Research Brief

First 24-h Sardjito Cardiovascular Intensive Care (SCIENCE) admission risk score to predict mortality in cardiovascular intensive care unit (CICU)

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ARTICLE INFO

ABSTRACT

Background and objectives: The application of prognostic scoring systems to identify risk of death within 24 h of CICU admission has significant consequences for clinical decision-making. Previous score of parameters collected after 24 h was considered too late to predict mortality. As a result, we attempted to develop a CICU admission risk score to predict hospital mortality using indicators collected within 24 h.
Methods: Data were obtained from SCIENCE registry from January 1, 2021 to December 21, 2021. Outcomes of 657 patients (mean age 58.91 ± 12.8 years) were recorded retrospectively. Demography, risk factors, comorbidities, vital signs, laboratory and echocardiography data at 24-h of patient admitted to CICU were analysed by multivariate logistic regression to create two models of scoring system (probability and cut-off model) to predict in-hospital mortality of any cause.
Results: From a total of 657 patients, the hospital mortality was 15%. The significant predictors of mortality were male, acute heart failure, hemodynamic instability, pneumonia, baseline creatinine ≥1.5 mg/dL, TAPSE <17 mm, and the use of mechanical ventilator within first 24-h of CICU admission. Based on Receiver Operating Characteristic (ROC) curve analysis a cut off of ≥3 is considered to be a high risk of in-hospital mortality (sensitivity 75% and specificity 65%).
Conclusion: The initial 24-h SCIENCE admission risk rating system can be used to predict in-hospital mortality in patients admitted to the CICU with a high degree of sensitivity and specificity,

1. Introduction

Cardiovascular disease (CVD) is a major cause of death worldwide. Cardiovascular intensive care unit (CICU), an intensive care unit for severe CVD patients, have developed in many hospitals to prevent death from cardiovascular disease.[1] Contemporary CICU patients frequently have primary cardiovascular problems in addition to multiple non-cardiovascular comorbidities or complications, diminishing the utility of standard diagnosis-specific risk scores derived from non-critically ill populations.[2] The development and validation of risk prediction models for common CICU conditions has been identified as a priority area of CICU research in the contemporary era.[3]

The application of prognostic scoring systems to identify patients at risk of death within 24 h of CICU admission has significant implications for triage and clinical decision-making. Risk stratification of patients with acute coronary syndrome aids in outcome prediction, therapeutic decision-making, and quality assurance in the modern cardiac care unit.[4]

Currently established intensive care unit (ICU) risk scores such as the Acute Physiology and Chronic Health Evaluation (APACHE) and Sequential Organ Failure Assessment (SOFA) are used to stratify

mortality risk, adjust for illness severity, and ensure an adequate balance of randomized groups in critically ill populations.[5,6] There have been no published studies examining the extent to which admission diagnoses affect risk score performance in CICU patients or the utility of these ICU risk scores in CICU patients with common cardiac diagnoses such as acute coronary syndrome (ACS) or heart failure (HF). Jentzer et al (2019) previously established a score for predicting patient mortality in the CICU, called the Mayo CICU Admission Risk Score (M-CARS) that has large sample size with high sensitivity and specificity. This score is composed of seven predictor factors for mortality during hospitalization that include cardiac arrest, shock, respiratory failure, the Braden skin score, blood urea nitrogen levels, anion gap values, and red blood cell distribution width value. The study's limitation is that it is a single-center study, which may limit the score's generalizability to other patient populations in the ICCU. Additionally, because this study did not include patients receiving ECMO or mechanical circulatory support, a group of patients who are quite common in the CICU, this score cannot be applied to this patient population.[7]

Prognostic scoring systems to identify risk of death within 24 h of CICU admission is needed because it has significant consequences for triage and clinical decision-making. Thus, the purpose of this study is to analyze the parameters present during the first 24 h of CICU admission which can be used as a predictors of mortality and to develop a scoring system to predict the mortality rate more early in the CICU of Sardjito General Hospital. This study can also be used as a preliminary study for further research.

