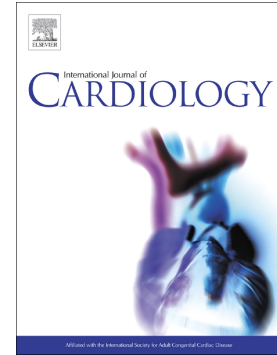


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## **Predictive Outcomes of APACHE II and Expanded SAPS II Mortality Scoring Systems in Coronary Care Unit**

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### **ABSTRACT**

**Objective:** We investigated the predictive values of the expanded Simplified Acute Physiology Score (SAPS) II and Acute Physiologic Score and Chronic Health Evaluation (APACHE) II score in predicting in-hospital mortality in coronary care unit (CCU) patients.

**Methods:** In this study, expanded SAPS II and APACHE II scores were calculated in the CCU of a single-center tertiary hospital. Patients admitted to CCU with any cardiovascular indication were included in the study. Both scores were calculated

according to previously determined criteria. Calibration and discrimination abilities of the scores in predicting in-hospital mortality were tested with Hosmer-Lemeshow goodness-of-fit C chi-square and receiver operating characteristics (ROC) curve analyses.

**Results:** A total of 871 patients were included in the analysis. The goodness-of-fit C chi-square test showed that both scores have a good performance in predicting survivors and nonsurvivors in CCU. Expanded SAPS II score has a sensitivity of 80% and a specificity of 91.8% with the cut-off value of 15.55, while APACHE II has a sensitivity of 75.9% and a specificity of 87.4% with the cut-off value of 16.5 in predicting mortality.

**Conclusion:** Expanded SAPS II and APACHE II scores have good ability to predict in-hospital mortality in CCU patients. Therefore, they can be used as a tool to predict short-term mortality in cardiovascular emergencies.

**Key words:** APACHE II; coronary care unit; Expanded SAPS II; mortality

## INTRODUCTION

Several scoring systems have been used for more than 20 years to predict the in-hospital mortality of patients in the intensive care unit (ICU). The Acute Physiologic Score and Chronic Health Evaluation (APACHE) was the first attempt described by Knaus et al. in 1981 and became one of the most frequently used scoring systems after revision of the original system (called APACHE II) in 1985 [1,2]. APACHE II score is derived from 12 physiological variables plus age and chronic health status of patients [2]. APACHE III and APACHE IV generated by adding several variables were not accepted and not used as often as APACHE II [3,4]. The Simplified Acute Physiology Score (SAPS) was first described in 1984 as a simpler and less time-consuming method than APACHE [5]. In 1993, a new score called SAPS II was developed from a large sample of surgical and medical patients to provide a method for converting the score to a probability of hospital mortality in 137 adult ICUs in 12 countries [6]. Afterward, an expanded SAPS II score was developed by adding six variables (age, sex, length of pre-ICU hospital stay, patient location before ICU, clinical category, and whether drug overdose was present) potentially associated with mortality [7]. Its objective was to improve the SAPS II for mortality prediction, thereby improving the standardized mortality ratio (SMR) and comparing the observed and predicted hospital mortality rate.

Despite APACHE II and SAPS II scoring systems having been evaluated in many population samples so far [8–11], coronary care unit (CCU) and burn patients were largely not included in the analyzes [6,12–15].

Early risk stratification plays a pivotal role in CCU patients, most of whom are high-risk patients such as acute coronary syndromes (ACS), fatal arrhythmias, and cardiogenic shock. Many risk scores derived from clinical trial populations and international registries other than SAPS II and APACHE II have been developed to facilitate risk assessment in ACS patients. They have been used efficiently for many years [17–20]. But so far expanded SAPS II and APACHE II scoring systems were not tested and compared in a study that included only CCU patients.

This study was undertaken to investigate the success of the aforementioned mortality scoring systems in predicting mortality in CCU patients.

