Fatih Kahraman[1], Ahmet Seyda Yılmaz[2], Mevlüt Demir[3], Fatih Beşiroğlu[4]

[1] Cardiology Clinic, Kutahya Evliya Celebi Research and Training Hospital, Kutahya, Turkey

[2] Recep Tayyip Erdogan University, Department of Cardiology, Rize, Turkey

[3] Kutahya Health Sciences University, Department of Cardiology, Kutahya, Turkey

[4] Cardiology Clinic, Yalova State Hospital, Yalova, Turkey

# APACHE II score predicts in-hospital mortality more accurately than inflammatory indices in patients with acute coronary syndrome

| | |
|---|---|
| *Aim* | This study evaluated the prognostic ability of the APACHE II score and compared it with inflammatory indices in patients with acute coronary syndrome (ACS). |
| *Material and Methods* | A total of 525 patients with ACS were retrospectively enrolled in the study. APACHE II scores were calculated and C-reactive protein (CRP), neutrophil-lymphocyte ratio (NLR), and systemic immune-inflammatory index (SII) were recorded. The APACHE II score was compared with inflammatory indices for predicting in-hospital mortality. |
| *Results* | Univariate logistic regression (LR) analysis showed that CRP, SII, NLR, ejection fraction, chronic kidney disease, gender, and APACHE II score were significant predictors of mortality. In multiple LR analysis, the APACHE II score was found to be a solitary, significant predictor of in-hospital mortality (OR: 1.201, 95% CI: 1.122–1.285; p<0.001). In the Receiver Operating Characteristics curve, using a cut-off point of 16.5, the APACHE II score predicted in-hospital mortality with 70.4% sensitivity and 92.9% specificity. |
| *Conclusion* | The APACHE II score may be used as a predictor of in-hospital mortality better than inflammatory markers in ACS patients. |

| | |
|---|---|
| *Keywords* | APACHE II; systemic immune-inflammatory index; acute coronary syndrome; C-reactive protein; neutrophil-lymphocyte ratio |
| *For citations* | Fatih Kahraman, Ahmet Seyda Yılmaz, Mevlüt Demir, Fatih Beşiroğlu. APACHE II score predicts in-hospital mortality more accurately than inflammatory indices in patients with acute coronary syndrome. Kardiologiia. 2022;62(9):54–59. [Russian: Фатих Кахраман, Ахмет Сейда Йылмаз, Мевлют Демир, Фатих Бешироглу. Шкала APACHE II точнее прогнозирует госпитальную летальность, чем показатели воспаления, у пациентов с острым коронарным синдромом. Кардиология. 2022;62(9):54–59]. |

| | |
|---|---|
| *Corresponding Author* | Fatih Kahraman, Email: drfkahraman@gmail.com |

## Introduction

Coronary artery disease (CAD), of which acute coronary syndrome (ACS) is a frequent complication, is the most common cause of morbidity and mortality worldwide. Most cases of ACS, an umbrella term encompassing ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris, are mostly caused by the erosion or rupture of an atherosclerotic plaque [1]. The inflammatory process plays a pivotal role in the pathogenesis of various stages of atherosclerosis, including plaque instability and rupture that results in ACS [2]. Many studies have shown that peripheral blood cells, such as platelets, neutrophils, and lymphocytes, and C-reactive protein (CRP) can be used as indicators of systemic inflammation [3]. Subsequently, the platelet/lymphocyte, the lymphocyte/monocyte, and the neutrophil/lymphocyte ratio (NLR) ratios and CRP have been evaluated and found to be associated with both stable CAD and ACS [4–6]. In addition to these parameters, the systemic immune-inflammatory index (SII) has been developed recently, based on platelet counts and the NLR (SII=platelets count x neutrophil/lymphocyte ratio) [7]. A high SII, which shows the inflammatory and immune status of patients simultaneously, was reported to be associated with poor outcomes in cancer and chronic heart failure (HF) patients. Furthermore, it more accurately predicted major cardiovascular events than did traditional risk factors in CAD patients after coronary intervention [8, 9].