2. Methods

This is a cross-sectional study with the objective of identifying factors that can be used to predict patient mortality within 24 h of CICU admission and developing a scoring system for predicting CICU mortality. We used an existing database of all adult patients (age above 18 years) who admitted to the CICU at Sardjito General Hospital between January 1, 2021 and December 21, 2021. During this time period, only data from the first 24 h of CICU admission were included. Based on the results of a previous study,[8] the study will need to recruit minimum of 125 subjects with a type I error of 0.05 and with at least 80% power of this study.

The SCIENCE Registry was used to obtain demographic, vital sign, laboratory, and other clinical and outcome data. All vital signs, clinical measurements, diagnosis, and laboratory values were used at their admission values, which were defined as either the first value recorded following CICU admission. In our study, hemodynamic instability is defined as the requirement for pharmacological and/or mechanical support to maintain a mean arterial pressure 65 mmHg in the presence of end-organ hypoperfusion.

In this study, the independent variables are all variables that can be used to predict mortality, while the dependent variable is any cause of death. The mortality data are restricted to those who died while receiving care in the CICU.

The association between predictive factors and mortality was examined using a bivariate analysis. The correlation was analyzed using the Chi-square test, with Fisher's test as an alternative. Additionally, a multivariate analysis was conducted using variables from the bivariate analysis with a *p* value of 0.25. Then, a logistic regression with a stepwise backward method was used. Multivariate analysis was then used to incorporate the B and SE scores from SPSS into the scoring system. This analysis yielded two scoring systems: 1) Probability; and 2) Cut-off scoring system based on the receiver operating characteristic (ROC) curve. SPSS ver. 23 was used to conduct all data analysis.

This study was approved by the Medical and Health Research Ethics Committee (MHREC) of Faculty of Medicine, Public Health

and Nursing, Universitas Gadjah Mada/Sardjito General Hospital Yogyakarta and the requirement for informed consent was waived by the Ethics Committee.

3. Results

This study enrolled 657 participants. The average age of the population is 60 years, and the majority of patients are male (69.1%). The most frequently encountered diagnosis is acute coronary syndrome (65.1%) (Table 1). The mortality rate is 15% in 102 patients regardless of the cause of death. Bivariate analysis revealed significant differences between several predictors associated with mortality events. Male gender, acute heart failure, hemodynamic instability, pneumonia, baseline creatinine >1.5 mg/dL, TAPSE 17, and mechanical ventilation are the seven predictors (Table 3).

Backward stepwise analysis revealed several variables that could be used as significant predictors of mortality within 24 h of CICU admission, including male gender (OR: 2.49), acute heart failure (OR: 2.87), hemodynamic instability (3.6), pneumonia (OR: 2.54), baseline creatinine >1.5 mg/dL (OR: 2.27), TAPSE 17 (OR: 2.06), and the use of mechanical ventilator (OR: 5.54) (Table 2).

Each independent predictor was evaluated in order to develop a calculation for the CICU scoring system. A multiple logistic regression analysis was used to develop a scoring system based on the probability of experiencing a mortality event. The probability of mortality scoring system used in this study (scores 1 to 8) revealed that a higher score is significantly associated with a greater likelihood of death (e.g. the mortality probability of patient with score 1 is 6.5%; while patient with score 7 is 64.3%). Another scoring system model used in this study is one that is based on the cut-off point from the ROC curve analysis depicted in the graphic with AUC value 0.75 for hospital mortality (Fig. 1).

A cut-off point of 3 was chosen based on the cut-off analysis. Thus, a score between 3 and 8 indicates a greater likelihood of death than a score between 1 and 8 (Table 4). This scoring system has a sensitivity of 75% and a specificity of 65% for predicting a mortality event (Fig. 2 and Table 5).