## MATERIALS AND METHODS

### Study Design and Patient Population

This retrospective, single-center, and cross-sectional study was conducted in the CCU of a tertiary referral hospital. All consecutive patients admitted for acute cardiovascular indications during the period 1 October 2019 to 31 May 2020 were included in the study. Data from 1153 patients were retrospectively analyzed, and 282 patients were excluded from the study because of various reasons: (I) were hospitalized to the CCU by other departments (internal medicine, chest diseases, general surgery, thoracic surgery, etc.) with noncardiac indications (acute renal failure, postoperative follow up, pulmonary embolism, acute hepatic failure, etc.), (II) discharged at the patient's request within 2 hours, (III) no vital signs despite adequate cardiopulmonary resuscitation during hospitalization, (IV) transferred to ward or another ICU within 4 hours, (V) patients with insufficient data (Figure S1). After applying these exclusion criteria, 871 patients were left to be included for the data analysis. Diagnosis of acute myocardial infarction (MI) was based on the third universal definition of MI [21], and decompensated heart failure (HF) was diagnosed according to clinical and laboratory findings defined in the European Society of

Cardiology (ESC) HF guidelines [22]. Arrhythmias like rapid ventricular rate atrial fibrillation (AF), sustained ventricular tachycardia (lasting longer than 30 seconds or hemodynamic instability occurring in less than 30 seconds), or severe bradycardia requiring intervention or follow-up were all diagnosed according to the guidelines [23–25]. According to the current guidelines, all other cardiac diagnoses (acute pulmonary edema, cardiogenic shock, myocarditis, pericarditis, and others) were also defined. All patients were followed in the CCU by experienced cardiologists, nurses, and health staff, and their vital parameters were recorded in patient follow-up cards and the hospital database system. The patients received routine clinical assessment with standard medical care currently performed in routine clinical practice according to the uptodate guidelines. The study was conducted with the principles stated in the Declaration of Helsinki and approved by the local ethics committee (17/09/2020, 2020/14-05).

### **Mortality Scoring Systems**

The expanded SAPS II and APACHE II variables were selected and collected during the first 24 h after CCU admission. The SAPS II score was calculated from the following parameters: age, heart rate, systolic blood pressure, body temperature, Glasgow coma scale, partial pressure of oxygen ( $PaO_2$ )/fraction of inspired oxygen ( $FiO_2$ ) (if on mechanical ventilation or continuous positive airway pressure (CPAP)), blood urea nitrogen, urine output, sodium, potassium, bicarbonate, bilirubin, white blood cells, presence of chronic disease and type of admission. Besides the length of pre-CCU hospital stay, patient location before CCU, clinical category, and presence/absence of drug overdose were added to get the expanded SAPS II score. Total SAPS II score ranging from 0 to 163 points was calculated according to score attributed to each parameter inside or outside the normal range and finally expanded SAPS II score calculated by adding the rest of the variables.

APACHE II score ranging from 0 to 71 is computed based on several measurements applied within 24 hours of admission of a patient to the CCU. Higher scores correspond to more severe disease and a higher risk of death. The score consists of the patient's age and 12 parameters:  $PaO_2$ , body temperature, mean arterial pressure, arterial pH, heart rate, respiratory rate, sodium, potassium, creatinine, hematocrit, leukocyte count, and Glasgow coma scale.

### **Data Collection**

Demographic data, hemodynamic and laboratory findings, primary admission diagnosis, length of CCU stay, and discharge status were recorded for all patients. APACHE II and expanded SAPS II scores were calculated using the data entered according to the previous definitions, with a higher score indicating higher mortality risk. The worst values of the clinical or laboratory findings within the first 24 hours or during CCU stay -if follow-up is less than 24 hours- were used for calculation. All parameters including Glasgow Coma Score, age, and chronic health status were used in the assessment. The probability of in-hospital mortality regarding APACHE II and expanded SAPS II scores for each patient were generated by computer database using the original regression equations [2,6].

