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## Predicting the Likelihood for Severe CAD and CABG Indication on Elective Patients: Comparison of Novel CHA2DS2-VASc-HSF with CHA2DS2 and CHA2DS2-VASc Score

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## Predicting the Likelihood for Severe CAD and CABG Indication on Elective Patients: Comparison of Novel CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF with CHA<sub>2</sub>DS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub> -VASC Score

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**Abstract.** Abundant scoring systems are available to assess the severity of coronary artery disease (CAD) and its intervention. However, the majority of them require advanced technologies. CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF is a novel and simple risk scoring, easily used for screening in primary care level. We hypothesize that CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF is predictive for severe CAD and indicative for coronary artery bypass grafting (CABG). Additionally, we compared its predictive value with CHA<sub>2</sub>DS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC score. A total of 210 consecutive patients who underwent elective coronary angiography were enrolled in our study. Anthropometric, laboratory, angiographic findings, and patient history were obtained from medical records and used to calculate CHA<sub>2</sub>DS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VASC, and CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF score. Severe CAD is defined as Gensini Score >20. CABG indication was defined based on Class I recommendation from the American Heart Association (AHA). Statistical analyses were done using SPSS 25.0. Receiver operating characteristic (ROC) curve analysis showed the CHA<sub>2</sub>DS<sub>2</sub> score (AUC [Area Under the Curve], 0.630; 95% CI, 0.555–0.706; p = 0.001), CHA<sub>2</sub>DS<sub>2</sub>-VASC score (AUC, 0.680; 95% CI, 0.608–0.752; p=0.000), and CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF score (AUC, 0.785; 95% CI, 0.723–0.846; p=0.000) were predictive of severe CAD. CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF score (AUC, 0.841; 95% CI, 0.711–0.971; p=0.00) were predictive of CABG indication. The CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF score provides the highest predictive value for severe CAD and CABG indication compared to the CHA<sub>2</sub>DS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC score, suggesting that CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF score may be used in primary care settings to suggest referral for coronary angiography and predict CABG possibilities.

### 1. Introduction

Coronary artery disease (CAD) remains the top cause of mortality and morbidity for a person aged 35 worldwide [1,2]. Failure to detect CAD and provide early treatment may cause CAD treatment to





become more expensive and higher mortality rate [2]. It is estimated that around one-third of middle aged population in the USA will suffer from CAD manifestation [3]. In Indonesia, the Indonesian Ministry of Health also showed that CAD is the leading cause of morbidity, responsible for 12.9% of deaths [4].

Determining the best risk factor assessment for CAD is extremely important for early prevention and treatment. Screening for CAD using angiography is easily available in the developed countries with short waiting lists. However, in the developing countries, the awareness and accessibility of the cardiovascular disease screening is still low [5]. To obtain cost-effective prevention and treatment of CAD at the patient level, stratification of the cardiovascular risk using simple method is crucial. Cardiovascular risk screening will have a relevant implication for decision-making in early referral and healthcare resource allocation [6].

Currently, CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC score have been established as clinical predictors for cardiac thromboembolism and indication of antithrombotic therapy [7]. Both CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC component has similarities with the risk factors of CAD development [8]. The components within the CHADS<sub>2</sub> score also have proven in large cohort studies to be associated with CAD in with ischemic stroke patients [9]. CHA<sub>2</sub>DS<sub>2</sub>-VASC is the refinement of CHADS<sub>2</sub> score which has been proven to outperform its predecessor in the various patient groups, including AF patient who received elective electrical cardioversion [10]. This suggests CHA<sub>2</sub>DS<sub>2</sub>-VASC score may predict the risk for both cerebrovascular and cardiovascular diseases. However, these scores did not include the major risk factors of CAD, such as smoking, hyperlipidemia and family histories. Hence, this research aims to improve the validity of the CHA<sub>2</sub>DS<sub>2</sub>-VASC score by including new major risk factors of CAD which are Hyperlipidemia (H), Smoking (S) and Family history of CAD (F) and compare it with the previous CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC scores to predict severe CAD and indication of CABG in the patient.

