.1
Platelet (10^3/µL)	0.995[0.992–0.998]	<0.001	0.999[0.996–1.014]	0.333	0.997[0.994–1.0]	0.02
NLR	1.023[0.995–1.051]	0.11	1.031[1.0–1.062]	0.05	1.035[1.003–1.068]	0.033
CAR	1.014[1.002–1.026]	0.02	1.005[0.996–1.014]	0.274	1.004[0.995–1.014]	0.371
Creatinine(mg/dL)	1.101[0.891–1.36]	0.374	0.838[0.687–1.022]	0.08	1.054[0.813–1.367]	0.69
APACHE II	1.219[1.162–1.278]	<0.001	1.238[1.188–1.29]	<0.001	1.129[1.088–1.171]	<0.001

not significant in the 85 years and older age group. The incidence of COPD was higher among those who were discharged in the 85 years and older age group than in those who died (*P*=0.011). The malignancy ratio was higher in patients who died in all age groups (*P*<0.001). While neurological impairment (*P*<0.001) and heart disease (*P*=0.013) were higher in those who died in the 75–84 and 85 years and older age groups, there were no differences in the 65–74 years age group.

The results of the logistic regression analysis presented in Table 4 were evaluated to determine whether the variables examined in the three age groups were independent risk factors affecting mortality. Accordingly, RDW (*P*<0.001), leukocyte count (*P*=0.04), PLT (*P*<0.001) (negative effect), CAR (*P*=0.02), and APACHE II (*P*<0.001) were determined to be effective independent risk factors in patients who died in the 65–74 years group. In the 75–84 years age group, the RDW (*P*<0.001) and APACHE II (*P*<0.001) variables were found to be effective independent risk factors for death. In the 85 years and older age group, RDW (*P*<0.001), leukocyte count (*P*=0.04), PLT (negative effect) (*P*=0.02), NLR (*P*=0.03), and APACHE II (*P*<0.001) scores were effective independent risk factors in patients who died.

When all older adult patients were evaluated regardless of age, the mortality prediction sensitivity of the APACHE II score was 76.2%, with a specificity of 76%. The cut-off APACHE II score was 23. The RDW sensitivity was 62.2%, with a specificity of 70.6%. The cutoff value for RDW was 17. The ROC curves showing the power of APACHE II, RDW, NLR, and CAR are shown in Figure 1.

Figure 1: ROC curves of APACHE II, RDW, NLR and CAR for predicting mortality



Discussion

In our study examining 1566 patients admitted to the ICU, the most common diagnosis was sepsis. The presence of COPD did not increase mortality in any age group. The presence of DM increased mortality in the 65–74 and 75–84 age groups, while neurological impairment and heart disease increased mortality in the two older age groups. Malignancy was associated with increased mortality in all age groups. The increase in the ICU LoS, RDW, leukocyte count, CAR, and APACHE II scores, and the decrease in PLT affected mortality. In the 75–84 age group, as the variables of ICU LoS, RDW, and APACHE II score increased, so did mortality. In the oldest age group, the increase in ICU LoS, RDW, leukocyte count, NLR, APACHE II score, and decrease in PLT were consistent with mortality.

As a result of health care developments, the older adult population is increasing in Turkey and worldwide. According to data provided by the Turkish Statistical Institute, the older adult population has increased by 24% in the last five years, reaching 8,245,124 people in 2021; The ratio of older adults to the total population has increased to 9.7% [7]. A decrease in physiological reserves caused by aging and chronic diseases can lead to increased susceptibility or death in many diseases [8]. In this advanced age period, when frailty increases, sepsis develops very easily and progresses with high mortality [9]. Additionally, in the older adult population, acute exacerbations or complications of chronic diseases, new-onset catastrophic diseases, and indoor and outdoor accidents are among the most common reasons for admission to the ICU [10]. The most common diagnoses and causes of treatment in our ICU were sepsis and organ failure associated with sepsis.

In the ICU follow-up, the search for guidelines to assist the clinician in terms of the patient's response to treatment continues. APACHE is of great importance in these guidelines and is frequently used [2]. In our study, the accuracy of APACHE scoring in predicting mortality in all older age groups in our ICU was evaluated.

NLR and CAR, which are ratios derived based on laboratory tests, are used by many clinicians in ICU follow-ups. In a study screening 4717 patients followed up in the ICU, RDW, NLR, and platelet-lymphocyte ratio (PLR) were examined. If the RDW ratio was 14.1 and above, atrial fibrillation (AF) rhythm disorder was common, and this may increase mortality. It was found that the NLR and PLR values did not affect AF [11]. In a study conducted in the palliative care unit, the effects of CRP, CAR, NLR, and the Glasgow scoring system on 90-day mortality were examined. The cut-off value for these parameters was indicated as CRP ≥6.7mg/L, CAR ≥2.0, leukocytes ≥9300/µL, neutrophils ≥7426/µL, and NLR ≥6.0. It has been reported that all these biomarkers (especially CAR) are below these threshold values and are indicators of a good prognosis [12].

