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Research Article

The Effect of CRP/Albumin, Platelet/Lymphocyte, SOFA, and APACHE II in Predicting Mortality in Covid-19 Patients in Intensive Care Unit

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ABSTRACT

Objectives: It is important to predict the prognosis during hospital admission of Covid-19 patients. The purpose of this study was to see how CRP/Albumin (CAR) and Platelet/Lymphocyte (PLR) ratios, obtained from patients in the intensive care unit (ICU) within the first 24 hours of their hospitalization with a Covid-19 diagnosis, predictmortality and how they correlated with acute physiology and chronic health evaluation (APACHE II) and sequential organ failure assessment (SOFA).

Methods: Using hospital records, records of 83 patients hospitalized in the ICU with a diagnosis of Covid-19 between 11.03.2020 and 01.01.2021 were retrospectively analyzed . Patients were divided into two groups discharged (Group I) and exits (ex) group (Group II). CAR and PLR were recorded during the first 24 hours of ICU admission, and APACHE II and SOFA scores were computed. The calculated CAR and PLR were correlated with APACHE II and SOFA scores and their association with mortality was investigated.

Results: SOFA, APACHE II, PLO, and age were higher, and albumin was lower in patients in the mortal course ($p<0.05$). ROC analysis revealed that APACHE II and SOFA scores could be employed to estimate mortality.

Conclusion: We believe that APACHE II and SOFA scores can be used to predict mortality in patients admitted to the ICU due to Covid-19, whereas CRP/Albumin and Platelet/Lymphocyte ratios cannot.

Keywords: APACHE II, Covid-19, CRP/Albumin Ratio, Mortality, Platelet/Lymphocyte Ratio.

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Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (Covid-19) has caused an unprecedented global pandemic of unprecedented magnitude. Covid-19 can causes everything from a minor infection to a life-threatening situation. The prospective course of Covid-19 at the time of admission is difficult to predict at patient admission.[1-3]

Different risk scores were and developed to predict Covid-19 prognosis and plan appropriate treatment. These scores included demographic and radiologic characteristics,[4] physiologic,[5] and biochemical parameters,[6] as well as various combinations of these. To calculate these risk scores, it is necessary to allocate time for further evaluations, and examinations. There is also no particular scoring system for Covid-19 yet, although it has been revealed in several studies.[4,5]

The Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores have long been used in intensive care units (ICUs). APACHE II is used to evaluate the prognosis and mortality of a patient.[6] SOFA evaluates organ dysfunction, morbidity, and mortality.[7] We believe that these two scoring systems can be used to predict mortality in Covid-19 patients, and we believe that more research should be done on this topic.

In a Covid-19 case, leukocytes, lymphocytes, and platelets decrease the.[18] Progressive lymphocytopenia indicates disease severity.[8] Several studies have shown that PLR can be used as an independent prognostic indicator in Covid-19 patients, both severe and non-severe.[8] Because CAR estimate the level of inflammation in two ways (increased CRP and decreased albumin), it may provide more information

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than only CRP and/or albumin alone.[9] CAR may also be a prognostic indicator for Covid-19 patients.

As a result, the purpose of this study was to assess the predictive power of CRP/Albumin ratio (CAR) and Platelet/Lymphocyte ratio (PLR), SOFA, and APACHE II scores in patients admitted to the ICU with Covid-19.

Methods

The study was planned retrospectively, and HNEAH - KAEK letter 2022/176-3860 was used to obtain ethics committee approval. The study included patients hospitalized in ICU between 11.03.2020 and 01.01.2021 in our hospital. The study included 83 older patients over the age of 18 , who had a positive Covid-19 PolymeraseChainReaction (PCR)test, were not diagnosed with t cancer, did not have any immunosuppressive disease, were not receiving immunosuppressive therapy, did not have the hematologic disease, and did not have the chronic liver disease. Patients under the age of 18 who had a negative Covid-19 PCR test, any malignancy that would affect the primary variables, immunosuppressive disease, receiving immunosuppressive therapy, and hematologic or chronic liver disease were excluded from the study.

The hospital system recorded age, gender, PCR positivity, date of ICU admission, type, and date of discharge from the ICU. Patients were divided into two groups according to the type of discharge from the ICU: discharged (Group I) and exits (Group II). Following, CAR, PLR, APACHE II, and SOFA scores were calculated by and analyzing the blood tests that were routinely taken during the first hospitalization to the ICU. The total APACHE II score the sum of three subscales, acute physiology score, age, and chronic health assessment. The highest score value is 71. Mortality rise from 25% a total score of 25 to 80% a score of 35 or higher. [10] A total of six organ systems are scored between 1 and 4 in the SOFA score. The evaluation is based on the total score. The total score between 6 and 24, with a higher score indicating worsening morbidity.[11]

Power Analysis

The TLO effect size between the study groups was found to be 0.56 [12] (alpha error probability=0.05) in the power analysis performed with the G*power 3.1 program related to our study; in the sample size analysis performed with the power value 0.80, the total number of samples required to be taken was found to be 83.

