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Usefulness of The CHADS2 and CHA2DS2–VASc Scores in Predicting In–Hospital Mortality in Acute Coronary Syndrome Patients: A Single–Center Retrospective Cohort Study

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Abstract

Background: Although the GRACE risk score is widely accepted as an established scoring system to predict in-hospital mortality in acute coronary syndrome (ACS) patients, this scoring system still depends on electrocardiography and laboratory findings to determine the results. Therefore, we aim to retrospectively evaluate the association between the CHADS2 and CHA2DS2-VASc score as an anamnesis-only mediated scoring system and in-hospital mortality in hospitalized ACS patients.

Methods: This retrospective cohort study analyzed data of ACS patients from the ACS registry in Dr. Hasan Sadikin Central General Hospital from 2018 to 2021. The outcome of this study was in-hospital mortality. The association between this scoring system and in-hospital mortality were evaluated using binary logistic regression analysis. Receiver operating characteristics (ROC) analysis was also performed to assess the success rate of this scoring system in predicting in-hospital mortality.

Results: A total of 1339 patients were included in this study, and 162 (12.1%) of them died in the hospital. High CHA2DS2-VASc score group (cut-off >2) was significantly associated with higher risk of in-hospital mortality before (OR=2.56 [1.75,3.75]; p<0.001) and after adjustment of several confounding factors (OR=3.39 [1.73,6.64]; p<0.001). Meanwhile, the high CHADS2 score (cutoff >2) only significantly increased the risk of in-hospital mortality in univariate analysis (OR=2.05[1.47,2.87];p<0.001), but was not significantly associated with in-hospital mortality after multivariate analysis (OR=1.31 [0.92,1.86];p=0.129). ROC analysis revealed that the predictive accuracy of the CHA2DS2-VASc score was significantly greater compared to the CHADS2 score (AUC: 0.653 vs 0.609, p<0.001). However, the predictive value of the CHA2DS2-VASc score was significantly lower than the GRACE risk score (AUC: 0.789 vs 0.653, p<0.001)..

Conclusion: Our study showed that the CHA2DS2-VASc score >2 was significantly and independently associated with higher in-hospital mortality in ACS patients compared to the CHA2DS2-VASc score of 1 or lower. Despite its lower predictive accuracy compared to the GRACE risk score, the CHA2DS2-VASc score can still be used in practical situations as an alternative scoring system for predicting in-hospital mortality in ACS patients, especially in primary healthcare settings located in rural areas that lack the diagnostic facilities.

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Keywords: acute coronary syndrome, CHA2DS2-VASc score, CHADS2 score, in-hospital mortality..

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Introduction

Acute coronary syndrome (ACS), as a critical and severe manifestation of coronary artery disease, has high in-hospital mortality, numbering up to 20%.[1,2] The Global Registry of an Acute Coronary Event (GRACE) risk score is widely known as a standard and validated scoring system to predict all-cause mortality in ACS patients within six months after admission.[3] This scoring system can identify high-risk patients who will benefit from aggressive therapies.[3] Additionally, KILLIP classification was also utilized to predict the risk of mortality in ACS patients. However, these scoring systems have limited applicability because they rely heavily on diagnostic modalities, including sphygmomanometer, electrocardiographic (ECG), and laboratory findings, a facility that not all rural healthcare centers carry.[4] Therefore, a simple and convenient scoring system may be useful for assessing in-hospital mortality risk in ACS patients.

Meanwhile, the CHADS2 score (congestive heart failure; hypertension; age ≥75 years; type 2 diabetes mellitus; previous stroke, transient ischemic attack, or thromboembolism [doubled]) and CHA2DS2-VASc score (congestive heart failure; hypertension; age ≥75 years [doubled]; type 2 diabetes mellitus; previous stroke, transient ischemic attack, or thromboembolism [doubled]; vascular disease; age 65–75 years; and sex category), an established scoring system for stroke risk stratification in atrial fibrillation (AF) patients,[5,6] were investigated by previous cohort studies to predict major adverse cardiovascular events (MACE)[7–10] and all-cause mortality in ACS patients.[11–14] These studies showed that high CHA2DS2-VASc scores were significantly associated with increased MACE and mortality risk in ACS patients. Of note, this scoring system was simple, feasible, and can be completed only through history taking. Hence, this scoring system was efficient in terms of time and resources and thus can be used in every healthcare facility.

