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Original Article

Comparative predictive value of APACHE-II, SAPS-II and GRACE scores for mortality in acute coronary syndrome (ACS) patients: Evidence from Indonesia intensive cardiovascular care unit registry

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Abstract

The Global Registry of Acute Coronary Events (GRACE) score is acknowledged for its ability to predict in-hospital mortality among patients with acute coronary syndrome (ACS). However, intensive care physicians often employ general prognostic scores such as Acute Physiologic and Chronic Health Evaluation II (APACHE-II) and Simplified Acute Physiology Score II (SAPS-II) to predict the mortality of ACS patients. However, their predictive values are not well-determined in predicting mortality in ACS treated in the cardiovascular care unit (CVCU). The aim of this study was to evaluate the performance of APACHE-II and SAPS-II scores in comparison with GRACE scores in predicting the CVCU mortality and in-hospital mortality of ACS patients admitted to CVCU. A multicenter retrospective cohort study was conducted using data from a registry of patients admitted to 10 hospitals in Indonesia between August 2021 and July 2023. This study evaluated the APACHE-II, SAPS-II, and GRACE scores for patients with ACS upon admission to CVCU. The area under the curve (AUC) of the receiver operating characteristic (ROC) was utilized to assess the discriminative ability for predicting mortality. Among the 12,950 admitted patients, 9,040 were diagnosed with ACS, and 6,490 patients were included in the final analysis. All three scoring systems had relatively good discriminative ability to predict CVCU mortality with APACHE-II having better results (AUC: 0.771; sensitivity: 63.9%; specificity: 78.7%) compared to GRACE (AUC: 0.726; sensitivity: 61.7%; specificity: 73.2%) and SAPS-II (AUC: 0.655; sensitivity: 38.9%;

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specificity: 85.2%). To predict in-hospital mortality, APACHE-II had better results (AUC: 0.815; sensitivity: 68.7%; specificity: 80.4%) compared to GRACE (AUC: 0.769; sensitivity: 64.6%; specificity: 77.5%) and SAPS-II (AUC: 0.683; sensitivity: 41.8%; specificity: 86.2%). APACHE-II had the best single risk factor for CVCU mortality (odds ratio (OR): 1.198; 95% confidence interval (CI): 1.181–1.214) and in-hospital mortality (OR: 1.259; 95%CI: 1.240–1.279). In conclusion, APACHE-II, SAPS-II, and GRACE scores moderately predict CVCU and in-hospital mortalities, with the APACHE-II score exhibiting the highest predictive capability in ACS patients admitted to CVCU.

Keywords: ACS, APACHE, GRACE, SAPS, mortality

Introduction

Cardiovascular disease remains the leading cause of mortality worldwide, primarily associated with ischemic heart disease [1]. Despite advancements in management and diagnostic strategies, in-hospital mortality rates for patients with acute coronary syndrome (ACS) remain significant, particularly among those with multiple comorbidities [2]. In the context of limited resources and the need for efficient patient management, judicious decision-making regarding the admission of high-risk patients to intensive care units is crucial to reducing morbidity and mortality. Increasingly, intensive care units are focusing on the use of scoring systems to objectively identify and prioritize high-risk patients.

Many specific prognostic risk scores have been validated for ACS; one of the well-known is the Global Registry of Acute Coronary Events (GRACE) score [3,4]. The GRACE score is a predictive logistic model that employs eight prognostic factors, the values of which can be computed to get a prognostic score estimating the probability of death or the cumulative risk of death within six months for individual ACS patients [5]. Despite the GRACE score's established efficacy, clinicians in intensive care units frequently employ broader scoring systems for mortality prediction, such as the Acute Physiologic Score and Chronic Health Evaluation II (APACHE-II) and the Simplified Acute Physiology Score II (SAPS-II) [6]. The APACHE-II score is derived from 12 physiological variables, along with the patient's age and long-term health status. The APACHE-II score has been employed for various medical conditions, particularly in cardiovascular settings. It has been demonstrated to moderately predict outcomes in several situations, including cardiomyopathy, out-of-hospital cardiac arrest (OHCA), in-hospital cardiac arrest (IHCA), and cardiac surgery, with a modified version designated for heart failure (APACHE-HF) [7-9]. The SAPS-II score was developed from a large cohort of surgical and medical patients to estimate the probability of hospital mortality [6]. SAPS-II was initially described as a simpler and faster alternative to APACHE-II [6] and it has been studied as a predictor for several cardiac conditions including cardiac arrest and cardiac surgery [9].

For widespread adoption, the effectiveness of each scoring system must be confirmed through diverse studies involving populations distinct from those used during their development [10]. Although numerous population samples have validated APACHE-II and SAPS-II, the analysis has not included the cardiovascular care unit (CVCU), particularly in patients with ACS. Therefore, the aim of this study was to investigate the predictive value of APACHE-II and SAPS-II scores compared to the current widely used score, GRACE, in predicting the mortality of ACS patients admitted to CVCU in 10 hospital centers in a limited health care resource country, Indonesia.

Methods

Study design and setting

This multicenter retrospective cohort study was conducted using data collected in the CVCU of 10 national reference hospitals in Indonesia participating in the "IndONEsia ICCU Registry" (ONE ICCU Registry) between August 1, 2021, and July 31, 2023 [11]. The hospitals involved were National Cardiovascular Center Harapan Kita (Jakarta, Indonesia), Dr. Saiful Anwar General Hospital (Malang, Indonesia), Dr. Sardjito General Hospital (Yogyakarta, Indonesia), Dr.

Wahidin Sudirohusodo General Hospital (Makassar, Indonesia), H. Adam Malik General Hospital (Medan, Indonesia), Prof. Dr. I.G.N.G. Ngoerah General Hospital (Denpasar, Indonesia), Dr. M. Djamil General Hospital (Padang, Indonesia), Prof. Dr. R. D. Kandou General Hospital (Manado, Indonesia), Dr. Iskak General Hospital (Tulungagung, Indonesia), and Dr. Kariadi General Hospital (Semarang, Indonesia).