## 2. Methods

### 2.1 Study Design

This cross-sectional study involves 210 consecutive patients who came to the outpatient department in Ramelan Navy Hospital, Surabaya, during January-December 2018. All participants were subjected to diagnostic coronary angiography for screening purposes. Coronary artery occlusion was assessed from angiograms using the Gensini score. Patients with infectious processes within two weeks before catheterization, hepatic dysfunction, thyroid dysfunction, cancer, and chronic kidney disease were excluded from the study. This study received ethical clearance (No.06/EC/KERS/2019) from the local ethics committee. Informed consents were obtained and details which disclosed patient's identity were omitted.

### 2.2 Risk Factor Data Collection

Clinical findings, 12-lead electrocardiogram, and echocardiographic examination were performed based on the American Society of Echocardiography guidelines [11]. The standard laboratory was performed to measure the fasting blood glucose, total cholesterol and renal function tests from the blood samples [12]. CHA<sub>2</sub>DS<sub>2</sub>-VASC-HSF scores, which consist of Congestive cardiac failure (C), Hypertension (H), Age >75 years (A), Diabetes Mellitus (D), Stroke (S), Vascular diseases (V), Age 65-74 years (A), Sex Category (Sc), Hyperlipidemia (H), Smoking (S) and Family history of cardiovascular disease (F), were obtained by thorough examination of medical records. Congestive cardiac failure (C) score was given if left ventricular ejection fraction was reduced (<45%) from echocardiography examination. Hypertension (H) was defined as systolic blood pressure >140mm Hg or diastolic <90mm Hg for repeated measurement, or when the patient was taking antihypertensive medications. Diabetes mellitus (D) type 2 was defined by fasting blood glucose >126mg/dl, previous diabetes diagnosis or when the patient was taking antidiabetic medications. Stroke (S) was defined as the history or current diagnosis of stroke or TIA which was given by the patients. Vascular disease (V)

was defined from the existence of a pathologic condition which causes stenosis of at least 50% in the non-coronary artery. Hyperlipidemia (H) was defined as cholesterol level of more than 200mg/dL based on the National Cholesterol Education Program or when the patient was consuming of lipid-lowering medications. Cigarette smoking (S) was defined as the habit of smoking of more than five cigarettes per-day without a quit attempt for a minimum of one year. Family history of cardiovascular disease (F) was defined as the presence of cardiovascular disease or sudden cardiac-related death of a first degree-relative.

### 2.3 Coronary Angiography and Gensini Scoring

Judkins technique 4 with 5-F catheters was used to perform cannulation of coronary arteries. Kodak 35mm cinefilm was used to record the images at 30 frames/second. Computer-assisted coronary angiography analysis system was used to detect coronary stenosis (Mipron 1; Kontron, Tokyo, Japan). One minute after the injection of ISDN (2.5mg/5mL for 20 s) through the Judkins catheter, several projections were taken to observe the coronary angiography. Coronary atherosclerosis severity was measured using the Gensini scoring method as described previously [12].

Calculation of the Gensini score was done for each patient through severity score assignment based on coronary occlusion. Narrowing between 1-25% will be scored 1, 26-50% will be scored 2, 51-75% will be scored 3, 75-90% will be scored 8, 91-99% will be scored 16 and 100% will be scored 32. The score is then multiplied based on the location and importance of the artery. We multiply by factor 5 for left main coronary artery occlusion, 2.5 for both proximal circumflex artery and proximal left anterior descending artery, 1.5 for a mid-left anterior descending artery, and 1 mid or distal circumflex artery, for distal left anterior descending artery, and the right coronary artery. The multiplication factor for any other branch is 0.5 [3].

