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# Comparison of the c-reactive protein-mean arterial pressure ratio with critical care prognostic scoring systems



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**Abstract**

Aim: We hypothesized that the C-reactive protein (CRP)-mean arterial pressure (MAP) ratio could predict short-term mortality in critically ill patients. In this study, our aim was to compare the CRP-MAP ratio with the acute physiology and chronic health evaluation (APACHE II) score in predicting the short-term mortality of critically ill patients.

Material and Methods: This research was designed as a prospective observational study and included critically ill patients aged over 18 years, who were admitted to the intensive care unit from the emergency department between December 10, 2021, and March 10, 2022. The patients' demographic and clinical data and 28-day mortality status were recorded.

Results: We included 169 patients in this study. The median age was 72 (25th-75th percentiles: 61-81) years, and 74 (43%) of the patients were female. The CRP-MAP ratio was significantly higher in the non-survivor group than in the survivor group [1.03 (0.194-2.24) and 0.207 (0.0346-1.1), respectively, p<0.001]. The APACHE II score was also significantly higher in the non-survivor group than in the survivor group [26 (20.8-30) and 21 (15-25.8), respectively, p < 0.001]. The odds ratio of the CRP-MAP value was similar to those of the APACHE II score and blood urea nitrogen-albumin ratio (3.819, 2.545, and 3.67, respectively).

Discussion: There was a significant difference in mortality between the patients with CRP-MAP ratios below and above the cut-off value of 4.2. According to the results of our study, the CRP-MAP ratio was as significant as APACHE II in the prediction of mortality

**Keywords**

C-reactive Protein, Mean Arterial Pressure, APACHE

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## Introduction

Critical care patients constitute a group that requires early diagnosis and prompt treatment at the emergency department. Various scoring systems have been developed to predict the clinical deterioration of patients and admit critical cases to the intensive care unit in the early period. These scores can be calculated not only with vital parameters but also with the combination of vital and laboratory parameters [1]. Many scoring systems, such as acute physiology and chronic health evaluation (APACHE II), have been developed to predict prognosis [2], and they are frequently used in intensive care. The APACHE II score is calculated based on the worst values recorded in the first 24 hours of patient admission.

C-reactive protein (CRP), an acute phase protein, is a marker of inflammatory response. It is a predictive biomarker in the prognosis of critically ill patients, with high CRP concentrations having been shown to be associated with poor outcome in patients with sepsis [3,4]. The mean arterial pressure (MAP) is a good predictor of organ perfusion [5]. It has been reported that organ perfusion is impaired in the presence of low MAP. Studies have found that fluctuation in MAP is associated with in-hospital mortality [6]. CRP and MAP alone can predict mortality and poor outcome in diseases such as sepsis. We hypothesized that a parameter to be created with the combination of CRP and MAP could predict mortality in sepsis, as well as other diseases. In this study, our aim was to compare the CRP-MAP ratio with the APACHE II score in predicting the mortality of critically ill patients.

## Material and Methods

This research was designed as a prospective observational study and conducted in the emergency department of Umraniye Training and Research Hospital with 657 beds and an average of 1,250 adult emergency admissions per day. Among the cases presented to the emergency department between December 10, 2021, and March 10, 2022, critically ill patients aged over 18 years, who were admitted to the intensive care unit from the emergency department, were included in the study. Trauma cases, patients whose consent could not be obtained, and those referred to other hospitals were excluded from the sample.

Patients' demographic data, Glasgow Coma Scale scores, vital parameters, comorbidities, laboratory parameters, inotropic agent requirement, and 28-day all-cause mortality were recorded at the time of admission. Heart rate, diastolic blood pressure, systolic blood pressure, and MAP were obtained as vital parameters. Blood parameters, such as hemoglobin, CRP, lactate, whole blood cell count, alanine transaminase, neutrophil count, lymphocyte count, hematocrit, albumin, aspartate aminotransferase, blood urea nitrogen (BUN), and creatinine values were recorded. Comorbidities were noted as congestive heart failure, coronary artery disease, diabetes mellitus, hepatic cirrhosis, chronic obstructive pulmonary disease, chronic kidney disease, hyperlipidemia, cerebrovascular disease, epilepsy, rheumatoid arthritis, malignancy, and hypertension. The mortality status of the patients was obtained from the national death registry system. The APACHE II score, CRP-albumin ratio, and CRP-MAP ratio were calculated. All evaluations were made at the time of the presentation. The primary outcome of the study was 28-day mortality.