Patients criteria and data collection

All patients, males and females over 18 years of age at the time of their index hospitalization, with ACS diagnoses admitted to the CVCU of each hospital, were documented in the "IndONEsia ICCU Registry." ACS was diagnosed according to the European Society of Cardiology (ESC) guideline [12]. It is divided into three categories: (a) ST-elevation myocardial infarction (STEMI) (characterized by myocardial necrosis as indicated by cardiac biomarkers (cardiac troponin or creatine kinase-MB (CK-MB)), new ST-segment elevation (considered new in the absence of prior ECG), or left bundle branch block (LBBB) observed on the initial electrocardiogram following hospitalization); (b) non-ST-elevation myocardial infarction (NSTEMI) (ACS which is proven by evidence of myocardial necrosis by evaluation of cardiac biomarkers such as troponin or CK-MB, without any elevation of new ST-segment on initial ECG examination following hospitalization); and (c) unstable angina pectoris (angina pectoris (an equivalent of ischemia pain) accompanied by one of the following three criteria: (1) resting angina that is persistent, typically lasting 10 minutes or longer, (2) newly developed angina classified as at least Canadian Cardiovascular Society (CCS) Class III, (3) progressive angina is defined by an escalation in severity from CCS Class I to CCS Class III. All diagnoses of ACS patients were based on clinical symptoms, ECG, and cardiac biomarkers (cardiac troponins (troponin-I or troponin-T) or CK-MB)).

Patients who were readmitted during the same hospital stay were excluded from the analysis. Data collection was undertaken by centrally trained research staff within 24 hours after admission to CVCU. Using standardized methods and accepted operational definitions of each variable in all centers (which has been agreed upon and become the guide for all data collectors), staff identified patients, reviewed their medical records, and conducted examinations. All parameters required for scoring APACHE-II, SAPS-II, and GRACE score were assessed. If any parameter was absent, the patient was excluded (listwise deletion approach).

Study variables

The APACHE-II score is a severity-of-disease classification system that is derived from 12 physiological variables plus age and chronic health status of patients to predict mortality risk. It includes the history of organ failure state (heart failure NYHA class IV, cirrhosis, end-stage renal disease (dialysis-dependent patients), surgical intervention (elective, emergency, and non-operative) and immunosuppression (e.g., CD4 count <200 cells/μL)), age, temperature, mean arterial pressure, pH, heart rate, respiratory rate, sodium, potassium, creatinine, acute renal failure status (increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours or increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days or urine volume <0.5 mL/kg/h for 6 hours), hematocrit, white blood cell count, Glasgow Coma Scale (GCS), and admission FiO_2 of patients [6,13]. Each variable (except age and chronic health condition) was scored from 0 to 4 based on how far it deviated from the normal range, whereas age was scored from 0 to 6, and chronic health condition was scored from 0 to 5 with a total range score from 0 to 71. The score was calculated using MDCalc (https://www.mdcalc.com/calc/1868/apache-ii-score) and assessed within 24 hours of admission to the CVCU.

The SAPS-II is a scoring system used to assess the severity of disease in ICU patients and predict mortality. This score assesses multiple variables, including age, heart rate, systolic blood pressure, temperature, GCS, PaO_2/FiO_2 ratio (profound hypoxemia (≤100 mmHg), severe hypoxemia (101–200 mmHg), moderate hypoxemia (201–300 mmHg), mild hypoxemia (300–400 mmHg) and normal (>400 mmHg)), blood urea nitrogen (BUN) or urea, urine output (first 24 hours urine output after admission to CVCU), sodium, potassium, serum bicarbonate, serum bilirubin, white blood cell count, chronic disease status (metastatic cancer, hematological malignancy, acquired immune deficiency syndrome (AIDS)), and type of admission (surgical, medical, unscheduled surgical) [6,14]. Each variable was scored on a predefined scale, with

different ranges and weights for each parameter with a range score from 0 to 163. The score was calculated using MDCalc (https://www.mdcalc.com/calc/4044/simplified-acute-physiology-score-saps-ii) and also assessed within 24 hours of admission to the CVCU.

The GRACE score is a scoring system used to estimate the risk of mortality in patients with ACS. It computes various factors, including age, Killip class (class I: no sign of heart failure, class II: mild heart failure (rales or third heart sound), class III: moderate to severe heart failure (pulmonary edema), and class IV: cardiogenic shock), systolic blood pressure, ST segment deviation (ST-elevation or ST-depression), cardiac arrest status at emergency department arrival, serum creatinine, positive cardiac biomarkers (troponin-I, troponin-T, CK-MB), and heart rate [15]. All scores were assessed within 24 hours of admission to the CVCU [15]. Each parameter was assigned a specific point value based on its severity or range, with a total range score from 1 to 372. All scores referenced were calculated based on physical examinations or laboratory results obtained within the initial 24 hours of CVCU. This score was also calculated using MDcalc website (https://www.mdcalc.com/calc/1099/grace-acs-risk-mortality-calculator).

In addition to data related to the scoring system, various other factors were collected, including sex, age, existing comorbidities, the necessity for mechanical ventilation, critical care medications administered (dobutamine, norepinephrine, dopamine), admission type (from CVCU of another hospital, emergency room, ward, Cath lab, polyclinic, COVID-19 isolation room, COVID-19 cohort room, or operation chamber), classification of ACS (STEMI, NSTEMI, or unstable angina pectoris), vital signs recorded within the first 24 hours of admission, laboratory data obtained during the same period, duration of stay in the CVCU, and overall hospital length of stay.