APACHE (Acute Physiologic Score and Chronic Health Evaluation) II is one of the most widely used and accepted mortality scoring systems, and it has been tested in many different patient populations admitted to intensive care units (ICU) [10]. It is derived from 12 physiological variables plus age and chronic health status of patients. Major trials that established the utility of the APACHE II score mostly excluded coronary care patients, but some small studies tested its ability to predict in-hospital mortality of coronary patients, especially those with ACS [11, 12]. In those studies



ISSN 0022-9040. Кардиология. 2022;62(9). DOI: 10.18087/cardio.2022.9.n1979

the APACHE II score showed good performance in assessing the short-term prognosis of patients with ACS.

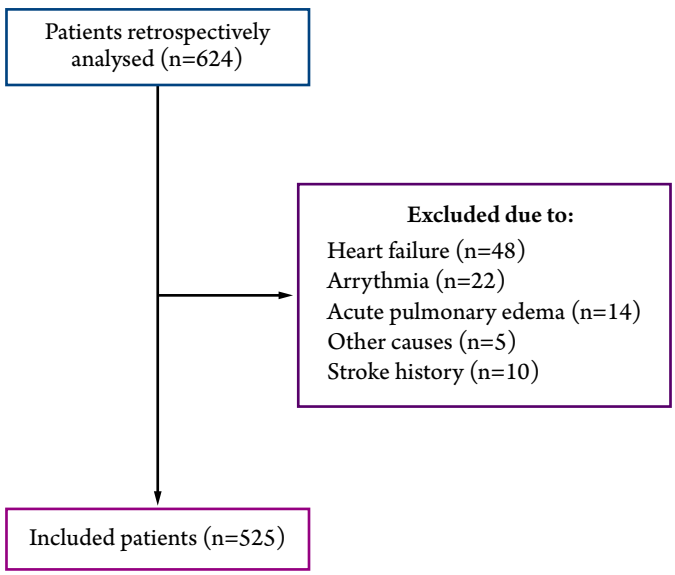
In the present study, we aimed to compare the in-hospital mortality predictive ability of the APACHE II score with inflammatory indices of ACS patients.

## Material and Methods

### *Study Design and Patient Population*

In this retrospective, cross-sectional study, 624 patients with all data available who were admitted to the coronary care unit (CCU) of a tertiary hospital during the period July 1, 2020 – December 31, 2020 were included. After the first evaluation, 99 patients were excluded from the study due to hospitalization for indications other than ACS, e.g., decompensated heart failure, acute pulmonary edema, arrhythmias, or other causes like pericarditis, myocarditis, cardiogenic shock, or for prior history of ischemic stroke (Figure 1). Apart from the 624 patients for whom complete data were available, we had excluded at the onset 4 patients with ACS due to lack of data. A total of 525 patients with ACS were included for further analysis. Demographic characteristics, laboratory findings, and clinical status of the patients were recorded. Diagnosis of ACS was based on the definitions of STEMI and NSTEMI according to previously published European Society of Cardiology guidelines [13, 14]. All patients were treated according to current guidelines. Primary percutaneous coronary intervention (PCI) was performed immediately for STEMI patients. Patients with NSTEMI were treated either with PCI within 24 hrs or with a noninvasive, medical approach at the physician's discretion. All patients were followed up in the CCU by well-trained staff and interventional cardiologists. The patients were divided into two groups according to their vital status, i.e., survivors or non-survivors, at hospital discharge. The study was performed according to the principles stated in the Declaration of Helsinki, and it was approved by the local ethics committee.

**Figure 1.** Inclusion and exclusion criteria




### *Biochemical and Hematological Parameters*

Blood tests were taken from all patients on admission to the CCU. Biochemical profiles were determined using standard methods. Hemogram variables were measured in blood samples collected in dipotassium EDTA tubes. An automatic blood counter (Beckman-Coulter Co, Miami, FL, USA) was used for whole blood counts. CRP and NLR values were recorded, and the SII was calculated.

### *APACHE II Score*

The APACHE II score, which quantifies the degree of abnormality of physiologic variables, was calculated within the first 24 hrs of admission to the CCU. This score is based on patients' age, chronic health status, and 12 physiological variables: body temperature, partial pressure of oxygen ($PaO_2$), arterial pH, heart rate, respiratory rate, concentrations of blood sodium, potassium, and serum creatinine, hematocrit, leukocyte count, Glasgow coma scale, mean arterial pressure. The score was computed according to a computer based program, and it ranged from 0 to 71. A higher score indicated a higher mortality risk.