This study will repurpose CHADS2 and CHA2DS2-VASc scores as prognostic tools to predict in-hospital mortality in ACS patients. However, a lack of studies investigated the association between CHADS2 and CHA2DS2-VASc scores with in-hospital mortality in ACS patients. Thus, the purpose of this cohort study was twofold: Firstly, to retrospectively evaluate the relationship between the CHADS2 and CHA2DS2-VASc score with in-hospital mortality of admitted ACS patients regardless of AF status. Secondly, to compare the predictive accuracy of CHADS2, CHA2DS2-VASc, and GRACE risk scores in predicting the in-hospital mortality in ACS patients

Methods

Study design and patient selection

This was a retrospective and single-center cohort study that included all ACS patients aged ≥ 18 years old hospitalized in Dr. Hasan Sadikin Central General Hospital from January 2018 to December 2021. The exclusion criteria were participants with missing at least one CHADS2 and CHA2DS2-VASc score component and in-hospital mortality data. This study was approved by the Medical Research Ethics Committee of Dr. Hasan Sadikin Central General Hospital, West Java, Indonesia. The informed patient consent was collected at the beginning of the study.

Definition of variables and outcome

Regarding baseline characteristics variables, all diagnoses were collected from the patient's medical records. Cerebrovascular disease was defined as stroke or transient ischemic attack. Chronic obstructive pulmonary disease was defined as asthma or chronic obstructive pulmonary disease.

ACS was classified into STEMI, NSTEMI, and UAP, and its diagnosis was based on European Society of Cardiology guidelines.[15,16] STEMI was diagnosed if the patient was admitted with acute chest pain with electrocardiographic findings of persistent ST-segment elevation >1 mm in 2 or more contiguous leads or new-onset left bundle branch block (LBBB).[15] Patients with acute chest pain, together with no ST-segment elevation in electrocardiography and increased cardiac enzyme level (troponin or creatinine kinase myocardial band), were diagnosed as NSTEMI.[16] Lastly, UAP was diagnosed if the patient presented with acute chest pain, with neither ST-segment elevation nor abnormal cardiac enzymes.[16]

Table 1. Baseline characteristics of all participants that stratified by scoring system cutoffs.

Variable	CHA_2DS_2-VASc score		P value	$CHADS_2$ score		P value
	<2 (n=555)	≥2 (n=784)		<2 (n=944)	≥2 (n=395)	
Demographic and lifestyle						
Age (years), median (IQR)	54 (48-60)	62 (54-70)	<0.001	57 (50-64)	62 (53-71)	<0.001
Age stratification						
Age ≤ 64, n (%)	526 (94.8)	421 (53.7)	<0.001	755 (80)	222 (56.2)	<0.001
Age 65-74, n (%)	29 (5.2)	228 (29.1)	<0.001	170 (18)	87 (22)	0.089
Age ≥ 75, n (%)	0 (0)	105 (13.4)	<0.001	19 (2)	86 (21.8)	<0.001
Female, n (%)	25 (4.5)	290 (37)	<0.001	172 (18.2)	143 (36.2)	<0.001
Smoking status						
Current, n (%)	428 (77.1)	371 (47.3)	<0.001	626 (66.3)	173 (43.8)	<0.001
Former, n (%)	65 (11.7)	123 (15.7)	0.039	117 (12.4)	71 (18)	0.007
Never, n (%)	62 (11.2)	288 (36.7)	<0.001	200 (21.2)	150 (38)	<0.001
Comorbidities						
Hypertension, n (%)	199 (35.9)	646 (82.4)	<0.001	475 (50.3)	370 (93.7)	<0.001
Type II DM, n (%)	32 (5.8)	254 (32.4)	<0.001	63 (6.7)	223 (56.5)	<0.001
Dyslipidemia, n (%)	70 (12.6)	181 (23.1)	<0.001	144 (15.3)	107 (27.1)	<0.001
Prior MI, n (%)	56 (10.1)	396 (50.5)	<0.001	270 (28.6)	182 (46.1)	<0.001
Prior peripheral artery disease, n (%)	0 (0)	38 (4.8)	<0.001	8 (0.9)	30 (7.6)	<0.001
Prior heart failure, n (%)	14 (2.5)	242 (30.9)	<0.001	45 (4.8)	211 (53.4)	<0.001
Prior cerebrovascular disease, n (%)	24 (4.3)	71 (9.1)	0.001	54 (5.7)	41 (10.4)	0.002
Prior obstructive pulmonary disease, n (%)	10 (1.8)	18 (2.3)	0.537	22 (2.3)	6 (1.5)	0.343
Family history of premature CAD, n (%)	50 (9)	77 (9.8)	0.617	90 (9.5)	37 (9.4)	0.924
Clinical presentation at admission						
Congestion, n (%)	102 (18.4)	274 (34.9)	<0.001	209 (22.1)	167 (42.3)	<0.001
Killip classification						
Killip I, n (%)	445 (80.1)	501 (63.9)	<0.001	724 (76.7)	222 (56.2)	<0.001
Killip II, n (%)	56 (10.1)	159 (20.3)	<0.001	109 (11.5)	106 (26.8)	<0.001
Killip III & IV, n (%)	53 (9.5)	121 (15.4)	0.002	108 (11.4)	66 (16.7)	0.009
ACS types						