These ratios are widely used in Turkey to predict mortality. In one study, 2147 patients in the ICU were screened retrospectively and these ratios were reported to be the best predictor of mortality in patients in the ICU. It was stated that among the laboratory rates, RDW, CAR, and NLR accurately determined mortality estimation. The mean age of the patients was 72.1 (15.8) years. In the patient group with exitus, this number increased to 75.3 (13.4) years, which was statistically significant. However, the patients were not divided into age groups, and the course of these values in the three older age subgroups was not examined [13].

In a study conducted on patients with acute ischemic stroke and intracerebral hemorrhage admitted to the neurology ICU, the effects of laboratory values used in the follow-up and their rates on mortality were examined. The calculated NLR, lymphocyte-monocyte ratio (LMR), PLR, and CAR were examined to determine the factors affecting 30-day and 90-day mortality. While NLR, and CAR were found to be significant predictors of 30-day mortality, only a high NLR has been reported as a valuable indicator of 90-day mortality [14].

The importance of these markers has been further elucidated, particularly during the COVID-19 pandemic. In a study in which independent risk factors predicting the severity of COVID-19 were determined, using logistic regression analysis, age, and CAR elevation were identified as independent risk factors. In the ROC curve analysis, the CAR threshold value was 0.9 in COVID-19 cases, and in cases with a higher value, the mortality rate was higher [15]. In a study examining the relationship between NLR and CAR ratio and mortality in geriatric patients diagnosed with COVID-19, creatinine, NLR, CRP, and CAR values were high in patients who died. Threshold values were determined as 4.02 for NLR, 23 for CAR, and 81.4 for CRP [16]. In the examination of 613 patients who were admitted to the emergency department due to COVID-19, it was found that acute-phase reactants were high in deceased patients. It was also emphasized that CAR, NLR, fibrinogen albumin ratio (FAR), and urea albumin ratio (UAR), which are the ratios obtained from these laboratory values, also affected mortality. Threshold values were determined as 2.1561 for CAR, 1.5622 for UAR, 7.7321 for NLR, and 11.1078 for FAR [17].

These rates are widely used to predict mortality not only in ICUs but also in emergency services. In a study in which patients with dyspnea who visited the emergency room were screened, the relationship between RDW and NLR and mortality was determined using ROC analysis. A low NLR has been previously reported to increase the chance of survival, but it is not an independent risk factor. There was no relationship with

RDW [18]. In another study conducted in Turkey, researchers examined emergency room applications. They reported that an increase in NLR and CAR increased mortality in the emergency room. It was determined that the risk of in-hospital mortality was 9.87 times higher in patients with high NLR and CAR values simultaneously (CAR >12.3, NLR >7.1). These values (NLR 7.21, CAR 12.65) were significantly higher among patients who were admitted to the ICU from the emergency room than in those who were discharged (NLR, 3.64; CAR, 2.88) [19].

Factors affecting resuscitation success were examined in a publication examining the issues affecting mortality in out-of-hospital cardiac arrests. Spontaneous circulation was restored in 91 of the 191 patients. It was determined that the first 24-hour mortality was affected by the neutrophil count, NLR, and lactate level at the time of admission, and if the NLR value was below 3.05, the first 24-hour mortality was low [20].

Surgeons also use these ratios to predict postoperative mortality. In a study examining patients aged >80 years who had undergone laparotomy, NLR and CAR values were high in patients with sepsis. It was found that the preoperative NLR increased the 30-day and 90-day mortality in patients with visceral perforation, while the CAR value did not affect mortality. It was emphasized that if the preoperative NLR value was 8 or above, mortality increased significantly [21].

Limitations

Our study was conducted with ICU patients at a single center. Only the NLR and CAR were calculated to evaluate their effects on mortality inpatients divided into age groups. Although these ratios have been shown to affect mortality, no threshold value was provided. Additionally, other ratios such as the LMR and PLR used in intensive care follow-up were not examined. New publications with a larger patient group and multicenter participation are needed to evaluate more ratios and determine threshold values to alert the attending physician.

Conclusions

In our study examining the factors affecting mortality in the ICU of three older age groups, we found that the LoS in the ICU, APACHE II score, and RDW were associated with mortality. Although CAR is an indicator of mortality in the 65–74 years age group, NLR has gained importance in the 85 years and older age group. We believe that follow-up on the APACHE II scores, laboratory values, and combinations of various laboratory parameters, considering the age of the patients, is meaningful in predicting mortality and in the follow-up of the clinical course. We are of the opinion that more randomized controlled studies are needed to support our findings.

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