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Original Article

Mayo Cardiac Intensive Care Unit Admission Risk Score (M–CARS) Validation Test to Assess Mortality During Treatment in Cardiovascular Care Unit (CVCU) Patients at Haji Adam Malik Hospital

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Abstract

Background: Approximately 85% of all in-hospital deaths occur in the Cardiovascular Care Units (CVCU) where M-CARS will be an important starting point for the development of CVCU-specific mortality risk prediction models.

Aim: This research aims to assess M-CARS validation to assess mortality during treatment in CVCU patients at Haji Adam Malik (HAM) General Hospital.

Methods: This research is prospective research that examines M-CARS score validity as a predictor of intra-hospital mortality in patients treated at CVCU HAM General Hospital Medan from September 2021 - January 2022. If correlation test results show a significant relationship, the cut-off value M-CARS score will be taken using ROC (Receiver Operating Characteristic) curve analysis, then analysis of the M-CARS score diagnostic value will be carried out according to the cut-off value obtained to predict mortality during hospitalization. Then Hosmer-Lemeshow test was carried out to assess the suitability of logistic regression on risk prediction assessment within a population that is being assessed.

Results: M-CARS had a very good discriminatory ability (AUC 0.93) to predict intrahospital mortality. The calibration value using the Hosmer Lemeshow test (R2 = 0.982; p = 1.516; p>0.05) shows that there is no significant difference between the observed and expected mortality rate by the two scoring systems therefore considered accurate.

Conclusion: M-CARS is valid to be used in assessing the risk of mortality events during CVCU treatment at H. Adam Malik Hospital Medan.

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Keywords: Mortality, Cardiovascular Care Unit, Mayo Cardiac Intensive Care Unit Admission Risk Score, Braden Score.

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Introduction

Cardiovascular Care Unit (CVCU) also known as Cardiac Intensive Care Unit (CICU) refers to specific systemic management for patients with severe cardiovascular disease, which consists of heart disease and vascular disease.[1] CVCU patients are often admitted with primary cardiovascular problems and multiple comorbidities or non-cardiovascular complications, therefore standard diagnosis-specific risk scores derived from non-critically ill population scores are less applicable. The development and validation of risk prediction models for CVCU conditions has been identified as a priority for contemporary CVCU research.[2,3]

Approximately one-third of CVCU patients are admitted with critical care diagnosis, and these patients account for about 85% of all in-hospital deaths. The overall calibration of ICU risk scores usage for CVCU patients is generally poor with most of these ICU risk scores, and consistent loss of discrimination in subgroups of patients with the highest risk indicates an urge for development and a more robust mortality risk stratification system for the CVCU population.[3]

Mayo Cardiac Intensive Care Unit Admission Risk Score (M-CARS) combines admission diagnosis and several new risk factors to predict in-hospital mortality in CVCU patients with better discrimination than risk scores in ICU patients.[4] If externally validated, M-CARS would be an important starting point for the development of CVCU-specific mortality risk prediction models analogous to APACHE-IV.[5]

The M-CARS used 7 variables available at CVCU admission, including relevant admission diagnoses (cardiac arrest, shock, and respiratory failure), markers of weakness (Braden skin score), and generally available laboratory parameters (Red Cell Distribution Width (RDW), Blood Urea Nitrogen (BUN), anion gap). Patients with M-CARS score lower than 2 had an in-hospital mortality of <1%, whereas patients with M-CARS above 6 had an in-hospital mortality of>50%. Using data available at the time of CVCU admission, M-CARS allows early risk stratification of death without waiting for 24 hours.[4]

Research Methodology

This research is prospective research that examines the validity of the M-CARS score as a predictor of intra-hospital mortality in patients treated at CVCU HAM General Hospital Medan from September 2021 to January 2022. The minimum number of samples for this research is 60 samples that meet inclusion criteria, namely patients treated at CVCU, patient age 18 years old, first CVCU admission during the research period, and exclusion criteria namely CVCU patients with incomplete data, congenital heart disease, history of coronary bypass surgery.