### 2.4 Statistical Analyses

Data analyses were performed using SPSS Statistics 25.0 and MedCalc 18.2.1. Continuous variables, presented as mean±SD, were compared using ANOVA test. Correlation between parametric variables was obtained using Spearman's rho followed by logistic regression. Specificity and sensitivity were obtained from the ROC curve and cutoff point analysis. AUC comparison was done using pairwise comparison as described previously [13].

## 3. Results

### 3.1. Clinical Characteristics of the Patients

A total of 210 patients were involved in this study. Table 1 shows the characteristics of the participants grouped based on the CAD severity. Of the 210 patients, 70 patients had normal angiogram (Gensini score=0, 33.3%), 48 patients had mild CAD (Gensini score=1-19, 22.9%) and 92 patients had obstructive/severe CAD (Gensini score >20, 43.8%) The comparison of the baseline demographics and characteristics of the three groups (normal coronary arteries, mild CAD, and severe CAD) are presented in Table 1.

**Table 1:** Characteristics of the patients based on CAD severity.

Variables	CAD Severity			P value
	Normal Angiogram (n=70)	Mild CAD (n=48)	Severe CAD (n=92)	
Age (years)	50.97±8.95 <sup>b,c</sup>	53.87±10.90 <sup>a</sup>	54.65±9.13 <sup>a</sup>	≤0.001
SBP (mmHg)	131.81±26.17	123.00±16.67	130.90±23.05	0.691
DBP (mmHg)	72.81±10.86	76.53±9.12	77.58±9.23	0.463



Weight (kg)	69.48±12.43	65.27±7.70	70.03±9.88	0.369
Height (m)	164.06±8.59	164.33±3.90	165.45±5.79	0.208
BMI (kg/m <sup>2</sup> )	25.67±3.26	24.22±3.28	25.55±3.15	0.341
Hb (g/dL)	14.01±1.11	13.63±1.73	14.60±3.75	0.474
WBC (cells/ $\mu$ L)	7434.2±1725.5	6746.0±1624.1	7350.1±2108.5	0.292
HCT (%)	41.63±3.64	41.20±4.89	42.46±4.36	0.897
Platelet (x 10 <sup>3</sup> cells/ $\mu$ L)	273.00±78.55	271.66±47.73	258.12±52.97	0.268
PT (seconds)	13.31±1.28	13.56±2.67	13.56±3.46	0.301
APTT (seconds)	32.56±3.23	31.33±6.19	33.39±5.27	0.097
FBG (mg/dL)	108.06±37.97 <sup>a</sup>	114.13±32.82	112.45±34.39 <sup>a</sup>	0.032
Ureum (mg/dL)	12.45±3.15 <sup>b,c</sup>	16.81±5.20 <sup>a</sup>	16.45±7.70 <sup>a</sup>	0.005
Creatinin (mg/dL)	1.00±0.31 <sup>b,c</sup>	1.27±0.25 <sup>a</sup>	1.16±0.26 <sup>a</sup>	0.005
Ejection Fraction (%)	57.65±18.31	64.73±5.96	52.15±16.85	0.474
CHADS <sub>2</sub> Score	0.68±0.65 <sup>b,c</sup>	0.60±0.99 <sup>a</sup>	1.08±0.94 <sup>a</sup>	≤0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc Score	1.32±0.83 <sup>b,c</sup>	1.47±1.06 <sup>a</sup>	1.95±1.04 <sup>a</sup>	≤0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc-HSF Score	2.06±0.77 <sup>b,c</sup>	2.33±1.23 <sup>a,c</sup>	3.43±1.20 <sup>a,b</sup>	≤0.001

SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BMI, Body Mass Index, Hb, Hemoglobin; WBC, White Blood Cells; HCT, Hematocrit; PT, Prothrombin time; APTT, Activated partial thromboplastin time; FBG, Fasting Blood Glucose. Values are presented as a mean  $\pm$  standard deviation; different annotation showed a significant difference ( $p < 0.05$ ) for the post-hoc LSD test to: normal angiogram (a), mild CAD (b) and severe CAD (c).