Statistical analysis and data calculation

A Kolmogorov-Smirnov test was employed to analyze the distribution of numerical variables. Continuous variables were reported as mean with standard deviation for the normal distributed data and as median with interquartile range (IQR) for the abnormally distributed data. Categorical variables were quantified as absolute values and percentages. Univariate analysis was conducted to evaluate factors associated with CVCU and in-hospital mortalities using the Chi-squared test, independent Student's t-test or the Mann-Whitney test as appropriate. A multiple logistic regression analysis was conducted to identify the independent risk factors for mortality by controlling the effect of potential confounding factors. Initially, all variables exhibiting significant associations in the univariate analysis ($p<0.05$) were incorporated into the preliminary model. Subsequently, a stepwise methodology was employed to enhance the model, retaining only those variables that remained statistically significant ($p<0.05$) or were deemed clinically pertinent. The main endpoints evaluated in this study were the ability of each scoring system to predict CVCU mortality (defined as patient death while receiving treatment in CVCU) and in-hospital mortality (death while receiving treatment in a hospital outside of CVCU).

The performance of the APACHE-II, SAPS-II, and GRACE scores in forecasting CVCU mortality or in-hospital mortality was evaluated in terms of their discriminative capability and calibration using the goodness-of-fit test. Effective discriminative ability is defined by the capacity to accurately differentiate between survivors and non-survivors, whereas calibration refers to the extent of alignment between the model's projected overall probability of death and the actual mortality rate [16]. The area under the curve (AUC) of the receiver operating characteristic (ROC) was used to evaluate the discriminative ability to predict CVCU mortality. The greater the AUC, the better the scoring system [17]. The AUCs of every score were further compared with the Hanley and McNeil test [18]. The association of each prognostic score with mortalities was re-analyzed with a binary logistic regression model. The calibration of the models to our data was assessed by the Hosmer-Lemeshow test. The sensitivity and specificity were measured using the Youden index to identify the optimal cutoff points, where a higher index indicates a better prediction at the cutoff point [19]. The $p<0.05$ was considered statistically significant. Statistical analysis and data calculations were conducted utilizing the Statistical Package for the Social Sciences (SPSS) version 30.0 (IBM, New York, USA).

Results

Characteristics of the patients

Out of 12,950 patients hospitalized at 10 hospital sites between August 1, 2021, and July 31, 2023, 9,040 patients were diagnosed with ACS. Finally, 6,490 patients were eligible to participate, as the remaining patients (2,550) were excluded using the listwise deletion method due to insufficient data and inability to be scored because of missing required data (**Figure 1**). The demographic characteristics of patients, based on CVCU and in-hospital mortality were summarized in **Table 1**. The most common comorbidities of patients were hypertension (n=3,809; 58.6%) followed by diabetes (n=1,941; 30%), pneumonia (n=1,152; 17.7%), chronic kidney disease (n=492; 7.6%), urinary tract infection (n=140; 2.1%), and acute heart failure (n=1,927; 29.7%). During their first admission to CVCU, 338 patients (5.2%) required intubation with mechanical ventilation, 943 patients required dobutamine (14.7%), 158 patients required dopamine (2.4%), and 533 patients required norepinephrine (8.2%) (**Table 1**). The emergency room was the most common source of patient admissions compared with others (n=4,951; 76.2%). The classification of ACS patients admitted was divided into STEMI (n=3,421; 52.7%), NSTEMI (n=2,377; 36.7%), and unstable angina pectoris (n=691; 10.6%).

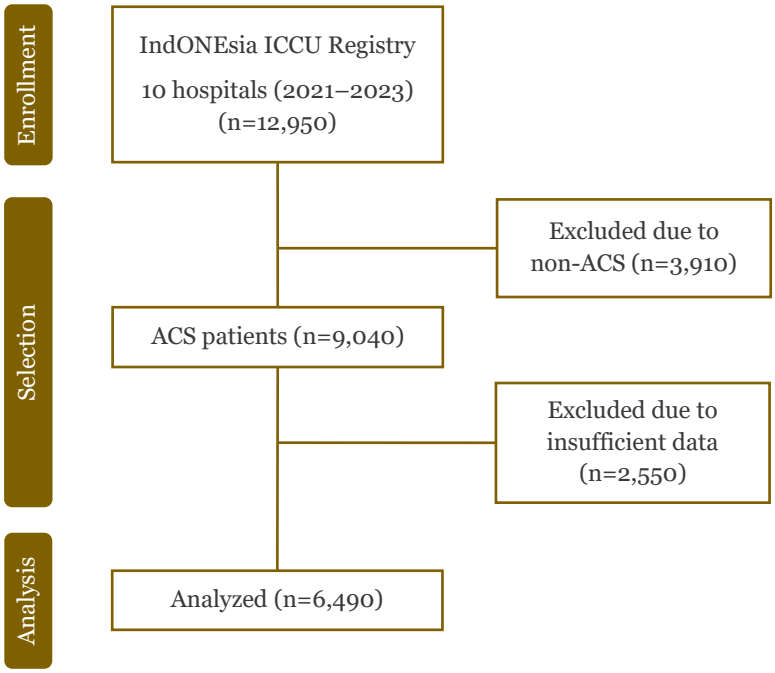

Figure 1. Study flow diagram showing the number of acute coronary syndrome (ACS) patients at each step.

Factors associated with CVCU and in-hospital mortalities

The results of statistical analyses performed to assess the disparities in comorbidities among the groups are presented in **Table 1**. The results indicated that the survivor group had a lower median age than the non-survivor group, in both CVCU mortality and in-hospital mortality assessments. In addition, there was a slightly higher number of males in the survivor group compared to the non-survivor group in the evaluation of CVCU mortality and in-hospital mortality. There was a higher number of patients with diabetes mellitus, chronic kidney disease, pneumonia, urinary tract infections, and acute heart failure in the non-survivor group, both in the analysis of CVCU and in-hospital mortalities. Critical care medication needs (dobutamine, norepinephrine, dopamine) were consistently higher in the non-survivor group in both analyses of CVCU and in-hospital mortalities. In the evaluation of laboratory findings, the non-survivor group consistently had higher creatinine levels but lower thrombocyte counts and pH in both analyses of CVCU and in-hospital mortalities (**Table 1**).