### **Statistical Analysis**

SPSS software package (Version 20.0, SPSS, Inc., Chicago, IL) and Minitab Version 18 were used for analyzing the gained data. The ability of the calibration (risk estimations corresponding to actual mortality rates) and discrimination (to classify survivors and non-survivors correctly according to the estimated probability of

death) were measured separately for both APACHE II and expanded SAPS II mortality scoring systems. In addition, Hosmer-Lemeshow C statistics were used to assess the goodness of fit for both models formally. In this technique, groups were formed using equal expected probability ranges and within each stratum, observed and predicted numbers of deaths were compared. A high p-value ( $>0,05$ ) which indicates slight differences in statistics, suggests that the model correctly reflects the actual outcome.

Receiver Operating Characteristics (ROC) analysis was used to assess discrimination for both models, and the area under the curve (AUC) was calculated and compared. The AUC by the plot of all possible pairs of false-positive and true-positive rates shows the satisfactory discrimination of the model (if the value is larger than 0,7). Student's t-test and chi-square tests were used to test statistical significance for continuous and categorical variables, respectively. The Shapiro-Wilk test assessed the normality assumption of data, and the homogeneity of variances was checked with Levene's test. Spearman correlation coefficient was used to check the correlation between predictive models and mortality probabilities because the parameters were not normally distributed. A p-value less than 0.05 was regarded as statistically significant.

## RESULTS

Of the 871 patients included in the analysis, the overall in-hospital mortality was 83 (9,5%). The median age of patients was 66 (58-75), while non-survivors were older than survivors (72 (65-80) vs. 66 (57-75),  $p<0.001$ ), and 32.4% of the population were female. Other demographic characteristics, laboratory findings, and clinical parameters in non-survivors and survivors are shown in Table 1, of which most of the parameters were significantly different between groups. Acute MI was the most common cause of admission to the CCU (79.3%). In comparison, HF constituted 21.7%, arrhythmias 4.1%, acute pulmonary edema 4.7%, and other causes (cardiogenic shock and sudden cardiac arrest, pericarditis, myocarditis) 2.9% of all hospitalizations. There were significant differences in mortality ratios according to the primary admission diagnoses, which were higher in HF and other causes groups compared to acute MI, arrhythmias, and acute pulmonary edema ( $p<0.001$ ) (Table S1). The presence of previous HF, chronic kidney disease, and stroke history were higher in non-survivors ( $p<0.001$ ,  $<0.001$ , and 0.041, respectively). Coronary artery disease, hypertension, and diabetes mellitus history were similar between groups ( $p=0.486$ , 0.564, and 0.403, respectively).

The relationship between the scores and mortality was evaluated separately, the results being shown in Table 2. The expanded SAPS II score was 4.3 (3.9-5.0), and the APACHE II score was 11 (9-15) for all patients. APACHE II and expanded SAPS II scores and predicted mortality rates were higher in non-survivors than survivors. Expanded SAPS II score was 4.3 (3.9-4.8) versus 6.5 (5.8-8.1), and APACHE II score was 11 (9-14) versus 23 (17-33) for survivors and non-survivors ( $p<0.001$  for all). SAPS II predicted mortality rate was 4.1 (2.5-5.8) versus 35.2 (20.9-69.2), and APACHE II predicted mortality rate was 12.8 (9.9-18.6) versus 42.4 (23.4-78.6) for survivors and non-survivors ( $p<0.001$  for all).

The prognostic performance of both systems was evaluated in terms of calibration and discrimination. Calibration, the degree of correspondence between predicted and