Statistical Methods

The SPSS 22 program was used for data analysis. The data were presented in the form of an arithmetic mean, standard deviation, median, range, frequency, and percentage distribution. The Kolmogorov–Smirnov test was used as a normal distribution test.The unpaired t-test was used to compare paired groups in the analysis of normally distributed data, the Mann–Whitney U test was used to compare paired groups of variables that did not show normal distribution, and the Chi Square test was used to evaluate qualitative data. The binary logistic regression test was used to determine the factors that influence mortality, and the Kaplan–Meier and LogRank analye were used to determine the effect of SOFA and APACHE II cut-off values on survival. Results were evaluated at the significance level of $p<0.05$.

Results

A total of 247 patients were analyzed from hospital records. 114 patients did not meet the inclusion criteria, and n 50 patients information was incomplete. Therefore, 164 analyzed patients could not be included in the study.The study included 83 patients, 25 of whom were discharged and 58 of whom passed. Sociodemographic characteristics of the patients according to group characteristics are given in Table 1.

Table 1. Demographic characteristics by group

Feature	Group X±SD or n (%)		p
	Discharged n: 25 (30.1)	Ex n: 58 (69.9)	
Age	58.48±16.68	72.71±9.692	<0.001*
Gender			
Female	6 (24.0)	16 (27.6)	0.945+
Male	19 (76.0)	42 (72.4)	
The time between PCR+ and ICU hospitalization (days)	6.64±3.32	5.78±4.17	0.170 ǂ
Duration of ICU stay (days)	12.04±9.43	12.84±7.28	0.219 ǂ
Total	25 (30.1)	58 (69.9)	

*Unpaired t-test ǂ Mann–Whitney U test+Chi Square test PCR: ICU: Intensive Care Unit; SD: Standard Deviation PCR: Polymerase Chain Reaction ICU: Intensive Care Unit.

It was found that albumin (p<0.001) was significantly lower, while SOFA (p<0.001), APACHE II (p<0.001), and TLO (p=0.034) were significantly higher in the ex-group (Table 2).

Age, Albumin, PLR, SOFA, APACHE II, and GCS variables were found to be significant in univariate tests, so a logistic regression analysis was performed to determine the factors affecting mortality. The variables age (p=0.893), Albumin (p=0.254), PLR (p=0.141), and GCS (p=0.978) were found to be statistically insignificant, whereas SOFA (p=0.042) and APACHE II (p=0.048) were found to be significant (Table 3).

Albumin, PLR, SOFA, APACHE II, and GCS variables used in a logistic regression analysis to determine the factors influencing mortality toby age. Albumin (p=0.142), PLR (p=0.150), and GCS (p=0.812) levels were found to be statistically insignificant,whereas SOFA (p=0.045) and APACHE II (p=0.049) levels were found to be significant (Table 3).

The ROC analysis revealed that the areas under the curve for APACHE II and SOFA scores were significant, whereas the areas under the curve for PLR and CAR were not (Table 4). The optimum cut-off value for mortality prediction was discovered to be 14 for APACHE II and 8 for SOFA score (Table 5).

Kaplan–Meier Survival Analyses were performed considering the recommended cut-off values for APACHE II and SOFA scores(Table 6, Table 7). The APACHE II of <14 group survival durations were statistically significantly longer than the APACHE II of >14 groups (LogRank:5.43 p=0.025) (Table 6 Fig. 1). There was no statistically significant difference in survival times between the SOFA groups (LogRank:3.07 p=0.080) (Table 7).

Discussion

According to our findings, hospitalization APACHE II and SOFA scores can be used to predict mortality in patients ad-

Table 3. Logistic regression analysis for mortality prediction

	OR 95% CI	p	OR 95% CI	p*
Age	1.01 (0.92–1.07)	0.893	-	-
Albumin	0.93 (0.75–1.08)	0.254	0.95 (0.89–1.02)	0.142
PLR	0.98 (0.93–1.02)	0.141	0.97 (0.99–1.03)	0.150
SOFA	2.18 (1.03–4.62)	0.042	1.08 (1.01–1.12)	0.045
APACHE II	1.19 (0.94–1.51)	0.048	1.04 (1.01–1.08)	0.049
GCS	0.99 (0.37–2.65)	0.978	0.97 (0.93–1.11)	0.812

*Adjusted Age; OR: Odds Ratio; CI: Confidence Interval; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow Coma Scale.