### *Statistical Analysis*

A SPSS software package (Version 20.0, SPSS, Inc., Chicago, IL, USA) was used for analyzing the data. Categorical variables were expressed as frequencies (%) and a chi-square ($\chi^2$) test was used to compare differences between the groups. A Kolmogorov-Smirnov test was used to examine the distribution of numerical variables. Normally distributed variables are expressed as mean±standard deviation, and those without normal distribution are expressed as the median with the $25^{th}$–$75^{th}$ percentile interquartile range (IQR). Student's t-tests and Mann–Whitney U tests were used to test normally and non-normally distributed variables, respectively. All statistical tests were two-sided, and $p<0.05$ was considered to be statistically significant for all analyses.

Univariate binary logistic analysis was performed to determine which parameters were independently associated with in-hospital mortality. Independent variables with a $p<0.05$ in the univariate analysis were assessed by multivariate binary logistic regression (LR) to estimate odds ratios (OR) and 95% confidence intervals (CI) for mortality. The receiver operating characteristics (ROC) curve method was applied to analyze the prognostic value of APACHE II and inflammatory indices to determine independent predictors of mortality. The threshold values of the parameters for predicting clinical outcomes were determined by ROC curve analysis. The optimal cut-off value was defined as the value yielding the maximal Youden index. The area under the curve (AUC, C statistic) was used to determine sensitivity and specificity.

## Results

The mean patient age was 65.3±12.2 yrs, and 144 (27.4%) of the 525 patients were female. 192 patients were admitted with STEMI, and 333 (36.6%) with NSTEMI. The overall in-hospital mortality was 9.5%, and mortality of the STEMI and NSTEMI groups did not differ significantly (24 (12.5%) vs 26 (7.8%), p=0.090). The demographic, clinical, and laboratory characteristics of survivors and nonsurvivors are shown in Table 1. While nonsurvivors were older than survivors (71.6±10.5 vs 64.7±12.2 yrs) p<0.001), in-hospital mortality was similar for both genders (p=0.109). The incidence of chronic kidney disease was higher in nonsurvivors (p<0.001), but there were no any differences in histories of coronary/peripheral artery disease, hypertension, diabetes mellitus, or HF between the groups (p>0.05 for all). Most of the laboratory values were significantly different between the patient groups, except platelet and lymphocyte counts, which are constituents of the SII index, and blood sodium concentration and hematocrit (Table 1). In terms of clinical characteristics and vital signs on admission, nonsurvivors had significantly lower mean arterial pressure, blood oxygen saturation, and higher heart rate (p<0.001 for all).

We used binary LR analyses to determine the independent predictors of in-hospital mortality. With univariate analysis, we evaluated components of APACHE II and excluded variables that are constituents of APACHE II to avoid multicollinearity. APACHE II was significantly associated with mortality (OR: 1.263, 95% CI: 1.202–1.328; p<0.001). Apart from the APACHE II score, gender (OR: 2.072, 95% CI: 1.140–3.768; p=0.017), history of chronic kidney disease (OR: 3.005, 95% CI: 1.705–5.295; p<0.001), CRP concentration (OR: 1.011, 95% CI: 1.007–1.015; p<0.001), ejection fraction (OR: 0.873, 95% CI: 0.818–0.931; p<0.001), NLR (OR: 1.052, 95% CI: 1.018–1.087; p=0.003), and SII (OR: 1.011, 95% CI: 1.003–1.020; p=0.007) were identified as significant predictors in the univariate regression analysis. We added all