Data were analyzed using Jamovi (Version 1.6.21.0; The Jamovi Project, 2020; R Core Team, 2019). Normally distributed data were presented as mean and standard deviation values, and non-normally distributed data as median and interquartile ranges. For the continuous data, Student's t-test was applied in the presence of normal data distribution, and the Mann-Whitney U test otherwise. Categorical variables were calculated with the chi-square test. A p value <0.05 was considered statistically significant.

Ethical approval was received from the local ethics committee of the hospital. Consent was obtained from the patients or their next of kin if their consciousness level was not sufficient. The study was carried out in full compliance with the rules of the Declaration of Helsinki.

## Results

This prospective observational study included 169 patients. The flow chart of the study is given in Figure 1. The median age was 72 (25th-75th percentiles: 61-81) years, and 74 (43%) of the patients were female.

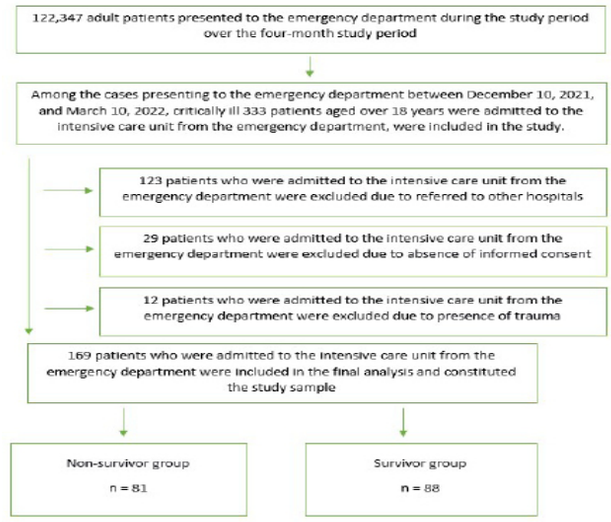


**Figure 1.** Flow chart of the study

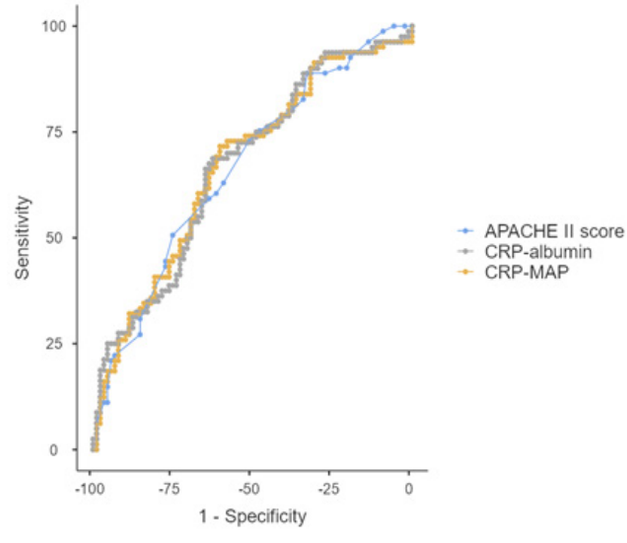


**Figure 2.** Receiver operating characteristic curves of the parameters in predicting short-term mortality

**Table 1.** Vital parameters and comorbidities of the enrolled patients and their comparison between the survivor and non-survivor groups

| Variables | Total n = 169 (%, 25th-75th percentile/±SD) | Survivor group n = 88 (%, 25th-75th percentile/±SD) | Non-survivor group n = 81 (%, 25th-75th percentile/±SD) | p |
|---|---|---|---|---|
| Age | 72 (61-81) | 67 (55.3-78) | 77 (68-84) | <0.001 |
| Female | 74 (43%) | 40 (45.5%) | 34 (42%) | 0.649 |
| Heart rate | 94.5 (82-111) | 89 (82-107) | 97 (85-115) | 0.052 |
| Systolic blood pressure | 130 (110-158) | 132 (111-163) | 127 (110-153) | 0.273 |
| Diastolic blood pressure | 74.4 (±19.3) | 74.2 (±18.8) | 74.6 (±19.9) | 0.888 |
| Mean arterial pressure | 94.5 (±22.5) | 95.1 (±22.1) | 93.8 (±23.1) | 0.698 |
| Hypertension | 98 (58.0%) | 51 (58%) | 47 (58%) | 0.993 |
| Diabetes mellitus | 56 (33.1%) | 28 (31.8%) | 28 (34.6%) | 0.704 |
| Hyperlipidemia | 9 (5.3%) | 5 (5.7%) | 4 (4.9%) | 0.830 |
| Coronary artery disease | 33 (19.5%) | 15 (17%) | 18 (22.2%) | 0.396 |
| Chronic obstructive pulmonary disease | 27 (16.0%) | 10 (11.4%) | 17 (21%) | 0.088 |
| Congestive heart failure | 25 (14.8%) | 11 (12.5%) | 14 (17.3%) | 0.382 |
| Chronic kidney disease | 15 (8.9%) | 6 (6.8%) | 9 (11.8%) | 0.327 |
| Hepatic cirrhosis | 2 (1.2%) | 0 (0%) | 2 (2.5%) | 0.138 |
| Cerebrovascular disease | 17 (10.1%) | 10 (14.8%) | 7 (8.6%) | 0.557 |
| Epilepsy | 6 (3.6%) | 3 (3.4%) | 3 (3.7%) | 0.918 |
| Rheumatoid arthritis | 3 (1.8%) | 1 (1.1%) | 2 (2.5%) | 0.512 |
| Malignancy | 19 (11.2%) | 9 (10.2%) | 10 (12.3%) | 0.663 |