4. Discussion

This study involved 657 participants between January 1st and December 21st 2021 at Sardjito General Hospital's CICU. Acute coronary syndrome was identified as the most frequent diagnosis for CICU admission (69.9%), with STE-ACS accounting for the majority of cases (67.7%). Other diagnoses for Sardjito CICU admission include shock or hemodynamic instability (16%), arrhythmia (8.7%), and acute heart failure (4.6%). This study also correlates with a previous study by Bohula et al, 2019, which found that the two most common primary reasons for cardiac CICU admission were acute coronary syndrome (ACS) (969 [31.8%]) and heart failure (567 [18.6%]). Only 448 (46.3%) of ACS admissions were for ST-segment elevation MI.[9]

During this study, 102 patients (15.5%) died, the majority from cardiogenic shock. Patient mortality rates varied significantly between previous studies (12.7%, 5.6%, and 13%.[10,11] Additionally, the leading causes of death are diverse, including cardiogenic shock, sepsis, and respiratory failure.[10]

Male gender is associated with a greater risk of death (OR 2.67). Estrogen has been shown to protect against cardiac ischemia in this case. According to De Kleijn et al (2002), women who have been exposed to estrogen for more than 18 years have a lower mortality rate, HR 0.8. (0.67–0.97).[12] While our study found that male gender is a predictor of CICU mortality, several other studies found the opposite. According to Herscovici et al (2020), there was no significant difference in CICU mortality by gender.[13] Other studies

Table 1
Baseline characteristic of the research subject (mortality versus No-mortality).

Parameter	N = 657	Mortality (Yes) N = 102	Mortality(No) N = 555	p value
Age, year +SD	58.91 ± 12.8	60.82 ± 15	55.85 ± 12	0.086
Age >60 years, n(%)	335 (51%)	60 (58.8)	275 (49.5)	
Age <60 years, n(%)	322 (49%)	42 (41.2)	280 (50.4)	
Gender				0.001*
Male	454 (69.1%)	56 (54.9)	398 (71.7)	
Female	203 (30.9%)	46 (45.1)	203 (36.5)	
Diagnosis				
Arrhythmia	28 (8.6%)	10 (16.6)	18 (3.2)	0.004[a]
ACS[a]	432 (65.1%)	55 (53.9)	377 (67.9)	0.065
STE_ACS[b]	290 (44%)	43 (42.1)	247 (44.5)	
NSTE_ACS[c]	142 (21%)	12 (11.7)	130 (23.4)	
Acute Heart Failure	57 (8.7%)	39 (38.2)	107 (19.3)	0.000*
Hemodynamic Instability	109 (16%)	55(53.9)	54 (9.7)	0.000*
Comorbid				
Hypertension	397 (60.4%)	55 (53.9)	342 (61.6)	0.145
Diabetes Mellitus	199 (30.3%)	33 (32.3)	166 (29.9)	0.622
Pneumonia	529 (80.5%)	44 (43.1)	86 (15.5)	0.000*
Sepsis	24 (3.7%)	16 (15.6)	8 (1.4)	0.000*
Smoker	350 (53.3%)	42 (41.1)	308 (88)	0.025
Use of mechanical ventilation	41 (6.2%)	30 (29.4)	11 (1.98)	0.000*
Hemodynamics				
Systolic Blood Pressure <140 mmHg	509 (77.4%)	90 (88.2)	419 (75.5)	0.006*
Systolic Blood Pressure >140 mmHg	148 (22.5%)	12 (11.7)	136 (24.5)	0.005*
Heart Rate >100	136(20.7%)	41 (40.2)	95 (17.1)	0.000*
Heart Rate ≤100	521 (79.2%)	61 (59.8)	460 (88.2)	0.125
Laboratory finding within the first 24 h				
Hemoglobin <12 g/dL	228 (34.7%)	55 (53.9)	171 (30.8)	0.000*
Creatinine >1.5 mg/dL	203 (30.9%)	65 (63.7)	141 (25.4)	0.000*
RBG >200 mg/dL	138 (21%)	24 (23.5)	114 (20.5)	0.496
Echocardiography				
EF <40%	182 (27.7%)	42 (41.2)	140 (25.2)	0.001*
TAPSE <17	169 (25.7%)	49 (48.0)	127 (22.8)	0.000*
Renal Replacement Therapy	9(1.3%)	4 (3.9)	5 (0.9)	0.027*

[a] ACS: Acute Coronary Syndrome.
[b] STE_ACS: ST Elevation Acute Coronary Syndrome.
[c] NSTE_ACS: Non-ST Elevation Acute Coronary Syndrome.