STEMI, n (%)	408 (73.5)	378 (48.2)	<0.001	609 (64.5)	177 (44.8)	<0.001
NSTEMI, n (%)	133 (24)	335 (42.7)	<0.001	285 (30.2)	183 (46.3)	<0.001
UAP, n (%)	13 (2.3)	65 (8.3)	<0.001	47 (5)	31 (7.8)	0.041
Physical examination at admission						
Body mass index (kg/m2), median (IQR)	23.5 (21.6-25.4)	23.5 (21.4-25.6)	0.943	23.5 (21.45-25.55)	23.5 (21.45-25.55)	0.515
Body mass index categories						
Underweight, n (%)	10 (1.8)	29 (3.7)	0.042	27 (2.9)	12 (3)	0.860
Normal weight, n (%)	148 (26.7)	212 (27)	0.879	242 (25.6)	118 (29.9)	0.111
Overweight, n (%)	186 (33.5)	227 (29)	0.075	303 (32.1)	210 (53.2)	0.125
Obese (class I), n (%)	163 (29.4)	227 (29)	0.869	270 (28.6)	120 (30.4)	0.514
Obese (class II), n (%)	29 (5.2)	65 (8.3)	0.031	67 (7.1)	27 (6.8)	0.864
SBP (mmHg), median (IQR)	120 (105.5-134.5)	120 (90-150)	<0.001	120 (107.5-132.5)	120 (105-135)	<0.001
DBP (mmHg), median (IQR)	77.5 (72.5-82.5)	80 (70-90)	0.128	80 (81-89)	80 (70-90)	0.112
Heart rate (bpm), median (IQR)	78 (67-89)	80 (67-93)	<0.001	80 (68-92)	82 (69-95)	0.002
Laboratory findings at admission						
Direct blood glucose (mmol/L)	6.7 (3.6-9.8)	7 (3.9-10)	0.104	6.7 (3.4-10)	7.1 (4-10.3)	<0.001
Haemoglobin (g/dL), median (IQR)	14.9 (13.6-16.2)	13 (11.4-14.6)	<0.001	14 (13-15)	13.3 (11.4-15.3)	<0.001
Hematocrite (%),median (IQR)	42.8 (39.3-46.3)	38.85 (34.8-42.9)	<0.001	41 (37.5-44.5)	39 (34.8-43.3)	<0.001
Leukocyte (10^9/L), median (IQR)	12 (9.1-14.9)	11.2 (8.5-13.9)	<0.001	11.9 (8.9-14.9)	11.2 (8.8-13.6)	0.002
Ureum (mmol/L), median (IQR)	1.7 (1.2-2.2)	1.8 (1.1-2.5)	<0.001	1.7 (1.2-2.2)	2 (1.3-2.7)	<0.001
Creatinine (µmol/L), median (IQR)	60.5 (48.4-72.6)	60.8 (45.5-76.1)	0.001	60 (47.2-76.7)	64.35 (45.8-83)	<0.001
Troponin-I (ng/L), median (IQR)	5.73 (0.9-10)	3.36 (0.01-8.06)	0.002	3.57 (0.01-8.4)	5.54 (0.7-10)	0.051
In-hospital medication						
Dual antiplatelet, n (%)	544 (98)	770 (98.2)	0.985	929 (98.4)	385 (97.5)	0.349
Anticoagulant, n (%)	488 (87.9)	679 (86.6)	0.532	828 (87.7)	339 (85.8)	0.429
Nitrate, n (%)	173 (31.2)	224 (28.6)	0.608	292 (30.9)	105 (26.6)	0.196
Beta blocker, n (%)	368 (66.3)	537 (68.5)	0.408	649 (68.8)	256 (64.8)	0.119
ACE-I, n (%)	303 (54.6)	445 (56.8)	0.379	536 (56.8)	212 (53.7)	0.298