Abbreviation: SD: standard deviation

**Table 2.** Laboratory values, scores, and other calculated parameters of the enrolled patients and their comparison between the survivor and non-survivor groups

| Variables | Total (%, 25th-75th percentile/±SD) n = 169 | Survivors (%, 25th-75th percentile/±SD) n = 88 (52.1 %) | Non-survivors (%, 25th-75th percentile/±SD) n = 81 (47.9 %) | p |
|---|---|---|---|---|
| White blood cell count ($10^3$ /µL) | 10.5 (7.22-13.7) | 8.53 (6.43-12.4) | 11.5 (8.26-14.6) | 0.004 |
| Neutrophil count ($10^3$ /µL) | 7.55 (4.75-11.3) | 6.08 (4.13-9.46) | 9.56 (6.37-12.3) | <0.001 |
| Lymphocyte count ($10^3$ /µL) | 1.33 (0.78-2.35) | 1.58 (0.915-2.5) | 1.01 (0.57-1.86) | 0.01 |
| C-reactive protein (mg/dL) | 48.8 (5.87-134) | 21 (3.8-114) | 84.1 (19.3-177) | <0.001 |
| Alanine aminotransferase (IU/L) | 26 (19-36.3) | 22.5 (17.8-31) | 29 (21-40) | 0.003 |
| Blood urea nitrogen (mg/dL) | 49.5 (32.5-85.2) | 43.1 (30.2-60.5) | 68.8 (38.9-118) | <0.001 |
| Creatinine (mg/dL) | 1.09 (0.77-1.57) | 0.995 (0.657-1.25) | 1.3 (0.91-1.92) | <0.001 |
| APACHE II score | 23.5 (18-28) | 21 (15-25.8) | 26 (20.8-30) | <0.001 |
| C-reactive protein/main arterial pressure ratio | 0.523 (0.058-1.61) | 0.207 (0.0346-1.1) | 1.03 (0.194-2.24) | <0.001 |
| C-reactive protein/albumin ratio | 1.31 (0.149-4.77) | 0.611 (0.0917-3.65) | 2.39 (0.531-6.1) | <0.001 |

Abbreviation: SD: standard deviation

The most common comorbidity was hypertension (n = 98, 58%), followed by diabetes mellitus (n = 56, 33.1%), coronary artery disease (n = 33, 19.5%), and chronic obstructive pulmonary disease (n = 27, 16.0%). In Table 1, the vital parameters and comorbidities of the patient are given in detail. The short-term mortality rate of our patients was 47.9% (n = 81), and the in-hospital mortality rate was 47.3% (n = 80).

The non-survivor group had significantly higher CRP [84.1

CRP: C-reactive protein; MAP: mean arterial pressure; APACHE: acute physiology and chronic health evaluation

(19.3-177) vs 21 (3.8-114), p < 0.001] and BUN [68.8 (38.9-118) vs 43.1 (30.2-60.5), p <0.001] values compared to the survivor group. The APACHE II score and CRP-MAP ratio were also significantly higher in the non-survivor group than in the survivor group [26 (20.8-30) vs 21 (15-25.8) and 1.03 (0.194-2.24) vs 0.207 (0.0346-1.1), respectively, p <0.001 for both]. The detailed laboratory data and scores of the patients are shown in Table 2.

The area under the curve (AUC) values of the CRP-MAP ratio and the APACHE II score in predicting short term mortality were calculated as 0.670 [95% confidence interval (CI): 0.589-0.752, p <0.001) and 0.665 (95% CI: 0.581-0.744, p < 0.001), respectively. There was no significant difference between the AUC values of the CRP-MAP ratio and the APACHE II score (p = 0.916, DeLong test). The calculated AUC values of the parameters are given in Table 3 and Figure 2. The odds ratio of the CRP-MAP ratio was determined as 3.819 (95% CI: 2.004-7.275, p <0.001).