Table 4. Areas under the ROC Curve in the differential mortality diagnosis

	AUC	SE	95% CI
CAR	0.606	0.0656	0.493 to 0.711
PLR	0.627	0.0644	0.514 to 0.731
SOFA	0.843	0.0425	0.746 to 0.913
APACHE II	0.865	0.0391	0.772 to 0.930

AUC: Areas Under Curve; SE: Standard Error; CI: Confidence Interval; CAR: CRP/Albumin Rate; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 5. Optimal values for APACHE II and SOFA score

	Cut-off	Sensitivity	Specificity	PPV	NPV	LR+
Apache II	14	0.966	0.640	0.851	0.937	2.683
SOFA	8	0.983	0.600	0.862	0.889	2.457

PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR: Likelihood Ratio; Apache II: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment.

Table 2. Comparison of biochemical values and scores by groups

	Discharged n: 25 (30.1)			Ex n: 58 (69.9)			
	M±SD	Median	Range	M±SD	Median	Range	p
CRP	14.52±8.34	13.90	29.50	19.98±21.22	15.30	127.20	0.336ǂ
Albumin	34.62±2.99	35.50	10.50	30.64±5.15	31.00	23.40	0.001*
CAR	0.42±0.26	0.40	1.07	0.67±0.71	0.48	3.95	0.128ǂ
Platelet	243.00±84.19	244.00	347.00	269.33±109.58	254.00	573.00	0.287*
Lymphocyte	0.76±0.46	0.69	2.27	0.67±0.40	0.60	2.19	0.297ǂ
PLR	416.66±301.2	356.00	1398.40	503.13±276.16	423.75	1197.0	0.034ǂ
SOFA	8.60±1.29	8.00	4.00	11.09±2.08	10.00	7.00	<0.001*
APACHE II	13.04±5.30	13.00	19.00	21.50±5.35	21.00	26.00	<0.001*

*Unpaired t-test ǂMann Whitney U test; M: Mean; SD: Standard Deviation; CRP: C Reactive Protein; CAR: CRP/Albumin Rate; PLR: Platelet/Lymphocyte Rate; SOFA: Sequential Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 6. Kaplan-Meier life analysis for APACHE II

	<14 APACHE II	>14 APACHE II	All Patients Group
Day 5	0.875	0.907	0.976
Day 10	0.875	0.735	0.833
Day 15	0.683	0.389	0.752
Day 30	0.683	0.203	0.426
Median±SE Lifetime	22.42±3.17	14.80±1.21	15.86±1.25
95% CI	16.20–28.64	12.42–17.18	13.42–18.31
LogRank: 5.43 p=0.025			

Apache II: Acute Physiology and Chronic Health Evaluation; CI: Confidence Interval.

Table 7. Kaplan–Meier life analysis for SOFA

	<8 SOFA	>8 SOFA	All Patients Group
Day 5	0.890	0.955	0.976
Day 10	0.890	0.746	0.833
Day 15	0.785	0.495	0.752
Day 30	0.785	0.218	0.426
Median±SE Lifetime	24.20±3.39	15.23±1.22	15.86±1.25
95% CI	17.54–30.86	12.83–17.63	13.42–18.31
LogRank:3.07 p=0.080			

SOFA: Sequential Organ Failure Assessment: CI: Confidence Interval.

mitted to the ICU due to Covid-19. We discovered that the optimum cut-off value for APACHE II was 14 and for SOFA score as 8, furthermore, TLO and CAR values not predict mortality in patients admitted to the ICU due to Covid-19.

Specific scoring systems may and in treatment selection, treatment success, and efficient, and effective use of available resources. Despite studies,[4,5] no specific scoring system Covid-19 mortality has been identified. SOFA and APACHE II scoring systems are commonly used in ICU. These scoring systems can and suggest the mortality of Covid-19 patients.