Morphine, n (%)	38 (6.8)	37 (4.7)	0.155	53 (5.6)	22 (5.6)	0.925
Statin, n (%)	544 (98)	759 (96.8)	0.095	924 (97.9)	379 (96)	0.014
Revascularication procedure						
Fibrinolytic, n (%)	75 (13.5)	69 (8.8)	0.033	114 (12.1)	30 (7.6)	0.072
PCI, n (%)	379 (68.3)	456 (58.2)	<0.001	615 (65.1)	220 (55.7)	0.001

1. All numerical variables were presented in median (interquartile range) and SI units.
2. All categorical variables were presented in n (%).
3. IQR: interquartile range; DM: diabetes mellitus; MI: myocardial infarction; SBP: systolic blood pressure; DBP: diastolic blood pressure; i.v: intravenous; PCI: primary coronary intervention; ACE-I: angiotensin converter enzyme inhibitor.

$CHADS_2$, CHA_2DS_2-VASc, and GRACE risk scores were collected accordingly based on patients' data in the medical record. We calculated the $CHADS_2$ score by assigning 1 point each for congestive heart failure, hypertension, age ≥75 years, and diabetes mellitus; and 2 points for prior stroke, TIA, or thromboembolism.6 We calculated the CHA_2DS_2-VASc score by assigning 1 point each for congestive heart failure, hypertension, diabetes mellitus, vascular disease (including prior CAD, myocardial infarct, peripheral artery disease, or aortic plaque), age 65-74 years, and female sex; and 2 points each for age ≥75 years and prior stroke, TIA, or thromboembolism.[5] In this study, $CHADS_2$ and CHA_2DS_2-VASc scores were categorized into two groups low and intermediate risk (score <2) and high risk (score ≥2). This categorization was performed based on previous literature and guidelines that investigated these scoring systems as a stroke risk stratification in the AF population.[5,17–19] Moreover, the GRACE risk score was calculated according to its several components including age, heart rate, SBP, ST-segment deviation on electrocardiography, cardiac arrest at admission, abnormal cardiac enzymes, baseline creatinine levels, and Killip class.

The outcome of this study was in-hospital mortality which is defined as all ACS patients who died in the hospital before discharge regardless of the cause of death.

Statistical analysis

$CHADS_2$ and CHA_2DS_2-VASc scores were analyzed as numerical and categorical variables (based on a cutoff of 2). Age, body mass index, blood pressure, heart rate, and laboratory findings were interpreted as numerical variables. Sex category, smoking, comorbidities, revascularization history, ACS types, and Killip classification were reported as categorical variables. A Kolmogorov-Smirnov test was performed to assess the normality of data distribution. Numerical variables with parametric distributions are presented as the mean ± standard deviation, whilst numerical variables with non-parametric distributions are presented as the median and interquartile range. Categorical variables are reported with counts and percentages. A Mann-Whitney U test was used to evaluate the differences between two numerical variables. To compare the differences between two categorical variables, we performed the Chi-Square test or Fisher's exact test, as appropriate. The association