## Discussion

In this prospective study, we compared the predictive ability of the CRP-MAP ratio and APACHE II score for short-term mortality in 169 critically ill patients presenting to the emergency department. There was a significant difference in mortality between the patients with CRP-MAP ratios below and above the cut-off value of 4.2. According to the results of our study, the CRP-MAP ratio was as significant as APACHE II in the prediction of mortality. When we compared the CRP-MAP ratio with the APACHE II score, we did not detect any significant difference in their AUC values.

It is important to make an early prediction of the clinical severity and mortality expectations of patients admitted to the emergency department. This assessment is essential for the care and earlier intervention of patients with high mortality or poor clinical outcome. Scoring systems and laboratory tests developed to predict the poor course of patients should be rapid, inexpensive, and widely available. Therefore, in general, vital parameters and blood values easily accessible at every emergency department are used in survival scoring.

CRP, an acute phase protein, has been used in mortality studies because it is a marker of inflammatory response [7-9]. High CRP concentrations are associated with poor outcomes in patients with sepsis. A study conducted with a multiethnic Brazilian population showed a consistent and independent relationship between CRP and all-cause mortality [7]. In another study, Lin et al. found that high CRP at the time of admission to the emergency department was an important independent risk factor for in-hospital outcome events in patients with

**Table 3.** Results of the receiver operating characteristics analysis for short-term mortality status

| | Cut-off point | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | AUC 95% confidence interval | p | Odds ratio | 95% confidence interval (lower-upper) |
|---|---|---|---|---|---|---|---|---|---|
| CRP-MAP ratio | 0.43 | 71.60% | 60.23% | 62.37% | 69.74% | 0.670 (0.589-0.752) | <0.001 | 3.819 | 2.043-7.275 |
| APACHE II score | 19 | 50.62% | 75% | 65.08% | 62.26% | 0.665 (0.581-0.744) | <0.001 | 2.545 | 1.368-4.734 |
| CRP-albumin ratio | 1.2 | 68.75% | 62.50% | 62.50% | 68.75% | 0.670 (0.589-0.751) | <0.001 | 3.670 | 1.93-6.95 |

Abbreviations: PPV: positive predictive value; NPV: negative predictive value; AUC: area under the ROC curve; CRP: C-reactive protein; MAP: mean arterial pressure; APACHE: acute physiology and chronic health evaluation

acute myocardial infarction. The same study also reported a significant positive correlation between CRP and the Global Registry of Acute Coronary Events risk score ($r = .191$, $p < 0.001$) (9). These studies suggest that CRP can be used to predict mortality in critically ill patients.

MAP is used to assess the adequacy of perfusion of vital organs. If MAP stays below 60 mmHg for a long time, end-organ damage may occur [10]. Zanella et al. showed that low MAP was associated with mortality in intensive care patients (hazard ratio: 0.988, CI: 0.982–0.995) [11]. Khanna et al., evaluating 2,766 intensive care patients, reported a significant correlation between low MAP and mortality. The authors also found that a decrease of 10 mmHg in MAP increased the risk of acute kidney injury [12]. According to these studies, MAP may be a predictor of organ damage and mortality.

The combined use of CRP and MAP in a single parameter can increase their ability to predict mortality. This modification is easy to calculate because it does not require additional blood tests or vital parameter measurements. Blood tests used in survival scoring both increase the cost and are difficult to use since they involve the calculation of many parameters. APACHE II is widely used for mortality prediction [13,14]. There are 14 different parameters in the APACHE II scoring system, and therefore this score is difficult to obtain without an automatic calculator [15]. Thus, predictive parameters involving only a few calculations, such as the CRP-MAP ratio are easier than scoring systems with many parameters. This will make the clinician's job easier.

In our study, the CRP-MAP ratio was as significant as the APACHE II score and the CRP-albumin ratio values in predicting mortality. The multivariate test showed that the CRP-MAP ratio was an independent predictive factor. The odds ratio of the CRP-MAP ratio was similar to the APACHE II score and the BUN-albumin ratio (3.819, 2.545, and 3.67, respectively). To the best of our knowledge, this is the first study to evaluate the CRP-MAP ratio as a predictor of mortality in critically ill patients presenting to the emergency department. We consider that the CRP-MAP ratio is a parameter that can be used to predict short- term mortality among these patients.