**Table 1.** Baseline clinical and laboratory characteristics of patients according to survival status.

| Variable | Survivors (n=475) | Nonsurvivors (n=50) | p value |
|---|---|---|---|
| Age (yrs) | 64.7±12.2 | 71.6±10.5 | <0.001 |
| Gender, female | 123 (25.9) | 21 (42) | 0.019 |
| **Acute coronary syndrome** | | | |
| • STEMI | 168 (87.5) | 307 (92.2) | 0.090 |
| • NSTEMI | 24 (12.5) | 26 (7.8) | |
| Chronic kidney disease | 106 (22.3) | 25 (50) | <0.001 |
| Heart failure | 10 (2.1) | 3 (6) | 0.118 |
| Hypertension | 228 (48) | 24 (48) | 0.560 |
| Diabetes mellitus | 173 (36.4) | 20 (40) | 0.645 |
| CAD/PAD | 249 (52.4) | 21 (42) | 0.182 |
| Ejection fraction (%) | 55 (46–60) | 35 (27–47) | <0.001 |
| Heart rate (bpm) | 80 (70–90) | 92 (80–110) | <0.001 |
| Mean arterial pressure (mm Hg) | 87 (77–96) | 53 (46–66) | <0.001 |
| Body temperature (°C) | 36.4 (36.2–36.6) | 36.3 (36.1–36.5) | 0.135 |
| $O_2$ saturation (%) | 96 (94–98) | 88 (82–93) | <0.001 |
| Respiratory rate | 16 (16-18) | 18 (6–26) | 0.162 |
| Creatinine (mg/dl) | 1 (0.9–1.2) | 1.4 (1.0–1.7) | <0.001 |
| GFR (ml/min) | 71.7 (58.3–84.5) | 44.4 (35.8–64.2) | <0.001 |
| CRP (mg/l) | 6 (3–17) | 21.3 (6.8–92.5) | <0.001 |
| Hematocrit (%) | 42.3 (38.6–45.5) | 41.6 (35.6–45.1) | 0.179 |
| WBC (g/dL) | 10.2 (8.2–12.7) | 13.2 (9.9–16.2) | <0.001 |
| Platelet ($10^3$/μl) | 236 (198–281) | 240 (179–294) | 0.851 |
| Neutrophil ($10^3$/μl) | 6.9 (5.2–9.3) | 9.5 (6.6–11.8) | <0.001 |
| Lymphocyte ($10^3$/μl) | 2 (1.3–2.8) | 2.3 (1.0–4.0) | 0.595 |
| NLR | 3.26 (2.06–5.80) | 4.66 (2.27–9.42) | 0.027 |
| SII | 742 (462–1392) | 1253 (539–2144) | 0.019 |
| Glucose (mg/dl) | 146 (98) | 220 (169) | <0.001 |
| Sodium (meq/l) | 138 (4) | 137.5 (5) | 0.374 |
| Potassium (meq/l) | 4.2 (0.6) | 4.5 (1.1) | <0.001 |
| APACHE II Score | 10 (4) | 20.5 (16.5) | <0.001 |

Data are mean ± SD, median (IQR), or frequency (%). bpm, beat per minute; BUN, blood urea nitrogen; CAD/PAD, coronary artery disease/peripheral artery disease; CRP, C-reactive protein; GFR, glomerular filtration rate; IQR, interquartile range; SD, standard deviation; NLR, neutrophil lymphocyte ratio; NSTEMI, non ST Elevation myocardial infarction; SII, systemic immune-inflammatory index; STEMI, ST elevation myocardial infarction; WBC, white blood cell.


ISSN 0022-9040. Кардиология. 2022;62(9). DOI: 10.18087/cardio.2022.9.n1979

**Table 2.** Independent predictors of in hospital mortality.

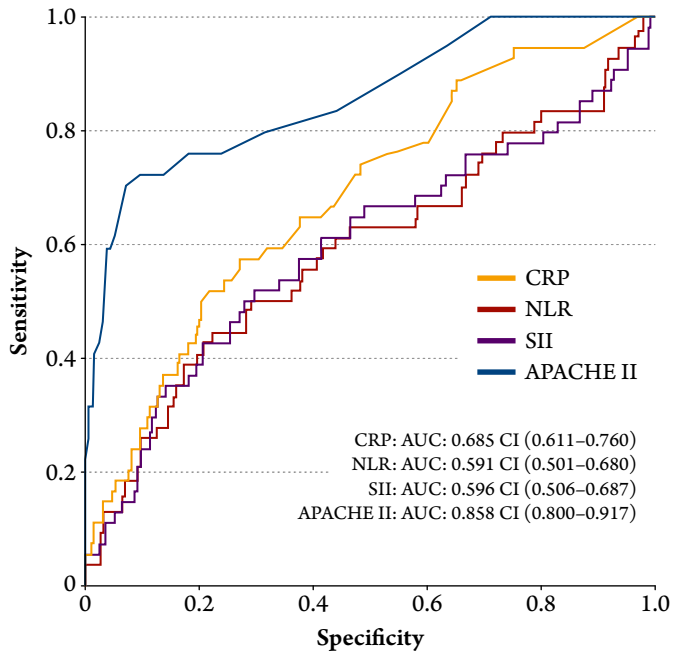
| Variables | Univariate analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p |
| Gender (female) | 2.072 (1.140–3.768) | 0.017 | — | — |
| Chronic kidney disease | 3.005 (1.705–5.295) | <0.001 | — | — |
| CRP | 1.011 (1.007–1.015) | <0.001 | — | — |
| EF | 0.873 (0.818–0.931) | <0.001 | — | — |
| SII | 1.011 (1.003–1.020) | 0.007 | — | — |
| NLR | 1.052 (1.018–1.087) | 0.003 | — | — |
| APACHE II Score | 1.263 (1.202–1.328) | <0.001 | 1.201 (1.122–1.285) | <0.001[a, b] |