From Table 1, significant differences between severe CAD and normal angiography group were observed on the age, Fasting Blood Glucose (FBG), ureum and creatinin, which are the CAD risk factors. CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VASc, and CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF scores were also significantly higher in patients with severe CAD compared to patients with normal angiography.

### 3.2. Correlations between Multiple Variables with CAD Severity

**Table 2:** Spearman's correlations between various independent variables with CAD Severity marked with Gensini score.

Variables*	Correlation Coefficient (r)
Age (years)	0.276**
FBG (mg/dL)	0.180*
Ureum (mg/dL)	0.232**
Creatinin (mg/dL)	0.204**
WBC	0.236**
Ejection Fraction (%)	-0.215**
CHA <sub>2</sub> DS <sub>2</sub>	0.315**
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.395**
CHA <sub>2</sub> DS <sub>2</sub> -VASc-HSF	0.612**

FBG, Fasting Blood Glucose; WBC, White Blood Cells;

\*: significant correlation at  $p < 0.05$ , \*\*: significant correlation at  $p < 0.01$

The correlation test was used to identify the factors associated with severity of CAD. Table 2 shows the results of Spearman's correlations between Gensini score and multiple independent variables in the subjects. Spearman's correlation analysis showed that the highest correlation was identified on the CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF score with Gensini score, which showed moderate to strong correlation ( $r = 0.612, p = \leq 0.001$ ).

### 3.3 Logistic Linear Regression Analysis of the Variables to Predict Severe CAD

**Table 3:** Univariate regression analysis for the predictors of severe CAD

**Table 4:** Multivariate regression analysis for the predictors of severe CAD

Variables	Odds Ratio	95% CI	<i>P</i> value
<b>With CHADS<sub>2</sub> Score</b>			
Age (years)	1.017	0.985-1.049	0.298
FBG (mg/dL)	1.002	0.994-1.011	0.588
Ureum (mg/dL)	1.067	1.008-1.130	0.026
Creatinin (mg/dL)	2.828	0.893-8.960	0.077
CHADS <sub>2</sub> Score	1.572	1.009-2.345	0.046
<b>With CHA<sub>2</sub>DS<sub>2</sub>-VAsC Score</b>			
Age (years)	1.008	0.976-1.042	0.613
FBG (mg/dL)	1.002	0.994-1.010	0.601
Ureum (mg/dL)	1.065	1.006-1.129	0.032
Creatinin (mg/dL)	2.323	0.731-7.380	0.153
CHA <sub>2</sub> DS <sub>2</sub> -VAsC Score	1.569	1.098-2.240	0.013
Variables	Odds Ratio	95% CI	<i>P</i> value
Age (years)	1.036	1.007-1.066	0.013
SBP (mmHg)	1.003	0.992-1.015	0.585
DBP (mmHg)	1.015	0.990-1.042	0.242
BMI (kg/m <sup>2</sup> )	1.016	0.933-1.106	0.721
Hb (g/dL)	1.072	0.861-1.335	0.551
WBC (cells/ $\mu$ L)	1.000	1.000-1.000	0.676
HCT (%)	0.995	0.899-1.102	0.929
Platelet ( $\times 10^3$ cells/ $\mu$ L)	1.000	1.000-1.000	0.615
FBG (mg/dL)	1.009	1.001-1.017	0.024
Ureum (mg/dL)	1.103	1.045-1.164	$\leq 0.001$
Creatinin (mg/dL)	5.000	1.756-14.233	0.005
Ejection Fraction (%)	0.390	0.059-2.563	0.474
CHA <sub>2</sub> DS <sub>2</sub> Score	1.834	1.304-2.580	$\leq 0.001$
CHA <sub>2</sub> DS <sub>2</sub> -VAsC Score	1.962	1.455-2.644	$\leq 0.001$
CHA <sub>2</sub> DS <sub>2</sub> -VAsC-HSF Score	2.716	1.996-3.696	$\leq 0.001$

SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BMI, Body Mass Index, Hb, Hemoglobin; WBC, White Blood Cells; HCT, Hematocrit; PT, Prothrombin time; APTT, Activated partial thromboplastin time; FBG, Fasting Blood Glucose

With CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF Score

Age (years)	0.997	0.962-1.033	0.871
FBG (mg/dL)	0.997	0.989-1.006	0.516
Ureum (mg/dL)	1.065	0.998-1.137	0.056
Creatinin (mg/dL)	1.511	0.421-5.419	0.527
CHA <sub>2</sub> DS <sub>2</sub> -VAsC-HSF Score	2.540	1.794-3.595	0.002

FBG, Fasting Blood Glucose; CI, Confidence Interval

Univariate and multivariate logistic linear regression analysis was done on various variables in predicting the outcome (severe CAD) as presented in Table 3 and Table 4. The analysis from Tables 3 and 4 showed that CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VAsC, and CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF were significant predictors for severe CAD. *3.4 Specificity and Sensitivity Test Using ROC Curves*

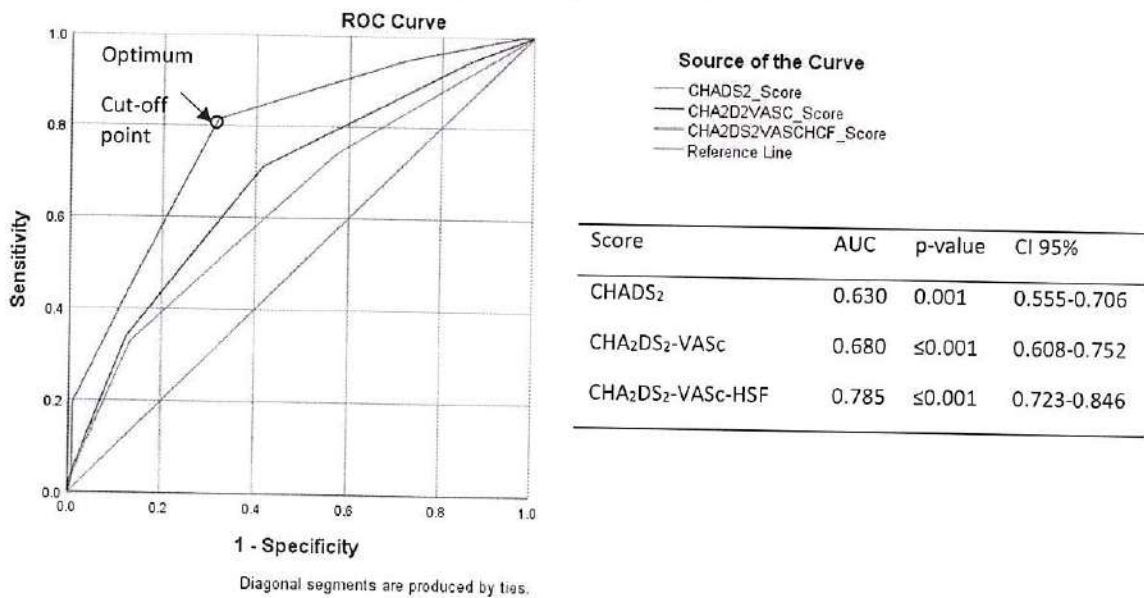


Figure 1: ROC curve of CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VAsC, and CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF score to predict severe CAD. AUC, Area Under the Curve; CI, Confidence Interval