Researchers collected data through history taking, physical examination, laboratory examination, ECG, and echocardiography. After that, all research subjects will be assessed for M-CARS score within the first 24 hours. All research subjects were observed until the last day of treatment at the hospital. This research got approval from the ethics committee of the Medical Faculty at, the University of North Sumatra.

Categorical variables are represented by number or frequency (n) and percentage (%). Numerical variables are represented by mean (mean) and standard deviation. For statistical analysis, a T-test will first be conducted between the M-CARS score and mortality to assess the correlation and strength of correlation between these two variables. If the results of the correlation test show a significant relationship, the M-CARS score cut-off value will be taken using ROC (Receiver Operating Characteristics) curve analysis, then analysis of the M-CARS score diagnostic value will be carried out according to the cut-off value. obtained to predict mortality during hospitalization.

The Hosmer-Lemeshow test was performed to assess the compatibility of logistic regression on the risk prediction assessment within a population that is being assessed. In statistical data analysis using statistical software, a p-value <0.05 is said to be statistically significant.

Results

The number of samples obtained was 70 patients who met the inclusion criteria and exclusion criteria so that they could be included in this research. Data were recorded after anamnesis, physical examination, and laboratories. Then evaluate Braden's Skin Score and M-CARS Score.

Based on the table above, it was found that patients

Table 1. Basic Characteristics of Research Samples.

Characteristics	Mortality during Admission (Mean ± SD)		P value
	Yes	No	
Age (years old)	62.92 + 13.43	58.95 + 11.71	0.478*
Body Weight (kg)	66.67 + 9.16	66.34 + 11.49	0.292**
Body Height (cm)	164.83 + 7.05	162.97 + 6.68	0.374*
Body Mass Index (BMI) (kg/m²)	24.55 + 3.36	24.87 + 3.46	0.994*
Gender	Mortality during Admission		**P value**
	Yes	No	Yes
Male	9 (12.9%)	37 (52.9%)	0.457#
Female	3 (4.3%)	21 (30.0%)	

chi-square test
* T-independent test
** Mann-Whitney test

Table 2. Laboratory Examination Results of Research Sample.

Laboratory Examination	Mortality during Admission (Mean + SD)		P value
	Yes	No	
Hemoglobin (g/dl)	12.25 + 2.65	12.54 + 2.39	0.581**
Leucocyte (/mm3)	14.349.17 + 7117.91	11.564.26 +5231.18	0.201*
Trombocyte (x103/mm3)	230.42 + 103.28	12693.43 + 54096.52	0.137*
Creatinin (g/dl)	3.05 + 2.71	2.07 + 2.69	0.080*
GFR (%)	48.48 +34.96	61.55 +37.20	0.275*
GDS (mg/dl)	175.67 + 104.18	158.55 + 88.38	0.956*
Natrium (mEq/L)	132.83 + 8.39	135.03 + 5.26	0.600*
Kalium (mEq/L)	9.08 + 15.43	5.49 + 7.39	0.012*
Chlorida (mEq/L)	98.42 + 8.51	102.52 + 5.19	0.066*
RDW	14.40 + 2.89	14.12 + 1.65	0.691*
BUN	43.75 + 37.5	26.5 + 21.97	0.154*
Anion Gap	14.89 + 8.4	12.80 + 5.33	0.149*
Braden Skin Score	12.83 + 3.51	18.26 +	0.000*
M-CARS Score	4.75 + 1.81	1.55 + 1.25	0.000*

* T-independent test
** Mann-Whitney test

who died during hospitalization with mean age 62.92 ± 13.43 years; body weight 66.67 ± 9.16 kg; body height 164.83 ± 7.05 cm and BMI 24.55 ± 3.36 kg/m^2. Meanwhile, in patients who survived, mean age was 58.95 ± 11.71 years; body weight 66.34 ± 11.49 kg, body height 162.97 ± 6.68 and BMI 24.87 ± 3.46 kg/m2. After the independent T-test and Man-Whitnney test was performed, there were no differences in age, body weight, body height, and body mass index between patients who died and survived during hospitalization (p value> 0.05). The majority of patients who died were male (12.9%) of which only 3 were female 4.3% as well surviving patients were dominated by male 37 patients (53.9%) and 21 patients (30%) were female. Based on the chi-square test, there was no gender difference between patients who died and survived during

Table 3. Research Sample Conditions at Admission and Risk Factors for Mortality During Hospitalization.