CKD: chronic kidney disease, CRP: C-reactive protein, EF: ejection fraction,
NLR: neutrophil lymphocyte ratio, SII: systemic immune-inflammatory index.
**a** – The variables (gender, CKD, CRP, NLR, EF, APACHE II) were tested in a multivariable analysis.
**b** – The variables (gender, CKD, CRP, SII, EF, APACHE II) were tested in a multivariable analysis.

variables which had a significant relationship with in-hospital mortality in the univariate analysis to the multivariate LR analysis. This analysis showed that the APACHE II score was the only predictor of in-hospital mortality for ACS patients (OR: 1.201, 95% CI: 1.122–1.285; p<0.001) (Table 2).

ROC curve analysis was performed to determine the cut-off values and predictive abilities of SII, NLR, CRP, and APACHE II score for predicting mortality. While SII had 50% sensitivity and 72.1% specificity with a value of 1278.5 (AUC: 0.596, 95% CI: 0.506–0.687, p=0.019), NLR had 44.4% sensitivity and 77.9% specificity with a value of 6.28 (AUC: 0.591, 95% CI: 0.501–0.680, p=0.027) and CRP had 51.9% sensitivity and 78.3% specificity with a value of 18.9 (AUC: 0.685, 95% CI: 0.611–0.760, p<0.001). APACHE II score had 70.4% sensitivity and 92.9% specificity with a value of 16.5 (AUC: 0.858, 95% CI: 0.800–0.917, p<0.001) (Figure 2). The Youden index, which was used to define the optimum cut-off values of all indices, was calculated according to maximum values of sensitivity and specificity (1.202 for CRP, 1.223 for NLR, 1.221 for SII, and 1.633 for APACHE II).

**Figure 2.** ROC curves of APACHE II, SII, NLR and CRP for predicting in-hospital mortality. AUC, area under the curve; CRP, C-reactive protein; NLR, neutrophil-lymphocyte ratio; SII, systemic immune-inflammatory index




## Discussion

The APACHE II score was more successful than systemic inflammatory indices in predicting in-hospital mortality in ACS patients.

Inflammation has a central role in development of atherosclerosis and in ACS pathogenesis [15, 16]. C-reactive protein (CRP), NLR, and white blood cell (WBC) count, which are significant predictors of inflammation, were previously tested separately in stable CAD and ACS patient groups [6, 17], and these parameters were found to be significantly correlated with atherosclerosis severity and with short and long-term outcomes of ACS patients.

C-reactive protein plays a direct pathophysiological role in atherosclerosis by causing endothelial dysfunction, foam cell formation, and activation of complement in atherosclerotic plaque intima [18, 19]. Previous studies showed that increased CRP concentrations may be associated with short and long-term mortality. Morrow et al. investigated short-term risk after ACS and found that CRP elevation may predict 14-day mortality [20]. In addition, in a prospective study of patients who underwent early invasive therapy for NSTEMI, Mueller et al. found that an increased concentration of CRP at admission was associated with an increased risk of death over a mean follow-up of 20 mos [21].

Neutrophils contribute to endothelial dysfunction by producing cytokines, chemokines, and proteases. Furthermore, they also secrete acute inflammatory substances like superoxide radicals and proteolytic enzymes which may decrease endothelial function. Low lymphocyte counts, which are the main cells of the immune system,

cause increased physiological stress and depress the immune system by increasing cortisol release. Additionally, T lymphocytes inhibit endothelial damage and, thus, inhibit atherosclerosis. Due to these physiologic properties, NLR was found to be an independent predictor of long-term mortality in STEMI, and it was associated with the severity and complexity of CAD [22, 23]. Decreased release of prostacyclin and nitric oxide by endothelium causes platelet activation, which is required for neutrophil adhesion and activation in the early phase of atherosclerosis. Thus, any changes in the numbers of these three blood cells may facilitate atherosclerosis.