Table 1. Patients' characteristics and factors associated with cardiovascular care unit (CVCU) and in-hospital mortality among acute coronary syndrome (ACS) patients

Variable	CVCU mortality[a]			In-hospital mortality		
	Survivor (n=5,791)	Non-survivor (n=689)	*p*-value	Survivor (n=5,661)	Non-survivor (n=829)	*p*-value
	n (%)	n (%)		n (%)	n (%)	
Male	4,522 (78)	504 (73)	0.003*[b]	4,420 (78)	614 (74)	0.010*[b]
Age (year), median ± interquartile (IQR)	60±18	69±13	0.001*[c]	59±17	70±12	<0.001*[c]
Comorbidities						
Hypertension	3,438 (59)	366 (53)	0.002*[b]	3,353 (59)	456 (55)	0.021*[b]
Diabetes	1,714 (30)	224 (33)	0.115[c]	1,645 (29)	296 (36)	<0.001*[b]
Chronic kidney disease	415 (7)	76 (11)	<0.001*[b]	397 (7)	95 (11)	<0.001*[b]
Pneumonia	932 (16)	220 (32)	<0.001*[b]	880 (16)	272 (33)	<0.001*[b]
Urinary tract infection	114 (2)	26 (4)	0.002*[b]	108 (2)	32 (4)	<0.001*[b]
Acute heart failure	1,503 (26)	420 (61)	<0.001*[b]	1,405 (25)	522 (63)	<0.001*[b]
Mechanical ventilation	129 (2)	208 (30)	<0.001*[b]	79 (1)	259 (31)	<0.001*[b]
Critical care medications						
Dobutamine	603 (10)	340 (49)	<0.001*[b]	521 (9)	422 (51)	<0.001*[b]
Norepinephrine	296 (5)	237 (34)	<0.001*[b]	232 (4)	301 (36)	<0.001*[b]
Dopamine	129 (2)	29 (4)	0.001*[b]	125 (2)	33 (4)	0.002*[b]
Admission						
CVCU	15 (0)	5 (1)	<0.001*[b]	14 (0)	6 (1)	<0.001*[b]
Emergency room	4,399 (76)	544 (79)		4,297 (76)	654 (79)	
Ward	184 (3)	40 (6)		175 (3)	49 (6)	
Cath lab	977 (17)	75 (11)		968 (17)	86 (10)	
Polyclinic	57 (1)	5 (1)		54 (1)	8 (1)	
Isolation room COVID-19	59 (1)	10 (1)		54 (1)	15 (1)	
Cohort room COVID-19	94 (2)	10 (1)		93 (2)	11 (1)	
Operation chamber	6 (0)	0 (0)		6 (0)	0 (0)	
Classification of ACS						
ST-elevation myocardial infarction (STEMI)	3,006 (52)	408 (59)	<0.001*[b]	2,957 (52)	464 (56)	<0.001*[b]
Non-ST-elevation myocardial infarction (NSTEMI)	2,127 (37)	248 (36)		2,046 (36)	331 (40)	
Unstable angina pectoris	657 (11)	33 (5)		657 (12)	34 (4)	
Laboratory data on CVCU admission						
Creatinine (mg/dL), median±IQR	1.22±0.81	2.65±2. 3	<0.001*[c]	1.16±0.81	2.16±1.62	<0.001*[c]
Leukocyte (10^3/µL), median±IQR	11.4±5.27	17.74±12.16	<0.001*[c]	11.4±5.5	13.39±7.62	<0.001*[c]
Thrombocyte (10^3/µL), median±IQR	243±115	210±120	0.017*[c]	246±115	221±119	0.001*[c]
pH, median±IQR	7.41±07	7.32±0.11	<0.001*[c]	7.41±0.7	7.38±0.12	<0.001*[c]
Length of CVCU stay (days), median±IQR	2±3	2±15	0.815[c]	2±3	3±15	0.003*[c]
Length of hospital stay (days), median±IQR	6±7	4±17	<0.001*[c]	5±6	7±15	<0.001*[c]
APACHE-II scores, median±IQR	12±7	26±10	<0.001*[c]	12±7	21±15	<0.001*[c]
SAPS-II scores, median±IQR	50±8	61±14	<0.001*[c]	50±7	51±16	<0.001*[c]
GRACE scores, median±IQR	120±62	175±35	<0.001*[c]	116±63	164±62	<0.001*[c]

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
[a]Excluding missing data from 10 patients
[b]Analyzed using Chi-squared test comparing survivors with non-survivors
[c]Analyzed using Mann-Whitney U test comparing survivors with non-survivors
*Statistically significant at $p<0.05$

The APACHE-II, SAPS-II, and GRACE scores of patients in the survivor group were consistently lower than those in the mortality group, both for CVCU mortality (12±7 vs 26±10, p<0.001; 50±8 vs 61±14, p<0.001; 120±62 vs 175±35, p<0.001, respectively) and for in-hospital mortality (12±7 vs 21±15, p<0.001; 50±7 vs 51±16, p<0.001; 116±63 vs 164±62, p<0.001, respectively) (**Table 1**).

A multiple logistic regression analysis was performed to identify factors influencing CVCU mortality by including the variables significant in univariate analysis. Initial multiple logistic regression findings showed that acute cardiac failure, mechanical ventilator usage, dobutamine administration, length of in-hospital stay, APACHE-II score, and GRACE score were statistically significant while SAPS-II score was not (**Table 2**). Subsequently, a second regression analysis was conducted through stepwise selection by only retaining factors found to be statistically significant (p<0.05) or deemed clinically relevant (SAPS-II). The final analysis showed that, for evaluation of CVCU mortality, usage of mechanical ventilator was the strongest significant independent factor (OR: 3.045; 95%CI: 2.168–4.277; p<0.001), followed by the usage of dobutamine (OR: 2.822; 95%CI: 2.255–3.531; p<0.001), acute heart failure (OR: 1.618; 95%CI: 1.313–1.995; p<0.001), APACHE-II score (OR: 1.100; 95%CI: 1.077–1.123; p<0.001), GRACE score (OR: 1.007; 95%CI: 1.004–1.010; p<0.001), and length of in-hospital stay (OR: 0.895; 95%CI: 0.873–0.917; p<0.001). It was found that SAPS-II score was not statistically significant (OR: 0.995; 95%CI: 0.984–1.006; p=0.353) (**Table 3**).