observed mortality, was assessed by the Hosmer-Lemeshow goodness-of-fit C chi-square tests. The goodness-of-fit C chi-square test revealed a good performance which implies a significant fit for both models (Table S2). We decided to compare the predictions of both models at a fixed decision (50%) and performed a cross-tabulation (Table S3). The two methods predicted the same outcome in 843 (96.7%) patients in the whole population. The two methods predicted the same outcome in 769 (97.6%) patients for survivors. While expanded SAPS II predicted 15 (78.9%) patients correctly, APACHE II predicted only 4 (21.1%) patients accurately for the 19 (2.4%) patients where the predictions did not agree. For non-survivors, the two methods predicted the same outcome in 74 (89.1%) patients. For the 9 (10.9%) patients where the predictions do not agree, expanded SAPS II predicted 3 (33.3%) patients correctly, while APACHE II predicted 6 (66.7%) patients accurately. While the difference in non-survivors was not statistically significant (McNemar's chi-square,  $p=0.508$ ), it was statistically significant in survivors and total population (McNemar's chi-square,  $p=0.019$ ,  $p=0.013$ , respectively). According to the comparison of the predictive abilities of both models, expanded SAPS II was more successful in predicting survivors (78.9% vs. 21.1%). APACHE II was numerically better than expanded SAPS II in predicting non-survivors, but the difference was not statistically significant (66.7% vs. 33.3%,  $p=0.508$ ).

Discrimination was considered as excellent, very good, good, moderate, and poor with AUC values of 0.9-0.99, 0.8-0.89, 0.7-0.79, 0.6-0.69 and  $<0.6$ , respectively. The expanded SAPS II AUC value was 0.908 (CI 0.869 – 0.947,  $p<0.001$ ), representing a statistically significant predictive marker. The cut-off value for expanded SAPS II was 5.55, with a sensitivity of 80% and a specificity of 91.8%. The APACHE II scoring system also represented a statistically significant predictor for mortality, of which the AUC value was 0.861 (CI 0.814 – 0.908,  $p<0.001$ ). The cut-off value for APACHE II was 16.5, with a sensitivity of 75.9% and a specificity of 87.4%. Figure 1 shows the AUC values for expanded SAPS II and APACHE II scoring systems. Furthermore, there was a statistically significant correlation between the scores and predicting risk of in-hospital mortality ( $R=0.691$ , and  $R=0.715$ ).

## DISCUSSION

Our study investigated the ability of the extended SAPS II and APACHE II scoring systems to predict in-hospital mortality conducted in a single tertiary center CCU patients. It showed that both scoring systems successfully predicted in-hospital mortality in patients hospitalized for CV reasons. To the best of our knowledge, this is the first study in which especially expanded SAPS II score has been tested and compared with APACHE II score, including only CCU patients.

APACHE II and SAPS II are widely used and accepted mortality scoring systems in ICU patients. Since their introduction to the literature, they were either tested

individually or compared to each other or other scoring systems. Furthermore, validation, customization, and predictive accuracy of SAPS II and APACHE II have been tested in single-center, multi-center, multinational retrospective, and prospective studies conducted in medical, surgical, or mix ICUs [12,13,15,26–29]. Nevertheless, coronary patients were mostly excluded from analysis in most of the trials. Le Gall et al. tried to develop a new SAPS II from a large sample of surgical and medical patients to provide a method to convert the score to a probability of hospital mortality using logistic regression analysis in a multicenter study [6]. Moreno et al. evaluated and compared the performance of SAPS II and APACHE II in the ICU population [12]. Capuzzo et al. investigated SAPS II and APACHE II validation in a single-center population in 2000 [15]. All three of these studies and many more excluded coronary patients from validation, regression, and prediction analysis [13,14,28]. Although there is no concrete reason to exclude this group of patients, there may be some valid reasons: I) coronary patients were not included in the development of original SAPS II and APACHE II scoring systems. So, including these patients may cause misinterpretation, II) ongoing efforts for the development of different scoring systems like GRACE (Global Registry of Acute Coronary Events) and TIMI (Thrombolysis in Myocardial Infarction) have been developed for ACS patients of which consisting of the vast majority of coronary care patients [19,20], III) usefulness of previously accepted three severity indexes in CCU patients [30–32].