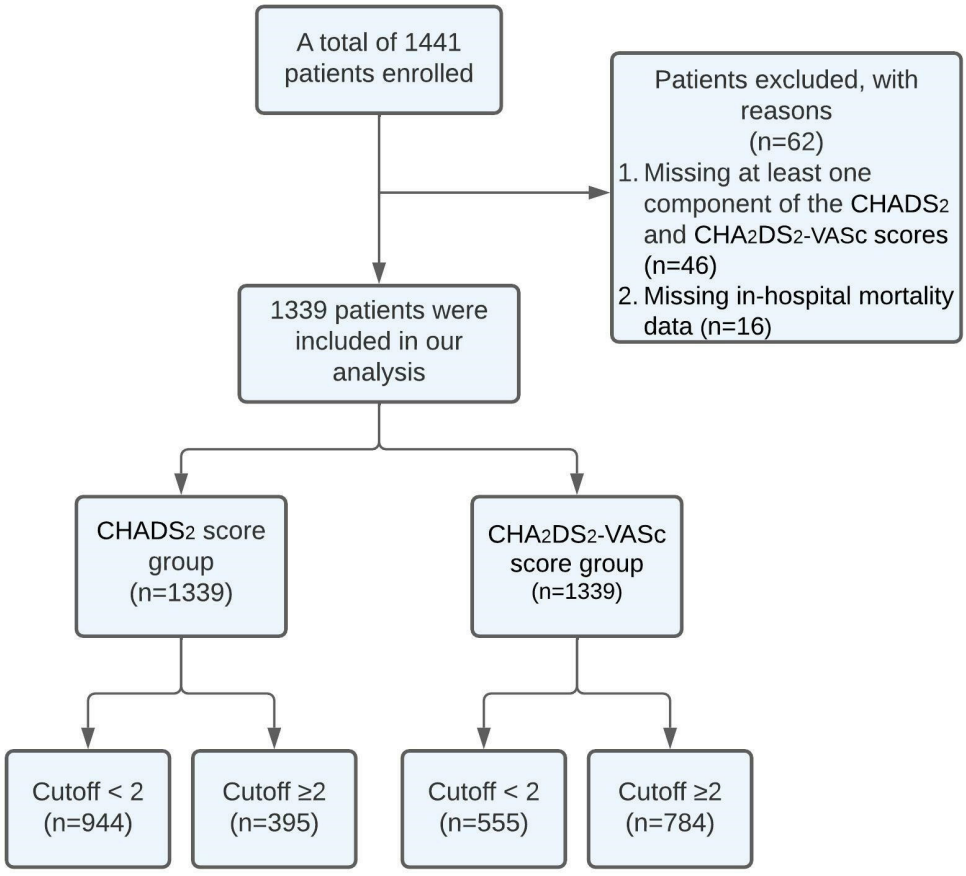

Figure 1. Patient selection process for this study. .

between $CHADS_2$ and CHA_2DS_2-VASc score and in-hospital mortality was evaluated using binary logistic regression analysis with the backward method according to each cutoff. Multivariate analysis was performed by adjusting several confounding factors with a p-value <0.25 based on univariate analysis. Statistical results were presented as odds ratio (OR) with a 95% confidence interval (CI) and a p-value. We used two-tailed p values with a significance set at ≤ 0.05. Receiver operating characteristics (ROC) analysis was also performed to assess the accuracy of these scoring systems in predicting in-hospital mortality. The area under the curve (AUC) between the two scoring systems was compared using De Long's method. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY).

Result

Participants' baseline characteristics

From January 2018 until December 2021, a total of 1441 ACS patients were enrolled in this study. However, 62 patients were excluded because of missing data. Therefore, 1339 patients were included in this study. These participants had a median age of 58 (50.5-65.5), 315 (23.5%) participants were female, and the total in-hospital mortality calculated for all participants was 162 (12.1%). The patients' selection process is described in **Figure 1.**

The baseline characteristics of participants that stratified by scoring system score were presented in **Table 1.** In the CHA_2DS_2-VASc group (score ≥2 vs <2), compared to those who had a low score, patients with

Table 2. Odds ratios for in-hospital mortality according to CHADS2 and CHA2DS2-VASc scores.

Variable	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
CHA_2DS_2-VASc score	1.45 [1.30,1.61]	<0.001	1.43 [1.18,1.75]	<0.001
CHA_2DS_2-VASc ≥2 vs <2	2.56 [1.75,3.75]	<0.001	3.39 [1.73,6.64]	<0.001
$CHADS_2$ score	1.57 [1.31,1.87]	<0.001	1.64 [0.90,2.96]	0.104
$CHADS_2$ ≥2 vs <2	2.05 [1.47,2.87]	<0.001	1.31 [0.92,1.86]	0.129

OR: odds ratio; CI: confidence interval.

Table 3. Odds ratios for in-hospital mortality according to CHADS2 and CHA2DS2-VASc components.