Recently, the SII formula containing platelet, neutrophil, and platelet counts has been developed based on their physiologic properties, and it has been proven valid in many different patient groups, including malignancies, heart failure, stable CAD, and ACS. Hu et al. first reported significant associations of SII with clinical outcomes, tumor size, vascular invasion, and early recurrence in hepatocellular carcinoma [24]. Seo et al. investigated the prognostic value of SII in HF patients and found that SII provided improved prediction of poor outcomes in congestive HF patients [9]. Furthermore, Liu et al. and Candemir et al. showed the clinical significance of SII in predicting the presence of coronary stenosis in patients with CAD [25, 26].

Huang et al. showed that SII is a potential indicator for predicting in-hospital and long-term clinical endpoints in elderly patients with acute MI undergoing PCI [27]. ROC curve analysis showed that the SII AUC value for long-term mortality was 0.64 (95% CI, 0.58–0.71). In the current study, we investigated the prognostic significance of SII in addition to CRP and NLR in patients with ACS. The AUC value for SII was 0.596 (95% CI: 0.506–0.687) for short-term mortality which is very similar to the study of Huang et al.

The APACHE II score was first described in 1981 by Knaus et al. and revised in 1985 by the same authors [28, 29]. Furthermore, it has been tested in a wide range of patient populations followed in surgical and medical ICUs for more than 20 yrs, but mostly excluding coronary patients [30, 31]. Most of the trials testing the ability of the APACHE II score showed good discrimination but poor calibration ability in terms of mortality [32, 33]. In addition, studies have tested the APACHE II score and have compared the prognostic accuracy of APACHE II and III with other scoring systems. Data of more than 15,000 patients were retrospectively analyzed. The ROC curve analysis was used for discrimination. These analyses also showed good discrimination, and it verified the findings of previous studies [34]. In addition to these studies, the APACHE II score was evaluated in small patient groups with acute MI. A trial conducted by Moreau et al. tested the short-term prognostic ability of APACHE II in 76 patients [12]. Sarmiento et al. investigated the ability of mortality prediction including 456 patients with acute MI in 17 different hospitals in Catalonia and the Balearic Islands [11]. APACHE II showed good performance along with other mortality scoring systems in this study. Despite these positive findings, the APACHE II score has not been widely used for acute MI patients as has been GRACE (Global Registry of Acute Coronary Events) or TIMI (Thrombolysis in Myocardial Infarction) risk scores.

One of the main aims of the current study was to compare the predictive abilities of CRP, NLR, and SII with APACHE II. Although CRP, NLR, and SII, which consist of only blood cell values, were found to be clinically significant for predicting mortality, adding clinical variables and vital signs may be more useful. Thus, the APACHE II score, which includes clinical findings, vital signs, and laboratory values, should give more accurate predictions. This study included a large number of acute MI patients, and it showed that the APACHE II score has a greater capability to predict in-hospital mortality than other inflammatory indices. According to these results, we conclude that evaluating the whole patient with all variables, i.e., clinical status, vital signs, laboratory findings, etc. is more important in order to be able to manage the clinical situation more effectively [11].

## Study Limitations

Despite positive results, this study has some limitations. First, it was a retrospective design and was conducted at a single center. Second, we did not consider GRACE and TIMI risk scores, which have been proven to be useful in predicting in-hospital mortality in ACS patients. Third, we did not include patients with missing data, although this was a very small group. Fourth, medications that patients used before hospitalization, i.e., statins, acetylsalicylic acid, and others, which may have affected the inflammatory factors, were not considered in the analysis. This deficiency may have also limited the validity of the findings. Lastly, other clinical risk factors present in the ACS patients were not compared.

## Conclusions

We found that the APACHE II score predicts in-hospital mortality of ACS patients more effectively than inflammatory indices. Larger, multicenter, and prospective studies may give more valid and reliable results.