Despite major trials excluded coronary patients while developing SAPS II and APACHE II and analysis of mortality prediction, a few small sample studies were conducted to test these scoring systems in this group, especially in ACS patients



[26,33–36]. Sarmiento et al. and Moreau et al. investigated SAPS II and APACHE II performance in small sample acute MI patients. Both studies showed the good performance of these prognostic indexes [33,36]. In a prospective, observational, and multicenter study, Reina et al. compared SAPS II and APACHE III in discriminating in-hospital mortality in acute MI patients. The results indicated good discrimination for both models [35]. Another study by Metnitz et al. tested the prognostic performance and customization of SAPS II score in 9 adults medical, surgical and mixed ICUs. They included patients with different CV indications in contrast to other studies, and its subgroup analysis showed better calibration and discrimination in CV disease groups than in others [26]. These trials showed that ICU scoring systems could be used in CCU patients, although they were conducted more than 20 years ago.

Moreover, many interventional techniques like primary percutaneous coronary intervention have been developed and become widespread in many centers, significantly decreasing in-hospital mortality. So, evaluating these scoring systems under current technological advances and well-developed hospital capabilities may be useful. In addition to these, a study conducted by Schuster et al., most similar to our research, investigated the ability of SAPS II in CCU patients [34]. They included 708 CCU patients whose population number and primary diagnosis were very similar to our study. However, unlike our study, they compared the outcomes with the ICU population and found that SAPS II is applicable to CCU patients.

In our study, different from the previous ones, we investigated expanded SAPS II in addition to APACHE II, which has not been analyzed in CCU patients so far. The expanded SAPS II model described first in 2005 by Le Gall et al. led to better calibration, discrimination, and uniformity of fit according to the original SAPS II model [7]. However, they also excluded coronary patients along with burn and

cardiac surgery patients. So investigating even including only CCU patients to test the ability of expanded SAPS II should be very important. Furthermore, our study showed that expanded SAPS II could also be used like older scoring systems to predict in-hospital mortality in CCU patients.

Considering results and trial designs of previous studies especially in groups including CCU patients, there are several noteworthy points of our study. First, all studies have been conducted before 2000s (between 1989 and 1999). At that time, interventional procedures (primary PCI and intraaortic balloon pump, etc.) and CCU capabilities were not as widespread and advanced as it is today. Therefore, our study is the most up-to-date study in investigating APACHE II and expanded SAPS II scores in CCU patients. Second, two of these five studies did not analyse CCU patients alone, but evaluated as a subgroup of other ICU patients [26,34]. The remaining three studies included only acute MI diagnoses, not all CCU patients [33,35,36]. Our study differs from these studies in that it included only CCU patients and all CV diagnoses. Furthermore, sample size in two studies including acute MI patients were lower than our population. The third study did not perform calibration analysis even though the sample size was higher than our study. Third, one of the most important features of our study is that it is the first study to use expanded SAPS II score when compared to previous studies involving CCU patients.

#### **LIMITATIONS OF STUDY**

Our trial has some limitations despite its satisfying results. First, it has been designed in a retrospective manner and is conducted in a single center. So, prospective and multicenter studies may yield more objective and reliable results in this regard. Second, we did not compare these scores with currently accepted and used cardiac mortality risk scores like GRACE and TIMI. If comparisons were made with these scores, it would increase the value of this study.

#### **CONCLUSION**

This study demonstrated that both models could predict in-hospital mortality in CCU patients as in other ICUs. They have a good calibration performance as well as discrimination, unlike other studies. Furthermore, expanded SAPS II has been evaluated for the first time in the CCU patients. It was demonstrated that it is a useful predictive model in this group of patients. Conducting prospective and multicenter studies may yield better and more objective results in the future.

#### **Disclosure of interest**

The authors report no conflicts of interest.