Table 2
Multivariable logistic regression model for prediction of hospital mortality.

SCORE	OR	95% CI		p value
		Lower Bound	Upper Bound	
Gender	2.67	1.23	5.78	0.013*
Acute Heart Failure	2.86	1.40	5.84	0.004*
Hemodynamic Instability	4.09	1.90	8.81	0.000*
Pneumonia Comorbid	2.71	1.26	5.86	0.011*
Creatinine ≥1.5 mg/dL	2.27	1.06	4.88	0.035*
TAPSE <17	2.06	1.00	4.28	0.051*
Use of Mechanical Ventilation	5.54	1.70	17.9	0.004*

Table 3
Assessment of the score value from each independent predictor factor.

SCORE	B	SE	B/SE	(B/SE)/x	Score
Gender	0.983	0.394	2.49	1.28	1
Acute Heart Failure	1.049	0.365	2.87	1.47	1
Hemodynamic Instability	1.409	0.391	3.60	1.85	2
Pneumonia Comorbid	0.998	0.393	2.54	1.31	1
Creatinine ≥1.5 mg/dL	0.820	0.390	2.10	1.08	1
TAPSE <17	0.725	0.372	1.95	1.00	1
Use of Mechanical Ventilation	1.713	0.600	2.85	1.46	1

Fig. 1. ROC curve analysis for our study with AUC value 0.75. ROC, receiver−operator curve.

found that female patients had a higher mortality rate than male patients.[13] Female gender was associated with a higher in-hospital mortality rate, OR 1.09, in a study conducted in Switzerland using the Swiss national registry AMIS Plus (0.95−1.24). This association, however, was not statistically significant. One possible explanation
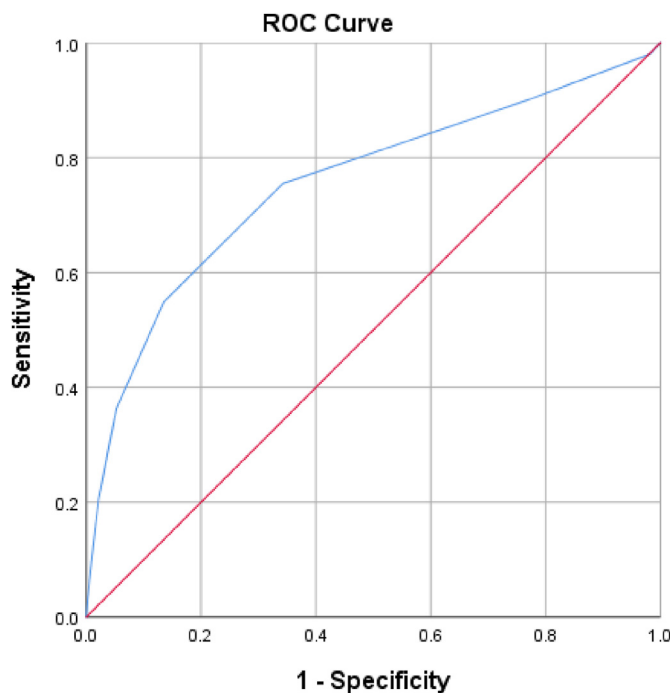
Table 4
Patient's probability on mortality event based on scoring system.