*No conflict of interest is reported.*

**The article was received on 25/12/2021**



ISSN 0022-9040. Кардиология. 2022;62(9). DOI: 10.18087/cardio.2022.9.n1979

## REFERENCES


1. Mackman N. Triggers, targets and treatments for thrombosis. Nature. 2008;451(7181):914–8. DOI: 10.1038/nature06797
2. Zakynthinos E, Pappa N. Inflammatory biomarkers in coronary artery disease. Journal of Cardiology. 2009;53(3):317–33. DOI: 10.1016/j.jjcc.2008.12.007
3. Kose N, Akin F, Yildirim T, Ergun G, Altun I. The association between the lymphocyte-to-monocyte ratio and coronary artery disease severity in patients with stable coronary artery disease. European Review for Medical and Pharmacological Sciences. 2019;23(6):2570–5. DOI: 10.26355/eurrev_201903_17406
4. Oylumlu M, Yildiz A, Oylumlu M, Yuksel M, Polat N, Bilik MZ et al. Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. The Anatolian Journal of Cardiology. 2015;15(4):277–83. DOI: 10.5152/akd.2014.5366
5. Kiris T, Çelik A, Variş E, Akan E, Akyildiz ZI, Karaca M et al. Association of Lymphocyte-to-Monocyte Ratio With the Mortality in Patients With ST-Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention. Angiology. 2017;68(8):707–15. DOI: 10.1177/0003319716685480
6. Ji H, Li Y, Fan Z, Zuo B, Jian X, Li L et al. Monocyte/lymphocyte ratio predicts the severity of coronary artery disease: a syntax score assessment. BMC Cardiovascular Disorders. 2017;17(1):90. DOI: 10.1186/s12872-017-0507-4
7. Yang Y, Wu C, Hsu P, Chen S, Huang S, Chan WL et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. European Journal of Clinical Investigation. 2020;50(5):e13230. DOI: 10.1111/eci.13230
8. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of Systemic immune-inflammation index in cancer: A meta-analysis. Journal of Cancer. 2018;9(18):3295–302. DOI: 10.7150/jca.25691
9. Seo M, Yamada T, Morita T, Furukawa Y, Tamaki S, Iwasaki Y et al. P589Prognostic value of systemic immune-inflammation index in patients with chronic heart failure. European Heart Journal. 2018;39(Suppl 1):70–1. DOI: 10.1093/eurheartj/ehy564.P589
10. Godinjak AG, Iglica A, Rama A, Tancica I, Jusufovic S, Ajanovic A et al. Predictive value of SAPS II and APACHE II scoring systems for patient outcome in medical intensive care unit. Acta Medica Academica. 2016;45(2):89–95. DOI: 10.5644/ama2006-124.165
11. Sarmiento X, Rué M, Guardiola JJ, Toboso JM, Soler M, Artigas A. Assessment of the Prognosis of Coronary Patients: Performance and customization of generic severity index. Chest. 1997;111(6):1666–71. DOI: 10.1378/chest.111.6.1666
12. Moreau R, Soupison T, Vauquelin P, Derrida S, Beaucour H, Sicot C. Comparison of two simplified severity scores (SAPS and APACHE II) for patients with acute myocardial infarction. Critical Care Medicine. 1989;17(5):409–13. DOI: 10.1097/00003246-198905000-00006
13. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal. 2018;39(2):119–77. DOI: 10.1093/eurheartj/ehx393
14. Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European Heart Journal. 2021;42(14):1289–367. DOI: 10.1093/eurheartj/ehaa575
15. Hansson GK. Inflammation, Atherosclerosis, and Coronary Artery Disease. New England Journal of Medicine. 2005;352(16):1685–95. DOI: 10.1056/NEJMra043430
16. Swirski FK, Nahrendorf M. Cardioimmunology: the immune system in cardiac homeostasis and disease. Nature Reviews Immunology. 2018;18(12):733–44. DOI: 10.1038/s41577-018-0065-8
17. Ates AH, Canpolat U, Yorgun H, Kaya EB, Sunman H, Demiri E et al. Total white blood cell count is associated with the presence, severity and extent of coronary atherosclerosis detected by dual-source multislice computed tomographic coronary angiography. Cardiology Journal. 2011;18(4):371–7. PMID: 21769817
18. Zwaka TP, Hombach V, Torzewski J. C-Reactive Protein–Mediated Low Density Lipoprotein Uptake by Macrophages: Implications for Atherosclerosis. Circulation. 2001;103(9):1194–7. DOI: 10.1161/01.CIR.103.9.1194