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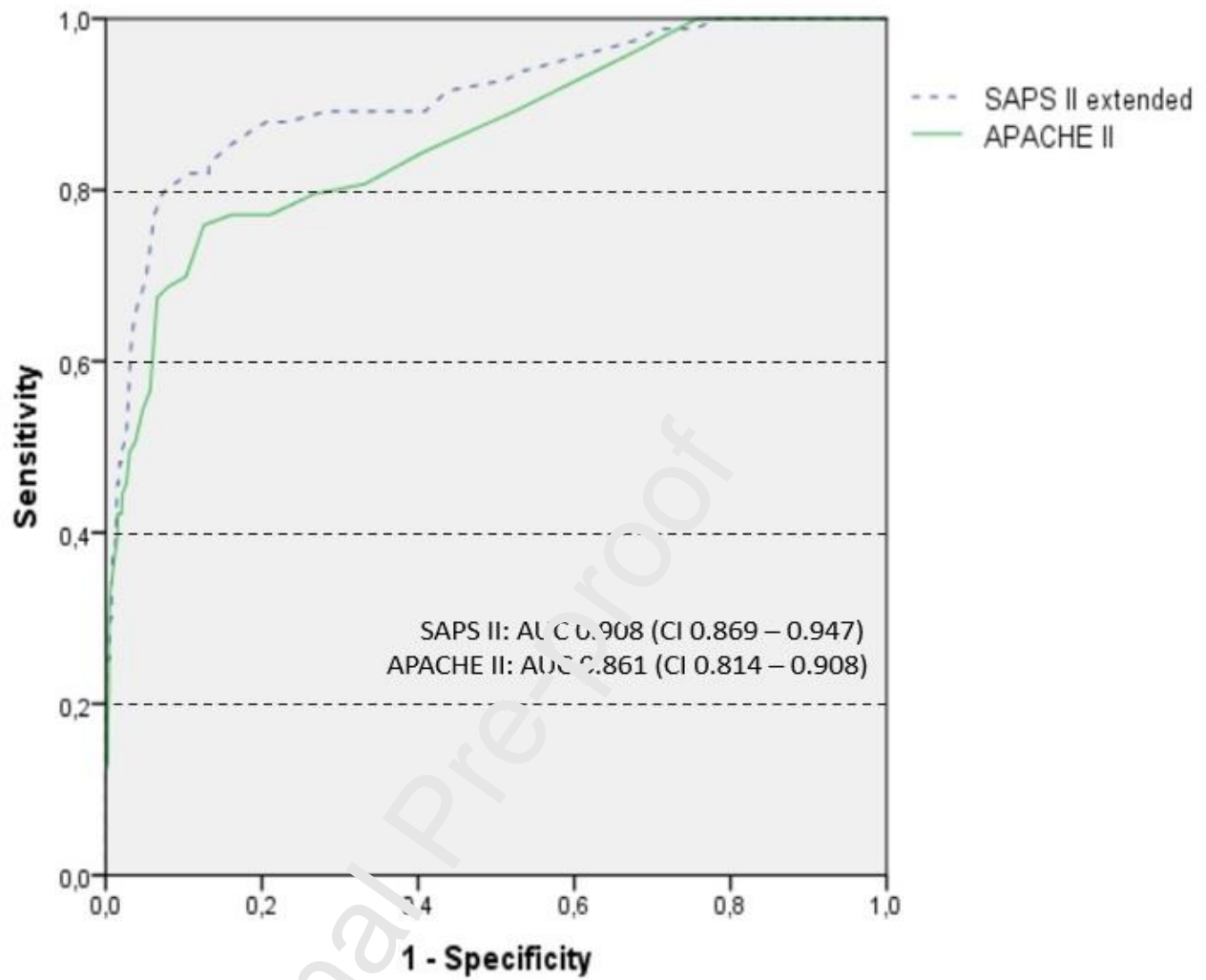
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**Figure.** Area under the ROC curves for expanded SAPS II and APACHE II. (CI: confidence interval, ROC: receiver operating characteristic)