Table 2. Initial model of multivariate logistic regression analysis showing factors associated with cardiovascular care unit (CVCU) mortality among acute coronary syndrome (ACS) patients

Variables	Adjusted odds ratio	95% confidence interval	p-value
Male	0.859	0.665–1.109	0.244
Age	0.996	0.983–1.008	0.494
Hypertension	0.884	0.702–1.112	0.239
Chronic kidney disease	1.196	0.783–1.828	0.407
Pneumonia	1.278	0.989–1.650	0.060
Urinary tract infection	1.062	0.575–1.963	0.847
Acute heart failure	1.467	1.144–1.880	0.003*
Mechanical ventilator use	2.828	1.947–4.107	<0.001*
Dobutamine use	2.306	1.726–3.079	<0.001*
Norepinephrine use	1.139	0.824–1.574	0.431
Dopamine use	0.804	0.465–1.392	0.436
Source of admission			0.263
Classification of ACS			0.327
Creatinine	1.004	0.938–1.075	0.909
Leukocyte	1.013	0.992–1.034	0.219
pH	1.471	0.773–2.799	0.239
Thrombocyte	1.000	0.998–1.001	0.467
In-hospital length of stay	0.896	0.872–0.920	<0.001*
APACHE-II score	1.060	1.031–1.090	<0.001*
SAPS-II score	1.012	0.998–1.026	0.101
GRACE score	1.004	1.001–1.008	0.016*

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
*Statistically significant at p<0.05

Table 3. Final model of multivariate logistic regression analysis showing factors associated with cardiovascular care unit (CVCU) mortality among acute coronary syndrome (ACS) patients

Variables	Adjusted odds ratio	95% confidence interval	p-value
Mechanical ventilator use	3.045	2.168–4.277	<0.001*
Dobutamine use	2.822	2.255–3.531	<0.001*
Acute heart failure	1.618	1.313–1.995	<0.001*
In-hospital length of stay	0.895	0.873–0.917	<0.001*
APACHE-II score	1.100	1.077–1.123	<0.001*
SAPS-II score	0.995	0.984–1.006	0.353
GRACE score	1.007	1.004–1.010	<0.001*

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
*Statistically significant at p<0.05

A separate analysis was conducted to evaluate in-hospital mortality. Initial multiple logistic regression findings showed that acute heart failure, mechanical ventilator usage, dobutamine administration, norepinephrine administration, leukocyte, thrombocyte, length of CVCU stay, length of in-hospital stay, APACHE-II score, SAPS-II score, and GRACE score were statistically significant (**Table 4**). Subsequently, a second regression analysis was conducted through stepwise selection by only retaining factors found to be statistically significant ($p<0.05$) or were deemed clinically relevant. Final analysis of evaluation for in-hospital mortality showed that use of a mechanical ventilator was the strongest significant independent factor (OR: 2.980; 95%CI: 2.092–4.244; $p<0.001$), followed by the administration of dobutamine (OR: 2.407; 95%CI: 1.887–3.070; $p<0.001$), administration of norepinephrine (OR: 1.623; 95%CI: 1.213–2.170; $p=0.001$), acute heart failure (OR: 1.525; 95%CI: 1.245–1.868; $p<0.001$), APACHE-II score (OR: 1.120; 95%CI: 1.096–1.144; $p<0.001$), CVCU length of stay (OR: 1.071; 95%CI: 1.035–1.108; $p<0.001$), leukocyte (OR: 1.020; 95%CI: 1.006–1.033; $p=0.004$), SAPS-II score (OR: 1.011; 95%CI: 1.000–1.022; $p=0.046$), GRACE score (OR: 1.008; 95%CI: 1.005–1.011; $p<0.001$), thrombocyte (OR: 0.999; 95%CI: 0.998–1.000; $p=0.018$), and in-hospital length of stay (OR: 0.966; 95%CI: 0.943–0.989; $p=0.004$) (**Table 5**).

Table 4. Initial model of multivariate logistic regression analysis showing factors associated with in-hospital mortality among acute coronary syndrome (ACS) patients

Variables	Adjusted odds ratio	95% confidence interval	*p*-value
Male	0.982	0.755–1.278	0.894
Age	0.996	0.983–1.009	0.536
Hypertension	0.999	0.790–1.265	0.995
Diabetes mellitus	1.159	0.913–1.470	0.225
Chronic kidney disease	0.826	0.545–1.251	0.367
Pneumonia	1.202	0.929–1.554	0.162
Urinary tract infection	0.738	0.395–1.379	0.341
Acute heart failure	1.459	1.139–1.868	0.003*
Mechanical ventilator use	2.596	1.767–3.814	<0.001*
Dobutamine use	2.394	1.795–3.191	<0.001*
Norepinephrine use	1.499	1.084–2.074	0.014*
Dopamine use	0.579	0.325–1.021	0.059
Source of admission			0.286
Classification of ACS			0.259
Creatinine	1.005	0.938–1.076	0.890
Leukocyte	1.020	1.000–1.041	0.046*
pH	1.560	0.835–2.913	0.163
Thrombocyte	0.998	0.997–1.000	0.008*
CVCU length of stay	1.084	1.042–1.128	<0.001*
In-hospital length of stay	0.935	0.907–0.965	<0.001*
APACHE-II score	1.107	1.076–1.139	<0.001*
SAPS-II score	1.023	1.008–1.038	0.003*
GRACE score	1.006	1.003–1.010	<0.001*

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; CVCU: cardiovascular care unit; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
*Statistically significant at $p<0.05$

Performance of APACHE-II and SAPS-II scores compared with GRACE scores in predicting the mortality of ACS patients

The binary logistic regression analysis revealed that the APACHE-II score had an OR: 1.198 (95%CI: 1.181–1.214), the GRACE score had an OR: 1.022 (95%CI: 1.019–1.024), and the SAPS-II score had an OR: 1.070 (95%CI: 1.061–1.079) for CVCU mortality in ACS patients (**Table 6**). In the analysis of in-hospital mortality, the APACHE-II system had an OR: 1.259 (95%CI: 1.240–1.279), while the GRACE and SAPS-II scores showed ORs: 1.027 (95%CI: 1.025–1.029) and 1.087 (95%CI: 1.078–1.096), respectively (**Table 6**).