### *Limitation*

There are several important limitations to our study. First, the limited sample size of our study reduces the generalizability of our results. Second, the MAP value alone is not associated with mortality in critically ill patients. However, this did not affect the significance of the CRP-MAP ratio in mortality prediction. Previous studies have shown the relationship between MAP and mortality, and we consider that this significant relationship will strengthen the ability of the CRP-MAP ratio to predict mortality in future studies with larger samples. We consider that the reason for the non-significance of the relationship between MAP and mortality in our study was due to the limited number of patients.

Finally, another factor limiting the generalizability of our findings is the single-centered design of the study.

### *Conclusion*

According to the results of our study, the CRP-MAP ratio is as good a predictor as APACHE II in predicting short term mortality in critically ill patients. However, due to the limited sample size and single-center design of our study, our findings should be validated by multicenter studies with larger samples.

***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 comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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***Conflict of interest***

*None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.*

***References***

*1. Akça H Ş, Algın A, Özdemir S, Sevimli H, Kokulu K, Eroğlu S E. Comparison of the efficacy of PSI, CURB-65, CALL and BCRSS in predicting prognosis and mortality in COVID-19 patients. J Exp Clin Med. 2021; 38(4): 434-9.*

*2. Basile-Filho A, Lago AF, Menegheti MG, Nicolini EA, Rodrigues LA de B, Nunes RS, et al. The use of APACHE II, SOFA, SAPS 3, C-reactive protein/albumin ratio, and lactate to predict mortality of surgical critically ill patients. Medicine (Baltimore). 2019 28;98(26):e16204.*

*3. Gunal O, Ulutan F. Diagnostic and Prognostic Value of Procalcitonin in Patients with Sepsis. Int J Infect Dis. 2008;(12):e463.*

*4. Lobo SMA, Lobo FRM, Bota DP, Lopes-Ferreira F, Soliman HM, Meélot C, et al. C-Reactive Protein Levels Correlate With Mortality and Organ Failure in Critically Ill Patientsa. Chest. 2003;123(6):2043–9.*

*5. Leone M, Asfar P, Radermacher P, Vincent JL, Martin C. Optimizing mean arterial pressure in septic shock: a critical reappraisal of the literature. Crit Care. 2015;19(1):101.*

*6. Gao Y, Wang Q, Li J, Zhang J, Li R, Sun L, et al. Impact of Mean Arterial Pressure Fluctuation on Mortality in Critically Ill Patients: Crit Care Med. 2018;46(12):e1167–74.*

*7. Maluf CB, Barreto SM, Giatti L, Ribeiro AL, Vidigal PG, Azevedo DRM, et al. Association between C reactive protein and all-cause mortality in the ELSA-Brasil cohort. J Epidemiol Community Health. 2020;74(5):421–7.*

*8. Lin XL, Sun HX, Li FQ, Zhao JY, Zhao DH, Liu JH, et al. Admission high-sensitivity C-reactive protein levels improve the Grace risk score prediction on in-hospital outcomes in acute myocardial infarction patients. Clin Cardiol. 2022;45(3):282–90.*

*9. Özdemir S, Algin A. Evaluation of the ability of the C-reactive protein-to-albumin ratio to predict short-term mortality in patients with COVID-19. J Clin Med Kazakhstan. 2021 27;18(6):35–9.*

*10. Campbell N, McGuire S, Carle C. Should all patients with septic shock have a mean arterial pressure threshold of 65 mmHg? Br J Hosp Med. 2020 2;81(9):1–2.*
*11. Zanella A, Florio G, Antonelli M, Bellani G, Berselli A, Bove T, et al. Time course of risk factors associated with mortality of 1260 critically ill patients with COVID-19 admitted to 24 Italian intensive care units. Intensive Care Med. 2021;47(9):995–1008.*
*12. Khanna AK, Maheshwari K, Mao G, Liu L, Perez-Protto SE, Chodavarapu P, et al. Association Between Mean Arterial Pressure and Acute Kidney Injury and a Composite of Myocardial Injury and Mortality in Postoperative Critically Ill Patients: A Retrospective Cohort Analysis. Crit Care Med. 2019;47(7):910–7.*
*13. Patel P, Gupta S, Patel H, Bashar MA. Assessment of APACHE II Score to Predict ICU Outcomes of Patients with AKI: A Single-center Experience from Haryana, North India. Indian Soc Crit Care Med. 2022;26(3):276–81.*
*14. Mierke J, Nowack T, Loehn T, Kluge F, Poege F, Speiser U, et al. Predictive value of the APACHE II score in cardiogenic shock patients treated with a percutaneous left ventricular assist device. Int J Cardiol Heart Vasc. 2022;40:101013.*
*15. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–29.*

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