Variable	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age 65-74	1.88 [1.30,2.73]	0.001	0.97 [0.48,1.94]	0.925
Age ≥ 75	3.93 [2.50,6.16]	<0.001	2.18 [0.77,6.14]	0.142
Female	1.87 [1.32,2.66]	<0.001	0.62 [0.27,1.43]	0.259
Hypertension	1.31 [0.92,1.87]	0.128	2.01 [1.07,3.77]	0.030
Type II DM	1.44 [0.99,2.09]	0.055	0.66 [0.34,1.31]	0.238
Prior MI	1.33 [0.95,1.86]	0.099	1.93 [1.10,3.37]	0.022
Prior PAD	1.99 [0.89,4.41]	0.086	2.06 [0.55,7.69]	0.284
Prior HF	1.76 [1.21,2.56]	0.003	1.23 [0.63,2.41]	0.537
Prior cerebrovascular disease	2.22 [1.33,3.72]	0.002	1.78 [0.76,4.22]	0.187

OR: odds ratio; Cl: confidence interval; DM: diabetes mellitus; MI: myocardial infarction; PAD: peripheral artery disease; HF: heart failure.

a high score were older (p<0.001) and had higher of female participants (37% vs 4.5%;p<0.001) and former smoker (15.7% vs 11.7%;p=0.039) but surprisingly had lower of current smoker (47.3% vs 77.1%; p<0.001). The incidence of several comorbidities including hypertension (82.4% vs 35.9%; p<0.001), type II DM (32.4% vs 5.8%;p<0.001), dyslipidemia (23.1% vs 12.6%;p<0.001), MI (50.5% vs 10.1%; p<0.001), prior PAD (4.8% vs 0%; p<0.001), HF (30.9% vs 2.5%;p<0.001) and cerebrovascular disease (9.1% vs 4.3%;p=0.001) were greater in high score group. Participants with a high score were more frequently admitted with congestion (34.9% vs 18.4%;p<0.001), Killip II (20.3% vs 10.1%;p<0.001), Killip III & IV (15.4% vs 9.5%; p=0.002), NSTEMI (42.7% vs 24%;p<0.001), UAP (8.3% vs 2.3%;p<0.001), underweight (3.7% vs 1.8%;p=0.042), obese class II (8.3% vs 5.2%;p=0.031), and had higher levels of SBP (p<0.001) and heart rate (p<0.001). Regarding laboratory findings, the ureum (p<0.001) and creatinine levels (p=0.001) were greater in the high CHA_2DS_2-VASc score group, whilst hemoglobin (p<0.001), hematocrit (p<0.001), leukocyte (p<0.001), and troponin levels were greater in low score group. Drug administration during hospitalization was not significantly different between the two groups. Moreover, participants with high scores were less frequently treated with fibrinolytic (8.8% vs. 13.5%;p<0.001) and PCI (58.2% vs. 68.3%;p<0.001).

In the $CHADS_2$ group (score ≥2 vs. <2), participants with high scores were older (p<0.001), and more frequently female (36.2% vs 18.2%;p<0.001), and former smokers (18% vs 12.4%; p<0.01) but lower of current smoker (66.3% vs 43.8%;p<0.01). The prevalence of several comorbidities at the baseline including hypertension (93.7% vs 50.3%; p<0.001), DM (56.5% vs 6.7%;p<0.001), dyslipidemia (27.1% vs 15.3%;p<0.001), MI (46.1% vs 28.6%;p<0.001), PAD (7.6% vs 0.9%; p<0.001), HF (53.4% vs 4.8%;p<0.001), and cerebrovascular disease (10.4%

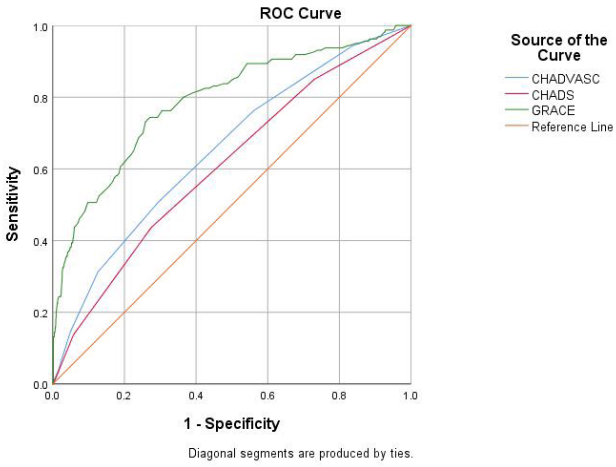

Figure 2. Results of ROC analysis.

vs 5.7%;p<0.001) were higher in high score group. At admission, participants with a high score were more likely to present with congestion (42.3% vs 22.1%;p<0.001), Killip II (26.8% vs 11.5%;p<0.001), Killip III and IV (16.7% vs 11.4%;p<0.001), NSTEMI (46.3% vs 30.2%;p<0.001), UAP (7.8% vs 5%;p=0.041) and had higher levels of SBP (p<0.001) and heart rate (p=0.002). The low score group was more likely to get statin administration (97.9% vs. 96%;p=0.014) and undergo PCI procedure (65.1% vs. 55.7%;p<0.001).