The results of ROC analysis assessing the performance of the scoring systems in predicting CVCU mortality and in-hospital mortality are presented in **Table 6**. The three scoring systems had substantial discriminative capability in predicting both CVCU and in-hospital mortalities, with the APACHE-II demonstrating the highest predictive accuracy (AUC: 0.771; sensitivity: 63.9%; specificity: 78.7%, and AUC: 0.815; sensitivity: 68.7%; specificity: 80.4%, respectively). This was followed by the GRACE score with AUC: 0.726 (sensitivity: 61.7%; specificity: 73.2%)

and AUC: 0.769 (sensitivity: 64.7%; specificity: 77.5%) for predicting CVCU and in-hospital mortalities, respectively. The SAPS-II score had AUC: 0.655 (sensitivity: 38.9%; specificity: 85.2%) and AUC: 0.683 (sensitivity: 41.7%; specificity: 86.2%) for predicting CVCU and in-hospital mortalities, respectively (**Figure 2**).

Table 5. Final model of multivariate logistic regression evaluating factors associated with in-hospital mortality among acute coronary syndrome (ACS) patients

Variables	Adjusted odds ratio	95% confidence interval	*p*-value
Mechanical ventilator	2.980	2.092–4.244	<0.001*
Dobutamine	2.407	1.887–3.070	<0.001*
Norepinephrine	1.623	1.213–2.170	0.001*
Acute heart failure	1.525	1.245–1.868	<0.001*
Leukocyte	1.020	1.006–1.033	0.004*
Thrombocyte	0.999	0.998–1.000	0.018*
CVCU length of stay	1.071	1.035–1.108	<0.001*
In-hospital length of stay	0.966	0.943–0.989	0.004*
APACHE-II score	1.120	1.096–1.144	<0.001*
SAPS-II score	1.011	1.000–1.022	0.046*
GRACE score	1.008	1.005–1.011	<0.001*

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; CVCU: cardiovascular care unit; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
*Statistically significant at $p<0.05$

The Hosmer-Lemeshow test indicated significant values for the GRACE and SAPS-II scores but not for the APACHE-II score, suggesting that APACHE-II demonstrated good calibration, in contrast to GRACE and SAPS-II (**Table 6**). The Hanley and McNeil test indicated substantial differences in the AUC comparisons between APACHE-II and GRACE, as well as between SAPS-II and GRACE (**Table 6**).

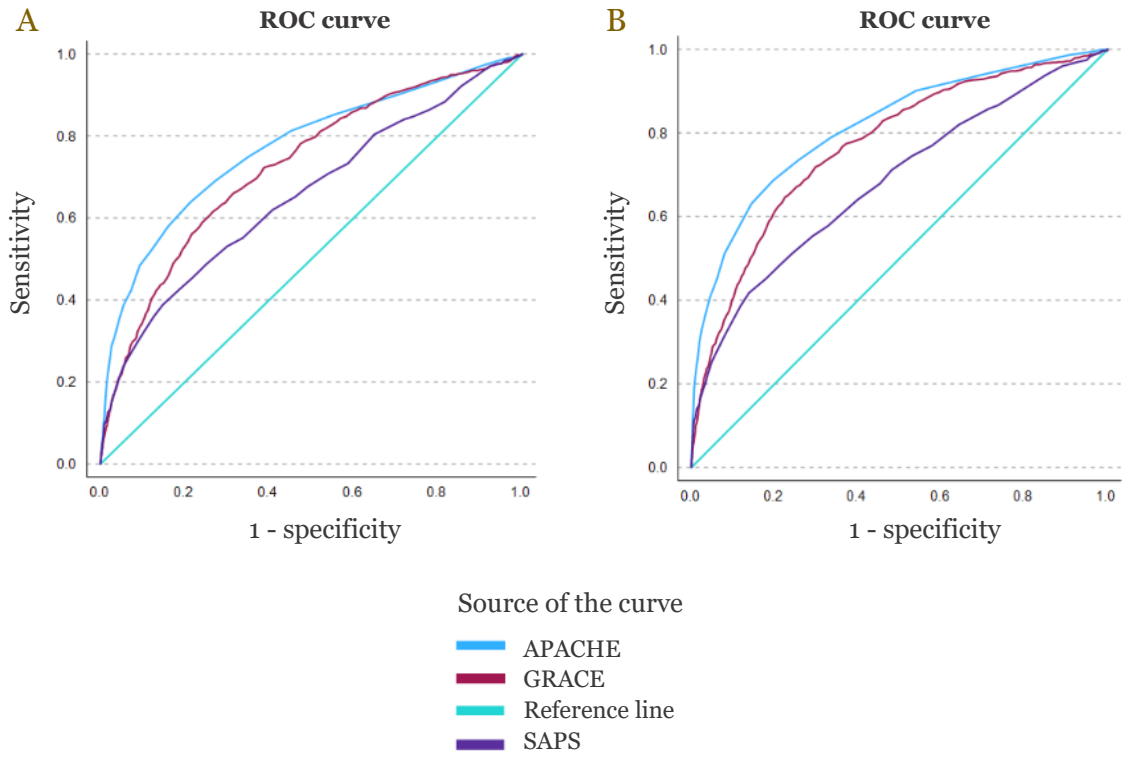

Figure 2. Receiver operating characteristic (ROC) curves of each scoring system to evaluate cardiovascular care unit (CVCU) mortality (A) and in-hospital mortality (B) among acute coronary syndrome (ACS) patients.