Conditions at admission	Mortality during Admission (Mean + SD)		P value
	Yes	No	
Cardiac Arrest			
Yes	5 (7.1%)	3 (4.3%)	0.000#
No	7 (10.0%)	55 (78.6%)	
Shock			
Yes	4 (5.7%)	5 (7.1%)	0.02#
No	8 (11.4%)	53 (75.7%)	
Respiratory Failure			
Yes	4 (5.7%)	1 (1.4%)	0.00#
No	8 (11.4%)	57 (81.4%)	

chi-square test

hospitalization (p-value> 0.05).

Numerical data with normal distribution, namely body weight, and hemoglobin, will be subjected to a T-independent test to obtain a p-value. For numerical data not normally distributed, the Mann-Whitney test is performed. Based on the T-independent test and the Mann-Whitney test results, it was found that there was a significant difference between patients who died and survived during hospitalization based on the potassium electrolyte examination (p = 0.012), Braden Skin Score (p = 0.000) and M-CARS Score (p = 0.012) with p-value <0.05.

Research Sample Conditions at Admission and Risk Factors for Mortality During Hospitalization.

For categorical data, a chi-square test was performed, and it was found that conditions of cardiac arrest (p=0.00), shock (p=0.02), and respiratory failure (p=0.00) at the time of admission were significantly different between patients who died and those who survived during hospitalization.

Multivariate Analysis of Multivariate Logistic Regression to Predict Intrahospital Mortality.

For logistic regression analysis, the Odds Ratio (OR) value is displayed where OR states how many events occur when accompanied by risk factors. For example, patients with cardiac arrest at admission have 31.897 times the risk of dying compared to patients without cardiac arrest at admission.

ROC Analysis for Discrimination of MCARS Scores on Intrahospital Mortality.

ROC analysis was performed to assess M-CARS discrimination in predicting intrahospital mortality. The area under the curve (AUC) value of M-CARS for

Table 4. Multivariate Analysis of Multivariate Logistic Regression to predict Intrahospital Mortality.

Conditions at Admission	OR	95% C.I.	Lower Limit
		Upper limit	
Cardiac Arrest	31.897	1.162	875.435
Diagnosis Shock	16.293	.901	294.775
Respiratory Failure	11.819	.489	285.497
RDW	3.591	.359	35.944
BUN	1.799	.180	17.942
Anion Gap	2.027	.226	18.203
Braden Skin Score	58.386	2.906	1173.163

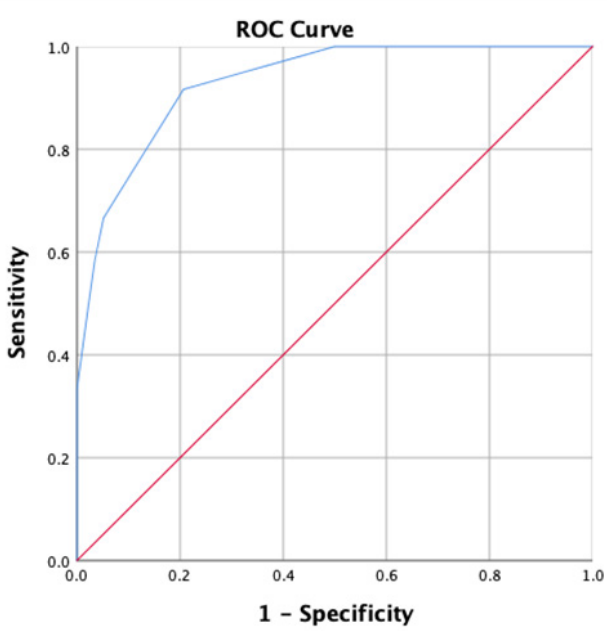

Figure 1. ROC Analysis for Discrimination of MCARS Scores on Intrahospital Mortality.

intrahospital mortality is 0.930, which indicates the excellent discriminatory ability of M-CARS to predict intrahospital mortality.