The association between CHADS2 and CHA2DS2-VASc scores with in-hospital mortality in ACS patients

Univariate analysis showed that the CHA_2DS_2-VASc score was significantly associated with in-hospital mortality in ACS patients (OR = 1.45 [1.30,1.61] ; p < 0.001). Multivariate analysis showed that statistical significance remained (OR = 1.43 [1.18,1.75] ; p < 0.001) after adjusting several potential confounding factors, including smoking status, prior obstructive pulmonary disease, congestion at admission, Killip classification, ACS types, BMI, SBP, DBP, heart rate, all laboratory findings, the use of DAPT, anticoagulant, nitrate, BB, ACE-I, and PCI procedure. Odds ratios for in-hospital mortality according to $CHADS_2$ and CHA_2DS_2-VASc scores were listed in **Table 2.**

The high CHA_2DS_2-VASc score (≥2) group was significantly associated with increased risk of in-hospital mortality in ACS patients compared to the low CHA2DS2-VASc score (<2) group in univariate analysis (OR=2.56[1.75,3.75];p<0.001). Moreover, the result becomes more significant with 3.39 odds ratios (OR=3.39[1.73,6.64];p<0.001) after adjustment for confounding factors,

Based on univariate analysis, the $CHADS_2$ score was significantly associated with higher in-hospital mortality risk (OR = 1.57[1.31,1.87] ; p < 0.001). However, $CHADS_2$ score was not significantly associated with in-hospital mortality (OR=1.64[0.90,2.96];p=0.104) after adjustment for several confounding factors including sex, smoking status, prior MI, prior PAD, prior obstructive pulmonary disease, congestion at admission, Killip III & IV, ACS types, BMI, SBP, DBP, heart rate, all laboratory findings, the use of DAPT, anticoagulant, nitrate, BB, ACE-I, and PCI procedure.

In univariate analysis, a higher $CHADS_2$ score (≥2) increased the risk of in-hospital mortality about two times higher compared to the lower one (OR=2.05[1.47,2.87];p<0.001), However, a higher $CHADS_2$ score was no longer associated with in-hospital mortality after performing the multivariate analysis (OR=1.31[0.92,1.86];p=0.129).

Additionally, we performed a univariate and multivariate analysis of every component of the $CHADS_2$ and CHA_2DS_2-VASc score. Among all components, age 65-74 years old (OR=1.88[1.30,2.73];p=0.001), age >75 years old (OR=3.93[2.50,6.16];p<0.001), female sex (OR=1.87[1.32,2.66];p<0.001), prior HF (OR=1.76[1.21,2.56];p=0.003) and prior cerebrovascular disease (OR=2.22[1.33,3.72];p=0.002) were significantly associated with increased risk of in-hospital mortality in univariate analysis. Furthermore, hypertension (OR=2.01[1.07,3.77];p=0.030) and prior MI (1.93[1.10,3.37];p=0.022) turned out to be significantly associated with in-hospital mortality after multivariate analysis was performed. Odds ratios for in-hospital mortality according to $CHADS_2$ and CHA2DS2-VASc scores components were described in **Table 3.**

Receiver operating characteristics (ROC) analysis of $CHADS_2$, CHA_2DS_2-VASc, TIMI, and GRACE risk scores in predicting in-hospital mortality in ACS patients

In the ACS population, ROC analysis demonstrated that $CHADS_2$, CHA_2DS_2-VASc, and GRACE risk scores were a good predictor of in-hospital mortality with the AUC of 0.609 (0.562-0.656), 0.653 (0.608-0.698), and 0.789 (0.748-0.830), respectively. This analysis showed that the predictive accuracy of CHA_2DS_2-VASc scores

was significantly higher compared to the $CHADS_2$ score ($p<0.001$) and significantly lower than the GRACE risk score ($p<0.001$). ROC analysis is described in **Figure 2**.