**Table 5: Pairwise Comparison Between ROC Curves**

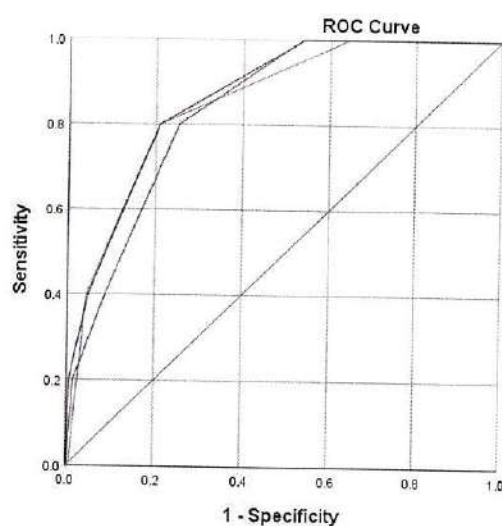
Variables	Differences	SE	95% CI	Z-	p-value
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	between areas			Statistic	
CHADS <sub>2</sub> and CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.0496	0.0227	0.0052-0.941	2.190	0.028
CHADS <sub>2</sub> and CHA <sub>2</sub> DS <sub>2</sub> -VASc-HSF	0.154	0.0320	0.0914-0.217	4.819	≤0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc and CHA <sub>2</sub> DS <sub>2</sub> -VASc-HSF	0.105	0.0255	0.0546-0.154	4.105	≤0.001

SE, Standard Error; CI, Confidence Interval

From the ROC curves in Figure 1, it is suggested that CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score have higher AUC compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc score. Optimum cutoff point analysis showed that the CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score  $\geq 2.5$  provided the highest predictive value for severe CAD (sensitivity = 81.4% and specificity = 68.1%). Pairwise comparison from Table 5 showed that the CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score was found to be the best scoring scheme to predict severe CAD compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc score.



#### Source of the Curve

- CHADS<sub>2</sub>\_Score
- CHA<sub>2</sub>DS<sub>2</sub>VASc\_Score
- CHA<sub>2</sub>DS<sub>2</sub>VAScHCF\_Score
- Reference Line

Score	AUC	p-value	CI 95%
CHADS <sub>2</sub>	0.854	0.007	0.709-0.999
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.867	0.005	0.739-0.996
CHA <sub>2</sub> DS <sub>2</sub> -VASc-HSF	0.841	0.009	0.711-0.971

Optimum cutoff point analysis showed that the CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score  $\geq 3.5$  provided the highest predictive value for CABG indication (sensitivity = 80.0% and specificity = 74.6%).

#### 4. Discussion

The major findings of this research were (1) CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score was significantly increased in both mild and severe CAD patients;(2) the CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VASc and CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF scores had positive and significant correlation with CAD severity measured by Gensini score;(3) CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VASc and CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF are significant predictors for severe CAD, with

the highest odds ratio found on the CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF score; (4) CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF was the best score to predict severe CAD with the cutoff point of  $\geq 2.5$ ; (5) CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF can predict severe CAD with the cutoff point of  $\geq 3.5$ .

The severe CAD may be fatal if remained undiagnosed and developed further into coronary total occlusion (CTO), which causes myocardial infarction. Hence, early detection of severe CAD is extremely important to prevent mortality and morbidity of the patients [3]. Coronary angiography is the gold standard to diagnose the severity of stable CAD; however, early coronary angiography screening is lacking in developing countries [14]. Hence, clinicians need reliable, simple, objective, and quantitative tools to identify these risk stratifications to refer the patient for early screening, modify the risk factor and provide early treatment [15]. Several scoring systems which involve major risk factors, such as European SCORE and Framingham risk score (FRS), have been developed to assess the risk of CAD [16]. FRS is the most widely used score and which estimates 10-year risk of developing CAD risk. However, this score cannot assess the severity of CAD. Furthermore, FRS also overestimates cardiovascular mortality rates in a low-risk population and underestimates it at the high-risk populations [17,18]. Because of its multiplicity and complexity, FRS, SCORE and other scoring system are considered to be impractical for daily use for primary care physicians [19, 20]. Hence, alternative scoring, such as that of CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VAsC and CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF, may offer a better alternative which is easy to be applied by the physician without any additional cost.