**Table 1.** Demographic and Clinical Characteristics of Patient Population in Coronary Care Unit

	All Patients (n=871)	Nonsurvivors (n=83)	Survivors (n=788)	<i>p</i>
Age (years)	66 (58-75)	72 (65-80)	66 (57-75)	<0.001
Hypertension, n(%)		37 (44.6)	382 (48.5)	0.564
Diabetes Mellitus, n (%)		34 (41)	285 (36.2)	0.403
CAD/PAD, n (%)		44 (53)	451 (57.2)	0.486
Stroke history, n (%)		7 (8.4)	28 (3.6)	0.041
Heart failure, n (%)		25 (30.1)	108 (13.7)	<0.001
Chronic Renal Disease, n (%)		42 (50.6)	222 (28.2)	<0.001
Glomerular Filtration Rate (ml/min)	67.39 (48.4-81.6)	39.9 (28.6-60)	69.5 (53.7-82.8)	<0.001
Heart rate (bpm)	84 (75-98)	96 (79-108)	82 (74-96)	0.003
Mean blood pressure (mmHg)	96 (83-103)	69 (53-83)	96 (86-103)	<0.001
Body temperature (°C)	36.5 (36.3-36.7)	36.6 (36.3-37)	36.5 (36.3-36.7)	0.510
Saturation (%)	96 (92-97)	86 (82-92)	96 (93-97)	<0.001
Respiratory rate (breaths/min)	17 (16-20)	20 (6-28)	16 (16-19)	0.810
Blood urea nitrogen (mg/dL)	19 (14-27)	33 (20-55)	18 (14-25)	<0.001
CRP (mg/L)	7.5 (3-22)	21 (6.4-74)	7 (3-19)	<0.001
Hematocrit (%)	42 (37.8-45.6)	40 (35.8-44.3)	42.1 (38.1-45.6)	0.060
WBC (10 <sup>3</sup> /μL)	10.34 (8.3-12.1)	12.2 (9.5-15.9)	10.2 (8.2-12.8)	<0.001
Platelet count (10 <sup>3</sup> /μL)	238 (193-285)	241 (179-295)	238 (196-283)	0.813
Neutrophil count (10 <sup>3</sup> /μL)	7.0 (5.1-9.7)	9.5 (6-12.5)	6.9 (5.1-9.4)	<0.001
Lymphocyte count (10 <sup>3</sup> /μL)	1.96 (1.2-2.8)	1.7 (0.9-3.2)	2 (1.3-2.8)	0.298
Glucose (mg/dL)	154 (119-230)	205 (134-311)	151 (117-221)	<0.001
Sodium (mEq/L)	138 (136-140)	137 (134-140)	138 (136-140)	0.178
Potassium (mEq/L)	4.2 (3.9-4.6)	4.6 (4-5.3)	4.2 (3.9-4.5)	<0.001
Glascow coma score	15 (15-15)	12 (3-15)	15 (15-15)	<0.001
CHA <sub>2</sub> DS <sub>2</sub> VASc score	3 (2-4)	4 (3-5)	3 (2-4)	<0.001

Continuous variables are presented as mean ± SD or median (IQR), categorical variables are presented as frequency (%)

bpm: beat per minute; BUN: blood urea nitrogen; CAD/PAD: Coronary Artery Disease/Peripheral Artery Disease; CRP: C-reactive protein; IQR: interquartile range; SD: standart deviation; WBC: white blood cell

**Table 2.** Relationship between scores and mortality

	Death	Median (IQR)	<i>p</i>
<b>Expanded SAPS II</b>	No	4.3 (3.9-4.8)	<0.001
	Yes	6.5 (5.8-8.1)	
<b>SAPS II Mortality</b>	No	4.1 (2.5-8.1)	<0.001
	Yes	35.2 (20.9-69.2)	
<b>APACHE II</b>	No	11 (9-14)	<0.001
	Yes	23 (17-33)	

<b>APACHE II Mortality</b>	No	12.8 (9.9-18.6)	<i>&lt;0.001</i>
	Yes	42.4 (23.4-78.6)	

IQR: interquartile range

### HIGHLIGHTS

- Although mortality scoring systems (APACHE II and SAPS II) have tested in different intensive care unit patients, data on CCU patients are very limited.
- The expanded SAPSS II score has better calibration and discrimination better than original SAPS II score has not been studied on CCU patients before.
- Our study showed that both mortality scores have good calibration and discrimination ability in CCU patients. So, with more extensive and multicenter trials, newer mortality scoring systems specific to CCU patients can be developed.