19. Torzewski J, Torzewski M, Bowyer DE, Fröhlich M, Koenig W, Waltenberger J et al. C-Reactive Protein Frequently Colocalizes With the Terminal Complement Complex in the Intima of Early Atherosclerotic Lesions of Human Coronary Arteries. Arteriosclerosis, Thrombosis, and Vascular Biology. 1998;18(9):1386–92. DOI: 10.1161/01.ATV.18.9.1386
20. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP et al. C-Reactive Protein Is a Potent Predictor of Mortality Independently of and in Combination With Troponin T in Acute Coronary Syndromes: A TIMI 11A Substudy. Journal of the American College of Cardiology. 1998;31(7):1460–5. DOI: 10.1016/S0735-1097(98)00136-3
21. Mueller C, Buettner HJ, Hodgson JM, Marsch S, Perruchoud AP, Roskamm H et al. Inflammation and Long-Term Mortality After Non–ST Elevation Acute Coronary Syndrome Treated With a Very Early Invasive Strategy in 1042 Consecutive Patients. Circulation. 2002;105(12):1412–5. DOI: 10.1161/01.CIR.0000012625.02748.62
22. Shen X-H, Chen Q, Shi Y, Li H-W. Association of neutrophil/lymphocyte ratio with long-term mortality after ST elevation myocardial infarction treated with primary percutaneous coronary intervention. Chinese Medical Journal. 2010;123(23):3438–43. PMID: 22166528
23. Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis. 2012;225(2):456–60. DOI: 10.1016/j.atherosclerosis.2012.09.009
24. Hu B, Yang X-R, Xu Y, Sun Y-F, Sun C, Guo W et al. Systemic Immune-Inflammation Index Predicts Prognosis of Patients after Curative Resection for Hepatocellular Carcinoma. Clinical Cancer Research. 2014;20(23):6212–22. DOI: 10.1158/1078-0432.CCR-14-0442
25. Liu Y, Ye T, Chen L, Jin T, Sheng Y, Wu G et al. Systemic immune-inflammation index predicts the severity of coronary stenosis in patients with coronary heart disease. Coronary Artery Disease. 2021;32(8):715–20. DOI: 10.1097/MCA.0000000000001037
26. Candemir M, Kiziltunç E, Nurkoç S, Şahinarslan A. Relationship Between Systemic Immune-Inflammation Index (SII) and the Severity of Stable Coronary Artery Disease. Angiology. 2021;72(6):575–81. DOI: 10.1177/0003319720987743
27. Huang J, Zhang Q, Wang R, Ji H, Chen Y, Quan X et al. Systemic Immune-Inflammatory Index Predicts Clinical Outcomes for Elderly Patients with Acute Myocardial Infarction Receiving Percutaneous Coronary Intervention. Medical Science Monitor. 2019;25:9690–701. DOI: 10.12659/MSM.919802
28. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE – acute physiology and chronic health evaluation: a physiologically based classification system: Critical Care Medicine. 1981;9(8):591–7. DOI: 10.1097/00003246-198108000-00008
29. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Critical Care Medicine. 1985;13(10):818–29. PMID: 3928249
30. McNelis J, Marini C, Kalimi R, Jurkiewicz A, Ritter G, Nathan I. A Comparison of Predictive Outcomes of APACHE II and SAPS II in a Surgical Intensive Care Unit. American Journal of Medical Quality. 2001;16(5):161–5. DOI: 10.1177/106286060101600503
31. Naved SA, Siddiqui S, Khan FH. APACHE-II score correlation with mortality and length of stay in an intensive care unit. Journal of the College of Physicians and Surgeons – Pakistan. 2011;21(1):4–8. DOI: 01.2011/JCPSP.0408
32. Moreno R, Morais P. Outcome prediction in intensive care: results of a prospective, multicentre, Portuguese study. Intensive Care Medicine. 1997;23(2):177–86. DOI: 10.1007/s001340050313
33. Katsaragakis S, Papadimitropoulos K, Antonakis P, Strergiopoulos S, Konstadoulakis MM, Androulakis G. Comparison of Acute Physiology and Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiology Score II (SAPS II) scoring systems in a single Greek intensive care unit: Critical Care Medicine. 2000;28(2):426–32. DOI: 10.1097/00003246-200002000-00023
34. Beck DH, Smith GB, Pappachan JV, Millar B. External validation of the SAPS II, APACHE II and APACHE III prognostic models in South England: a multicentre study. Intensive Care Medicine. 2003;29(2):249–56. DOI: 10.1007/s00134-002-1607-9