This study showed that CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VAsC, and CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF as having a positive and significant correlation with CAD severity measured by Gensini score. The highest correlation was found in the CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF score. This was in accordance with previous research that showed both CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VAsC score are significantly correlated with the Gensini score with almost similar r-value ( $r = 0.383, p < 0.001$ ;  $r = 0.300, p = 0.001$ ) [15]. When CHA<sub>2</sub>DS<sub>2</sub>-VAsC score was modified by adding hyperlipidemia (H) and smoking (S), a stronger and significant correlation was found between CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HS score and Gensini score ( $r=0,813, p<0.001$ ) [21]. Similar to this research, CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF also have a stronger and significant correlation with severity of CAD measured by syntax score in NSTEMI patients compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VAsC [22]. This suggested that CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF score has a superior association with CAD severity compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VAsC scores.

We investigated whether the CHADS<sub>2</sub>-VAsC-HSF scores could help clinicians to predict the patient who has higher odds of severe CAD and which needs immediate diagnosis and treatments. This research showed that CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF has the highest odds ratio to predict severe CAD compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VAsC. Previously, the CHADS<sub>2</sub> score, as one of the rapid and very practical scores for risk stratification for thromboembolism, was also shown able to predict CAD in ischemic stroke patients [23]. Development of CHADS<sub>2</sub> into CHA<sub>2</sub>DS<sub>2</sub>-VAsC score also has been shown to have better predictive power for long-term mortality for patients with severe CAD [24]. This suggested that the improvement of CHA<sub>2</sub>DS<sub>2</sub>-VAsC into CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HSF may provide a better prediction for the odds of having severe CAD.

The CHADS<sub>2</sub> score is considered as rapid, wide ranged and very practical for risk stratification for thromboembolism, which was also developed to predict CAD in ischemic stroke patients [23]. CHA<sub>2</sub>DS<sub>2</sub>-VAsC is the development of CHADS<sub>2</sub> score, which showed better predictive power for long-term mortality for patients with CAD [24]. When compared with TIMI, GRACE score, CHA<sub>2</sub>DS<sub>2</sub>-VAsC showed the capability to predict severe CAD measured by syntax score [25]. Modification of CHA<sub>2</sub>DS<sub>2</sub>-VAsC into CHA<sub>2</sub>DS<sub>2</sub>-VAsC-HS score has also been shown to improve its predictive value for severe CAD compared to both CHADS<sub>2</sub> into CHA<sub>2</sub>DS<sub>2</sub>-VAsC with the sensitivity of 85.2% and specificity of 57.5% at the cutoff value of  $>2$  [13]. In this research, modification of



CHA<sub>2</sub>DS<sub>2</sub>-VASc into CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score also showed higher AUC area compared to both CHADS<sub>2</sub> into CHA<sub>2</sub>DS<sub>2</sub>-VASc score with the sensitivity of 81.4% and specificity of 68.1% at the cutoff value of >2.5. CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF has also been shown to be the best scoring scheme for severe CAD prediction compared to CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc score. This suggests that CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score is a better scoring method which can easily be used by a physician to screen patient with angina, which may require referral for coronary angiography and early treatment.

To predict the CABG indication, this research also showed that CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF is able to predict the likelihood of CABG indication at cutoff value of >3.5 with the sensitivity and specificity of more than 70%. Previous research showed that the prediction of CABG indication can be done using GRACE score. However, the sensitivity and specificity of GRACE score to predict CABG indication was only less than 70% [26]. Hence, it is suggested that CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF may be superior to previous scoring methods.

However, this study is not possible to be generalized since it only involved single-center as the source of data. This study also used consecutive samplings from all patients who were admitted for diagnostic coronary angiography. Hence, selection bias might occur. In the future, it is suggested to involve more cardiac centers and stratify the sample based on several factors, such as race and social status, to ensure the validity of the score among various demographic characteristics.

## 5. Conclusion

The CHA<sub>2</sub>DS<sub>2</sub>-VASc-HSF score provides the highest predictive value for severe CAD and CABG to suggest referral for coronary angiography and predict CABG possibilities.