Table 6. Performance of APACHE-II, SAPS-II, and GRACE scoring system to predict cardiovascular care unit (CVCU) and in-hospital mortality among acute coronary syndrome (ACS) patients

Analysis type	CVCU mortality			In-hospital mortality		
	APACHE-II	GRACE	SAPS-II	APACHE-II	GRACE	SAPS-II
Logistic regression						
Odds ratio	1.198	1.022	1.070	1.259	1.027	1.087
95% confidence interval	1.181–1.214	1.019–1.024	1.061–1.079	1.240–1.279	1.025–1.029	1.078–1.096
Hosmer-Lemeshow test						
χ^2	9.951	18.429	38.220	15.468	25.180	33.417
Degrees of freedom	8	8	8	8	8	8
p-value	0.269	0.018*	<0.001*	0.051	0.001*	<0.001*
ROC curve analysis						
Area under the curve	0.771	0.726	0.655	0.815	0.769	0.683
95% confidence interval	0.751–0.792	0.705–0.747	0.631–0.678	0.798–0.832	0.752–0.787	0.662–0.704
Youden Index	0.426	0.241	0.349	0.491	0.279	0.422
Best cutoff	13.5	135.5	55.5	13.5	135.5	55.5
Sensitivity (%)	63.9	61.7	38.9	68.7	64.6	41.8
Specificity (%)	78.7	73.2	85.2	80.4	77.5	86.2
Hanley-McNeil test						
p-value	0.003*	<0.001*		0.0003*	<0.001*	

APACHE-II: Acute Physiologic Score and Chronic Health Evaluation II; GRACE: Global Registry of Acute Coronary Events; SAPS-II: Simplified Acute Physiology Score II
*Statistically significant at $p<0.05$

Discussion

ACS continues to be a worldwide concern and is a major contributor to admissions at CVCU. Considering the varied clinical situations of patients, judicious decision-making regarding the admission and management of appropriate patients to the critical care unit is essential to mitigate mortality and morbidity rates among high-risk individuals. Therefore, prognostic scoring systems are essential for objectively performing this purpose in the current context. This study indicated that the discriminative capacity of the APACHE-II score, as measured by the AUC, was notably good, with an AUC of 0.771, sensitivity of 63.9%, and specificity of 78.7%, utilizing a cutoff score of 13.5 for assessing CVCU mortality. Logistic regression indicates that the use of APACHE-II scores has an odds ratio of 1.198 in forecasting CVCU mortality. The investigation of the discriminative capacity of APACHE-II is significant in assessing in-hospital mortality, with an AUC of 0.815, sensitivity of 68.7% and specificity of 80.4% at a cutoff score of 13.5. Logistic regressions indicate that the use of APACHE-II scores has an odds ratio of 1.259 in forecasting in-hospital mortality. Our findings suggest that, in terms of discrimination capability, the APACHE-II, SAPS-II, and GRACE scores are appropriate for predicting CVCU mortality and in-hospital mortality, with the APACHE-II score exhibiting the highest predictive ability, sensitivity, specificity, and OR relative to the other assessed scoring systems.

Our findings align with previous studies indicating the predictive capacity of the APACHE-II and SAPS-II scores in patients admitted to the ICU [16,20,21]. In the context of CVCU, including ACS patients, the results were consistent, demonstrating that both scores exhibit robust predictive power for in-hospital mortality in either ICU or CVCU patients [6]. The study by Kahraman *et al*. shows good ability of APACHE-II and SAPS-II to predict in-hospital mortality of ACS patients admitted to CVCU with good calibration with a cutoff point of 16.5. It yields 75.9% sensitivity and 87.4% specificity [6]. Sarmiento *et al*. and Moreau *et al*. examined the efficacy of SAPS-II and APACHE-II in small sample sizes of ACS patients, with both studies demonstrating the favorable performance of these prognostic indices [22,23].

In typical ICU settings, APACHE-II and SAPS-II are two widely utilized models, originally developed to evaluate illness severity and predict death in patients undergoing medical treatment [16,24,25]. Nonetheless, limitations pertain to the application of this scoring method within the CVCU environment, necessitating validation across many nations, particularly for ACS patients admitted to CVCU in comparison with the GRACE score. This study illustrates that APACHE-II and SAPS-II exhibit comparable effectiveness in predicting mortality when used in conjunction with the GRACE score, owing to a significant and varied participant cohort from a multicenter study across 10 hospitals in Indonesia. APACHE-II demonstrated the highest predictive accuracy and calibration, establishing it as the most robust tool for risk stratification. To optimize its clinical utility, healthcare systems could integrate the APACHE-II scoring system into electronic or non-electronic health record platforms, enabling automated risk assessment and facilitating objective decision-making regarding ICU admissions.

This study had some key strengths, particularly the utilization of data from a large multicenter registry, which enhanced statistical power and facilitated a thorough investigation of various clinical and laboratory parameters, including the implementation of a scoring system for patients diagnosed with ACS admitted to CVCU. However, our present investigation also had limitations that may affect the validity of the findings. The calibration of SAPS-II and GRACE scores was inadequate, potentially affecting the results of our study, as evidenced by significant HL test results. This means that the model of SAPS-II and GRACE may overestimate or underestimate the risk of CVCU or in-hospital mortalities. Potential factors contributing to the insufficient calibration of the data could be: (1) potential inconsistencies in the interpretation of the defined parameters and data collection, notwithstanding the presence of recognized operational definition and trained research personnel; or (2) fluctuations in the timing of diagnoses (lead-time bias).