Discussion

The main results of this study can be concluded as follows: first, the incrementation of each CHA_2DS_2-VASc score is independently associated with a 1.43 times higher risk of in-hospital mortality in ACS patients. Second, the high CHA2DS2-VASc score (cutoff > 2) was independently associated with a 3.[39]-fold increased risk of in-hospital mortality in patients with ACS, whilst the $CHADS_2$ score was not independently associated with in-hospital mortality. Third, the CHA_2DS_2-VASc score was a good predictor of in-hospital mortality. Its predictive value was significantly higher compared to the $CHADS_2$ score but still significantly lower than the GRACE risk score.

$CHADS_2$ and CHA_2DS_2-VASc were previously known as risk stratification risk scores in AF patients.5,6 Nonetheless, it is reasonable to use this scoring system to predict ACS patients' mortality because each of its components was prognostic factors associated with increased mortality risk in ACS.[20,21] However, in this study, only hypertension and prior MI that independently associated with in-hospital mortality. Thus, although not all components of the CHA_2DS_2-VASc score independently increased the risk of mortality in this study, the combination of all these risk factors into one scoring system was confirmed to be useful in predicting in-hospital mortality in the ACS population.

A previous prospective cohort study conducted by Chua et al also provided a similar outcome to our study, which showed that the CHA_2DS_2-VASc score had better diagnostic performance compared to the $CHADS_2$ score in predicting the incidence of death in ACS patients.[12] However, a higher $CHADS_2$ score is still significantly associated with greater mortality risk after adjusting confounding factors in this study. In contrast, similar to our findings, a prospective cohort study by Ma et al. found that the $CHADS_2$ score was no longer associated with MACE after multivariate analysis.8 It may explain that the addition of three variables in CHA_2DS_2-VASc score, including age 65-74 years, female sex, and vascular disease (MI, PAD, or aortic plaque), were significant risk factors of mortality in ACS.[20,22] However, in this study, only prior MI was independently associated with in-hospital mortality.

Interestingly, this cohort showed that revascularization therapy was performed less often in the high CHA_2DS_2-VASc score group compared to the low scores group. This result is the same as that of Rozenbaum et al. and Chua et al. studies.[11,12] These studies showed that coronary intervention was significantly lower in the higher CHA_2DS_2-VASc score group. It may be caused by patient-related factors, including patient preference, vulnerability, functional and mental status, or clinician-related factors, including misjudgment of patient risk at baseline. However, since patient factors are fixed, the CHA_2DS_2-VASc score can help clinicians determine the best management approach for patients with ACS based on the CHA_2DS_2-VASc score (cutoff ≥2) as an additional scoring system to support the GRACE risk score.

The European Society of Cardiology (ESC) guideline recommends early risk stratification in ACS patients using the GRACE risk score to plan the appropriate treatment.[16] However, unlike the GRACE risk score that required the electrocardiographic and laboratory findings to complete the calculation, the CHA_2DS_2-VASc score can be completed only through anamnesis, which was more convenient and feasible to use in the clinical setting, especially in primary health care facilities in a rural area which had lack of ancillary test. Thus, despite having less predictive value than the GRACE risk score, the CHA_2DS_2-VASc score may be a more practical model for early risk stratification in ACS patients.

Our study has several limitations. First, this study was limited by a single-center retrospective cohort study with all the shortcomings. Second, our center is the highest referral hospital in West Java; therefore, adverse events that could be potential confounders from previous hospitals were not recorded. Third, this study only included Indonesian populations, which does not reflect the racial heterogeneity of the global ACS population. Therefore, prospective multicentre cohort studies with larger numbers of participants, multi-ethnicity, and long-term duration follow-up are needed to understand better the association of $CHADS_2$ and CHA_2DS_2-VASc scores with mortality risk in ACS patients.

Conclusion

In ACS patients, a high CHA_2DS_2-VASc score (cutoffs ≥ 2) is independently and significantly associated with an increased risk of in-hospital mortality. Despite its lower predictive accuracy compared to the GRACE risk score, the CHA_2DS_2-VASc score still has a potential role in predicting in-hospital mortality, especially in primary healthcare settings located in rural areas that lack the necessary facilities. However, the importance of ECG and troponin measurements is not replaceable to truly predict the risk of mortality in ACS patients.

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