Ghaith et al.[13] and studied critical Covid-19 patients admitted to the ICU and discovered that mortality was higher (83%) in patients over the age of 60. Du et al.[14] also found that advanced age was associated with mortality in Covid-19 patients. In our study, we discovered that advanced age was associated with higher mortality in Covid-19 patients, as has been shown in other similar studies.[12,15-17]

Deligöz et al.[18] found that low albumin level is a risk factor for mortality, furthermore, they stated that low albumin levels are have been linked to a poor prognosis in various studies. In the study by Tseng et al.,[15] albumin was found

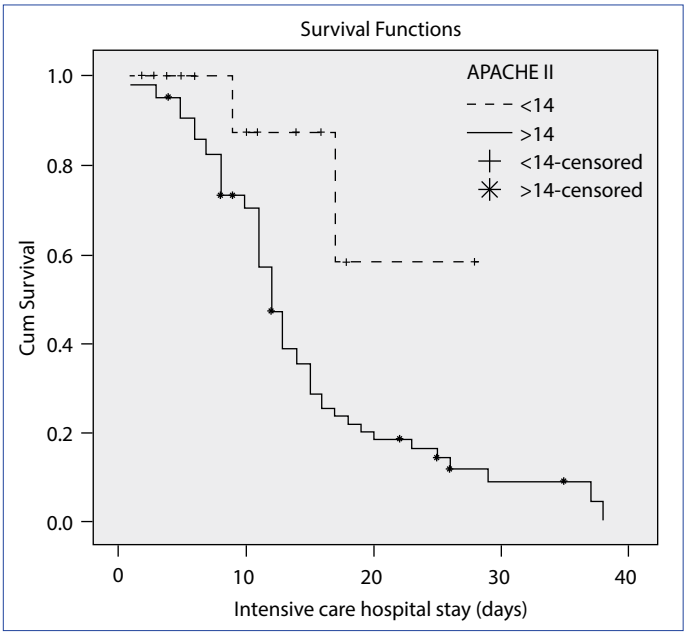

Figure 1. The relationship of APACHE II score with an intensive care life expectancy.

Apache II: Acute Physiology and Chronic Health Evaluation.

to be an important predictor of mortality. We discovered that Covid-19 patients with low albumin levels had a more fatal course.

In our study, PLR was significantly higher in the mortal group. This conclusion is supported by numerous studies. Korkmaz et al.[8] discovered that PLR was significant in predicting disease severity and prognosis in hospitalied Covid-19 patients. Uzundere et al.[17] also reported that PLR was a risk factor for mortality in patients with Covid-19 admitted to ICU.

Vicka et al.[19] compared the (SAPS) II, APACHE II, and SOFA scores and discovered that APACHE II had the best mortality prediction in Covid-19 patients hospitalied in the ICU. Vahedi et al.[7] showed that higher SOFA and APACHE II scores indicate higher mortality in ICU patients. Beigmohammadi et al.[20] discovered that APACHE II and SOFA scores were higher in Covid-19 patients who died. Discovered that SOFA and APACHE II scores at the time of ICU admission could be used to predict mortality in Covid-19 patients, similar to these studies. Bayrak et al.[16] found that an APACHE II score of >15 was linked with ICU mortality according to Kaplan–Meier curves and found that the APACHE II score predicted mortality. In our study, we discovered that APACHE II score greater than 14 on the Kaplan–Meier curve associated with ICU mortality.

Hocanlı et al.[21] discovered that CAR was statistically significantly higher in ICU patients than in ward patients and that this rate was associated with mortality. Another study

found that a high CAR at baseline was associated with 28-day mortality.[22] CAR was also found to be higher in the fatal group of Covid-19 patients by Özdemir et al.[9] Lucijanić et al.[23] and studied 2309 Covid-19 patients admitted to the ICU and discovered that high CAR values were associated with 30-day and post-discharge mortality. Kalabin et al.[24] used multivariate logistic regression analysis to examine CAR in the first 24 hours in Covid-19 patients (OR 1.21, 95% CI 0.96.–1.51, p=0.06) and discovered that CAR was not an independent predictor of mortality. We also found that CAR was not an independent predictor of mortality in our study.

Conclusion

We believe that APACHE II and SOFA scores can be used to predict mortality in patients admitted to the ICU due to Covid-19, whereas CRP/Albumin and Platelet/Lymphocyte ratios cannot.These results need to be supported by the results of other studies for clarity.

Disclosures

Ethics Committee Approval: The study was planned retrospectively, and HNEAH - KAEK letter 2022/176-3860 was used to obtain ethics committee approval. The study included patients hospitalized in ICU between 11.03.2020 and 01.01.2021 in our hospital.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Authorship Contributions: Concept – Ü.T., Ö.D.; Design – Ü.T., Ö.D.; Supervision – Ö.D., O.E.; Fundings – Ü.T., Ö.D.; Materials – Ü.T., Ö.D.; Data collection &/or processing – Ü.T., Ö.D.; Analysis and/or interpretation – Ü.T., Ö.D.; Literature search – Ü.T., Ö.D.; Writing – Ö.D.; Critical review – Ö.D., O.E.

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