In this research, the calibration value was assessed with the Hosmer Lemeshow test and found R2 value = 0.982 with p-value = 1.516. The p-value> 0.05 indicates that there is no significant difference between the observed and expected mortality rate by the two scoring systems, therefore considered accurate.

Discussion

M-CARS On Admission and Intrahospital Mortality

M-CARS had a very good discriminatory ability (AUC 0.93) to predict intrahospital mortality. The calibration value using the Hosmer Lemeshow test (R2 = 0.982; p = 1.516; p>0.05) shows that there is no significant difference between the observed and expected mortality rates by the two scoring systems and assessed as accurately. In the Jentzer et al. study, based on a database of CVCU patients admitted from January 1, 2007, to April 30, 2018, M-CARS showed a stratified association with in-hospital mortality (odds ratio 1.84 for each 1-point increase in M-CARS, 95% CI 1.78-1.89). In the validation group, M-CARS had an area below ROC 0.86 for hospital mortality, with good calibration (P=0.21). 47.1% of patients with M-CARS <2 had an in-hospital mortality of 0.8%, and 5.2% of patients with M-CARS>6 had an in-hospital mortality of 51.6%.[3] In a study involving 12,428 patients, a total of 2839 patients (22.8%) died within 1 year of hospitalization, including 1149 (9.2%) in-hospital deaths and 1690 (15.0%) of 11,279 survivors at the hospital. 1-year survival decreased gradually as increasing function of M-CARS (P<.001), and all components of M-CARS were significant predictors for 1-year mortality (P<.001). 1-year survival among patients decreased gradually as increasing M-CARS function for scores below 3 (all P<.001); however, there was no further reduction in 1-year survival for patients who were later discharged from hospital with M-CARS > 3 (P=.99). The M-CARS components associated with 1-year mortality among hospital survivors included BUN, RDW, BSS, and respiratory failure (all P<.001).[6] Based on this research results and previous studies, using 7 variables available at the time of CVCU admission, M-CARS can predict hospital mortality in CVCU patients with good discrimination.

BUN Value on Admission and Intrahospital Mortality

Different study results were shown by previous studies which stated that BUN was associated with in-hospital mortality in logistic regression analysis (HR 1.03; 95% CI 1.01-1.05; p < 0.001). Per quartile, (BUN 0-5.4 mmol/L, 5.4-9.0 mmol/L, 9.0-15.9 mmol/L, and above 15.9 mmol/L) hospital deaths increased by 51% (HR 1.51; 95% CI 1.23 -1.85; p < 0.001).[7] In patients with acute decompensated heart failure (ADHF), high BUN levels are a more potent marker of mortality than creatinine.[8] This relationship has also been shown in patients with ACS, where ACS patients show significantly elevated BUN levels.[9] In a study examining the association between renal dysfunction and mortality in CVCU patients, overall hospital mortality was 8.6% and was higher in patients with a history of chronic kidney disease than in patients without chronic renal failure (12.2% vs 7, 8%, OR 1.65, p < 0.001). Initial

Table 5. Hosmer Lemeshow Analysis for MCARS Score Calibration on Intrahospital Mortality.

Characteristics	Discrimination Test		Calibration Test	P value
	AUC	CI 95%	R2 Hosmer-Lemeshow	
MCARS Score	0.930	0.861-1.000	0.982	1.516

BUN (OR 1.014, p < 0.001) was a significant predictor of in-hospital mortality.[10]