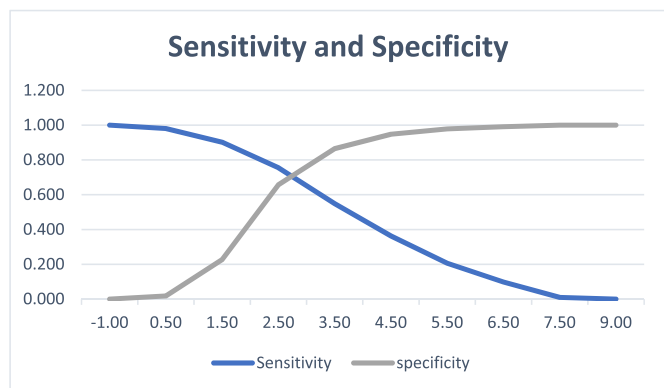| Score	Probability of Mortality (%)
1	6.50%
2	5.90%
3	15.40%
4	29.20%
5	48.50%
6	61.10%
7	64.30%
8	100.00%

Fig. 2. Sensitivity and specificity graphic based on ROC curve analysis. The sensitivity and specificity graph crosses at the value of 3 indicating a balance sensitivity and specificity. ROC.

Table 5
Sensitivity and specificity graphic based on ROC curve analysis.

Positive if Greater Than or Equal To	Sensitivity	Specificity
−1,00	1000	0,000
0,50	0,980	0018
1,50	0,902	0227
2,50	0,755	0658
3,50	0,549	0865
4,50	0,363	0948
5,50	0,206	0978
6,50	0,098	0991
7,50	0,010	1000
9,00	0,000	1000

for this discrepancy is that some female patients did not receive the same level of care as male patients. For instance, some female patients who were indicated for PCI were not treated as quickly as their male counterparts.[14] The same conclusion was reached in a study conducted in China, where women with AMI frequently did not receive the same level of intervention as men. Nonetheless, we treat males and females equally as the guideline requires.[15]

Acute heart failure symptoms are defined as a gradual or rapid change in the signs and symptoms of heart failure (HF), necessitating urgent therapy. It can result in a high rate of morbidity and mortality in emergency departments and contributes to the menpower burden associated with hospitalization care. Acute heart failure was identified as a predictor of mortality in CICUs in our study (OR: 2.86). Despite therapeutic advances, acute heart failure has a poor prognosis, with in-hospital mortality ranging from 4% to 7%, 60- to 90-day mortality ranging from 7% to 11%, and 60- to 90-day rehospitalization ranging from 25% to 30%.[16] There have been reports of in-hospital mortality rates as high as 10% and rehospitalization rates greater than 50% within one year.[17] In the

prospective cohort of hospitalized patients with AHF (ADHERE), in-hospital mortality was 4%.[18] The Second EuroHeart Failure Survey (EHFS II) revealed a 6.7% in-hospital mortality rate.[19]

Pneumonia accounts for 15–20% of CICU mortality. In our setting, we discovered that Pneumonia has an OR of 2.71 as a predictor of CICU mortality 95% CI 1.26–5.86. Pneumonia can exacerbate underlying cardiac disease in a variety of ways. The first mechanism is by increasing pro-inflammatory cytokines, which have a toxic effect on heart muscle, promoting myocarditis, and also by activating the coagulation cascade, which promotes vascular events. Coagulation may aggravate the underlying cardiac ischemia. Additionally, newer evidence indicates that certain well-known pathogens responsible for pneumonia, such as pneumococcus, can directly invade heart muscle, resulting in cardiomyocyte apoptosis.[20]

In our setting, mechanical ventilation is also a predictor of mortality, with an OR of 5.54 (1.70–17.9). A study conducted in Canada discovered an overall mortality rate of 29.4% for ventilated patients. Respiratory failure, in and of itself, increases the risk of hospitalization and death from any cause. According to one study, patients with AHF who requiredmechanical ventilation had a higher mortality rate than those who did not require mechanical ventilation, with an adjusted risk ratio of 2.03 (1.29–3.21).[21] This variable has the potential to affect mortality because the patients who required mechanical ventilation were already in poor health, and prolonged use or a high tidal volume of mechanical ventilation can cause diffuse alveolar damage. Additionally, hyperoxia contributes to elevated oxidative stress, which damages the alveolus. When these factors are combined, they can have an effect on the mortality of patients admitted to the CICU.[22]