The principal error in the scoring method may result from the inconsistency in identifying the data employed between the maximum and minimum values [26]. Lead-time bias may significantly impact the results, as patients evaluated and admitted to the CVCU early may exhibit different outcomes compared to those who were not. Addressing these limitations necessitates recalibration of the models. The absence of external validation further constrains the

generalizability of these findings. Training healthcare personnel in the application and interpretation of APACHE-II and SAPS-II scores, and also the presence of external validation future studies could improve its calibration. Moreover, various patients' characteristics deviated from the original GRACE score cohort, such as the percentage of patients with ST-elevation (52.7% in our study versus 35.3% in the original GRACE cohort), which may clarify the reduced effectiveness of the comprehensive risk stratification score in practical applications [15]. The study's retrospective design also introduces potential selection bias, as listwise exclusion of patients with incomplete data may lead to the exclusion of a non-random subset of patients, thereby skewing the results. Moreover, despite the use of standardized operational definitions, the presence of data heterogeneity across the 10 participating hospitals may have contributed to variability in scoring performance. This highlights the need for further study to enhance the sensitivity and specificity of mortality prediction algorithms through improved data.

Conclusion

This study indicated that APACHE-II, SAPS-II, and GRACE moderately predicted CVCU and in-hospital mortalities, with APACHE-II exhibiting the highest predictive capability. However, SAPS-II and GRACE exhibit inadequate calibration, potentially impacting the projected overall chance of death in relation to the actual mortality rate in the real-world context. Future direction should focus on improving these scoring tools to maintain their clinical relevance.

Ethics approval

This study was conducted in accordance with the ethical standards of the institutional and national research committees, as well as the 1964 Helsinki Declaration and its subsequent amendments. Ethical approval was obtained from the Ethics Committee of the National Cardiovascular Center Harapan Kita, Jakarta (ethic registration number: 240227018). The scientific and ethics committee of each hospital approved the study.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study used artificial intelligence (AI) during the process of manuscript writing support. An AI-based language model (QuillBot) was employed for language refinement. We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

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References

1. Bergmark BA, Mathenge N, Merlini PA, *et al.* Acute coronary syndromes. The Lancet 2022;399(10332):1347-1358.
2. Omer MA, Tyler JM, Henry TD, *et al.* Clinical characteristics and outcomes of STEMI patients with cardiogenic shock and cardiac arrest. JACC Cardiovasc Interv 2020;13(10):1211-1219.
3. Poldervaart JM, Langedijk M, Backus BE, *et al.* Comparison of the GRACE, HEART and TIMI score to predict major adverse cardiac events in chest pain patients at the emergency department. Int J Cardiol 2017;227:656-661.
4. Silva-Obregon A, Arroyo Espliguero R, Viana-Llamas MC, *et al.* Comparison of APACHE II, SAPS II and GRACE 2.0 risk scores to estimate early and late mortality in patients with ST-segment elevation acute myocardial infarction. Eur Heart J 2019;40 Suppl 1:ehz745.0277.
5. Cakar MA, Sahinkus S, Aydin E, *et al.* Relation between the GRACE score and severity of atherosclerosis in acute coronary syndrome. J Cardiol 2014;63(1):24-28.
6. Kahraman F, Yılmaz AS, Ersoy İ, *et al.* Predictive outcomes of APACHE II and expanded SAPS II mortality scoring systems in coronary care unit. Int J Cardiol 2023;371:427-431.
7. Joe BH, Jo U, Kim HS, *et al.* APACHE II score, rather than cardiac function, may predict poor prognosis in patients with stress-induced cardiomyopathy. J Korean Med Sci 2012;27(1):52.
8. Donnino MW, Salciccioli JD, Dejam A, *et al.* APACHE II scoring to predict outcome in post-cardiac arrest. Resuscitation 2013;84(5):651-656.
9. Tsaousi GG, Pitsis AA, Ioannidis GD, *et al.* Implementation of EuroSCORE II as an adjunct to APACHE II model and SOFA score, for refining the prognostic accuracy in cardiac surgical patients. J Cardiovasc Surg 2015;56(6):919-927.
10. Altman DG, Vergouwe Y, Royston P, Moons KGM. Prognosis and prognostic research: Validating a prognostic model. BMJ 2009;338(7708):b605.
11. Juzar DA, Bagaswoto HP, Muzakkir AF, *et al.* The IndONEsia ICCU registry. IJC 2024;44(4):152-157.
12. Collet JP, Thiele H, Barbato E, *et al.* 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2021;42(14):1289-1367.
13. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120(4):c179-c184.
14. Le Gall JR. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993;270(24):2957.
15. Granger CB. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med 2003;163(19):2345.
16. Khwannimit B, Geater A. A comparison of APACHE II and SAPS II scoring systems in predicting hospital mortality in Thai adult intensive care units. J Med Assoc Thai 2007;90(4):643-652.
17. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143(1):29-36.
18. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1983;148(3):839-843.
19. Youden WJ. Index for rating diagnostic tests. Cancer 1950;3(1):32-35.
20. Kostoglou A, Kotanidou A, Marvaki C, *et al.* Mortality rate of ICU patients according to APACHE II and SAPS II score. Health Res J 2018;4(4):219.
21. Godinjak A, Iglica A, Rama A, *et al.* Predictive value of SAPS II and APACHE II scoring systems for patient outcome in a medical intensive care unit. Acta Med Acad 2016;45(2):97-103.
22. Sarmiento X, Rué M, Guardiola JJ, *et al.* Assessment of the prognosis of coronary patients. Chest 1997;111(6):1666-1671.
23. Moreau R, Soupison T, Vauquelin P, *et al.* Comparison of two simplified severity scores (SAPS and APACHE II) for patients with acute myocardial infarction. Crit Care Med 1989;17(5):409-413.
24. Knaus WA, Draper EA, Wagner DP, *et al.* APACHE II: A severity of disease classification system. Crit Care Med 1985;13(10):818-829.
25. Le Gall JR, Loirat P, Alperovitch A, *et al.* A simplified acute physiology score for ICU patients. Crit Care Med 1984;12(11):975-977.
26. Holt AW, Bury LK, Bersten AD, *et al.* Prospective evaluation of residents and nurses as severity score data collectors. Crit Care Med 1992;20(12):1688-1691.