Anion Gap Value on Admission and Intrahospital Mortality

The anion gap is an excellent predictor of severe hyperlactatemia defined as lactate above 4 mmol/l or 5 mmol/l. The anion gap can miss diagnosing patients at risk of death because a sufficiently large degree of hyperlactatemia is required to push the anion gap beyond its normal reference range if the baseline anion gap is low. Based on a meta-analysis, a single anion gap measurement cannot be recommended for risk stratification in critically ill patients.[11] Different results were found in the Breen et al. study, where a negative correlation was seen between chloride intake and anion gap (r = -0.425, p < 0.001). In this study, the anion gap increased in 32.1% of patients. Patients with an increased anion gap >12 mEq/L had a higher overall mortality than those with an anion gap of 12 mEq/L at all levels of chloride admission (p<0.001). An increase in anion gap during acidosis (often due to lactic acidosis) has been identified as an important predictor of adverse outcomes in CVCU patients and may contribute to hypochloremia in patients without metabolic alkalosis.[6]

Braden skin score on admission and intrahospital mortality

BSS at admission was inversely associated with in-hospital mortality (OR 0.70; 95% CI, 0.68-0.72; P<.001; receiving operator AUC, 0.80; 95% CI, 0.78-0,82), with an increase in short-term mortality as a function of a decrease in BSS at admission. After adjustment for disease severity and comorbidities using multivariable analyses, admission BSS remained inversely related to in-hospital mortality (OR 0.88; 95% CI, 0.85–0.92; P<.001). In patients discharged from the hospital, BSS at admission was inversely associated with post-discharge mortality after adjustment for disease severity and comorbidities (hazard ratio 0.89; 95% CI, 0.88–0.90; P<.001). It can be concluded that BSS at admission, a simple and inexpensive nursing assessment that could potentially reflect overall disease severity and acuity, was independently associated with in-hospital and post-hospital mortality when added to multiparametric disease severity scores in CVCU patients.[4]

Different results were found in the Pan et al. study, which showed that RDW was significantly associated with mortality from cardiovascular disease (HR = 1.39, 95% CI: 1.21-1.59). Delayed clearance of red blood cells, thereby increasing RDW, can be a physiological reaction to stress and ill health. This could potentially explain the association between RDW and mortality and this association with poor prognosis in many different patient groups (Pan, Borné and Engström, 2019). A retrospective cohort study of CVCU patients between January 1, 2007, and December 31, 2015, involving 9,644 patients also showed similar results, with RDW at admission (OR 1.12 per 1%, 95% CI 1.07-1.18, p < 0.001) was significantly associated with in-hospital mortality. Patients discharged from the hospital with a higher RDW had lower post-discharge survival. An increase in RDW on admission was independently associated with higher hospital mortality in CVCU patients. These data emphasize the importance of hematological abnormalities for mortality risk stratification in the CVCU population.[12]

Diagnosis at admission and Intrahospital Mortality

Diagnosis at admission can influence risk prediction by CVCU risk score, especially critical care diagnoses such as cardiac arrest, respiratory failure, sepsis, and shock as well as acute kidney injury. Critical care diagnoses are more common in patients who experience intrahospital death than in patients who survive during hospitalization. Patients with at least one critical care diagnosis at admission had a significantly higher intrahospital mortality rate than other patients (24.1%

vs 2.0%, OR 15.16, 95% CI 12.58-18.29, P< 0.001). Patients with respiratory failure had higher hospital mortality than patients without this diagnosis (19.0% vs. 3.0%, OR 7.52, 95% CI 6.36-8.89, P<0.001). Patients without a diagnosis of critical care admission or acute renal failure accounted for only 8% of all in-hospital deaths (1.4% vs. 19.0% hospital mortality, OR 0.06, 95% CI 0.05–0.08, P<0.001).[5] Similar results were also found by Bohula et al., where in mortality risk stratification based on primary admission diagnosis, the highest mortality rate was found in patients with cardiac arrest, which was 45.3%. Apart from cardiac arrest, indications for CVCU care that carried the highest mortality rate were shock (cardiogenic, 30.6%; others, 23.8%), need for renal replacement therapy (34.5%), neurological emergencies (30.6%), respiratory failure (24.1%), or use of mechanical circulation aids (26.6%).[13]

Conclusion

M-CARS had a very good discriminatory ability (AUC 0.93) to predict intrahospital mortality. M-CARS is valid to be used in assessing the risk of mortality events during CVCU treatment at H. Adam Malik Hospital Medan.

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