Hemodynamic instability is a factor in determining CICU mortality in our setting. In our study, hemodynamic instability is defined as the requirement for pharmacological and/or mechanical support to maintain a mean arterial pressure 65 mmHg in the presence of end-organ hypoperfusion. Patients admitted to the CICU with hemodynamic instability may present with low blood pressure and a rapid heart rate, resulting in a shock state. A study conducted in the United States of America on the severity of shock and mortality in CICU patients with and without heart failure discovered that the higher the SCAI shock stage, the higher the mortality rate in each age group. $P < 0.01$.[7] Numerous studies have concluded that the presence of cardiogenic shock is associated with an increased risk of death. According to one study, the mortality rate for ADHF patients was 6%, for acute de novo heart failure patients was 8%, but once cardiogenic shock was present, the mortality rate increased to 46%.[23] Shock, in and of itself, results in decreased perfusion and cardiac output, both of which impair oxygen delivery to the human body. When the oxygen demand exceeds the oxygen supply during a shock, the body cannot function normally and all organ functions deteriorate over time, resulting in a multiple organ dysfunction syndrome. This will result in an increased mortality rate.[24]

The right ventricle is a critical component of heart function. It can be used to predict outcome in patients with heart failure, non-ischemic cardiomyopathy, or pulmonary hypertension. Tricuspid Annular Plane Systolic Excursion (TAPSE) was validated for the first time in 1984 and was found to correlate with the RV ejection fraction. It is one of several parameters that have been used to quantify RV function. Additionally, it represents the RV's longitudinal function.[25] Lasin et al, (2021) demonstrated that RV function is associated with 28-day mortality in patients with myocardial infarction complicated by cardiogenic shock, but the author stated that while the TAPSE was lower in the non-survivor group (mean = 15, compared to the survivor group, mean = 16), the difference between the groups was not statistically significant.[26] In

our setting, we use a cut off value of 17 as a predictor of CICU mortality with an OR of 2.06. (1.00–4.28). It also confirmed that, in our setting, RV function is a significant predictor of CICU mortality.

Acute kidney injury (AKI) is a significant issue in the management of acute coronary syndromes (ACS). It is an unresolved clinical problem in critically ill patients, with a high mortality rate, rising incidence, and no definitive treatment. AKI is a significant risk factor for in-hospital and long-term mortality following acute cardiovascular disease. Acute Kidney Injury is defined as a sudden decrease in kidney function (within hours), which includes both injury (structural damage) and impairment (loss of function). Chronic renal failure has also been identified as an independent risk factor for cardiovascular mortality in patients with coronary artery disease (CAD).[27] In our setting, a serum creatinine level of 1.5 mg/dL is considered to be elevated. We discovered that serum creatinine levels greater than 1.5 mg/dL were a significant predictor of CICU mortality, with an OR of 2.27. (1.06–4.88). Serum creatinine levels greater than 1.5 mg/dL were associated with a 70% increase in the risk of all-cause mortality. Serum creatinine is only a crude indicator of glomerular filtration rate. A concentration greater than 1.5 mg/dL is associated with a decrease in glomerular filtration rate. According to The HOPE Randomized Trial, those with serum creatinine levels greater than 1.4 mg/dL had a higher risk of cardiovascular or all-cause mortality.[28] Elevated serum creatinine concentrations are thought to be associated with the severity of atherosclerotic damage. This can aggravate the underlying atherosclerotic process, increasing the risk of death.[28]

As is the case with all single-center studies, this study has a few limitations that may affect the scoring system's generalizability to other CICU populations. Our center, Sardjito General Hospital Yogyakarta, is a tertiary-care referral CICU that is likely to be unique in terms of demographics, characteristics, and logistics compared to other institutions. Additionally, additional research is required to validate the scoring system's external applicability in another population.

5. Conclusion

The first 24-h Sardjito Cardiovascular Intensive Care (SCIENCE) admission risk scoring system, which incorporates male gender, the presence of AHF, hemodynamic instability, pneumonia, serum creatinine >1.5 mg/dL, TAPSE 17 mm, and the use of mechanical ventilation, can be used to accurately predict in-hospital mortality in patients hospitalized in CICU with good sensitivity and specificity.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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