## References

- [1]. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, Hong Y. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2008; **117**:e25.
- [2]. American Heart Association. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation* 2018; **137**:e67.
- [3]. Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. *Lancet* 1999; **353**:89.
- [4]. Ministry of Health Indonesia. 2015. *Indonesia: Sample Registration System 2014*. NIHRD Library Cataloguing in Publication Data. Available at <https://www.litbang.kemkes.go.id/wp-content/uploads/2017/10/final-report-SRS-2014.pdf>. Accessed on 20 March 2019
- [5]. Viktor Kočka. The coronary angiography – An old-timer in great shape. *Cor et Vasa* Volume **57**, Issue 6, December 2015, Pages e419-e424
- [6]. Modesti PA, Agostoni P, Agyemang C, Basu S, Benetos A, Cappuccio FP, Ceriello A, Del Prato S, Kalyesubula R, O'Brien E, Kilama MO, Perlini S, Picano E, Reboli G, Remuzzi G, Stuckler D, Twagirumukiza M, Van Bortel LM, Wafiq G, Zhao D, Parati G; ESH Working Group on Hypertension and Cardiovascular Risk in Low Resource Settings. Cardiovascular risk assessment in low-resource settings: a consensus document of the European Society of Hypertension Working Group on Hypertension and Cardiovascular Risk in Low Resource Settings. *J Hypertens*. 2014 May;**32**(5):951-60.
- [7]. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW; ACC/AHA Task Force Members. 2014. AHA/ACC/HRS Guideline for the



- Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2014 **64**: e1–e76.
- [8]. Henriksson KM, Farahmand B, Johansson S, Asberg S, Terént A, Edvardsson N. Survival after stroke — the impact of CHADS2 score and atrial fibrillation. *Int J Cardiol*, 2010; 141: 18–23.
- [9]. Loh E, Sutton MS, Wun CC, Rouleau JL, Flaker GC, Gottlieb SS, Lamas GA, Moye LA, Goldhaber SZ, Pfeffer MA. Ventricular dysfunction and the risk of stroke after myocardial infarction. *N Engl J Med*. 1997;**336**:251–257
- [10]. Yarmohammadi H, Varr BC, Puwanant S, Lieber E, Williams SJ, Klostermann T, Jasper SE, Whitman C, Klein AL. Role of CHADS2 score in evaluation of thromboembolic risk and mortality in patients with atrial fibrillation undergoing direct current cardioversion (from the ACUTE Trial Substudy). *Am J Cardiol*. 2012;**110**(2):222-26
- [11]. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005 Dec;**18**(12):1440-63.
- [12]. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;**18**:499e502
- [13]. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;**44**:837e845
- [14]. Zhao Y, Shaista M, Nathan D. Evidence for Coronary Artery Calcification Screening in the Early Detection of Coronary Artery Disease and Implications of Screening in Developing Countries. *Global Heart*; Volume 9, Issue 4, December 2014, Pages 399-407
- [15]. Cetin M, Cakici M, Zencir C, Tasolar H, Baysal E, Balli M, Akturk E. Prediction of coronary artery disease severity using CHADS2 and CHA2DS2-VASc scores and a newly defined CHA2DS2-VASc-HS score. *Am J Cardiol*. 2014; 113(6):950-956.
- [16]. Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. *Am Heart J* 1991;**121**:293e298.
- [17]. Menotti A, Puddu PE, Lanti M. Comparison of the Framingham risk function-based coronary chart with risk function from an Italian population study. *Eur Heart J* 2000;**21**:365e370.
- [18]. Onat A, Can G, Hergenç G, Küçükdurmaz Z, Ugur M, Yüksel H. High absolute coronary disease risk among Turks: involvement of risk factors additional to conventional ones. *Cardiology* 2010;**115**:297e306.
- [19]. Siontis GC, Tzoulaki I, Siontis KC, Ioannidis JP. Comparisons of established risk prediction models for cardiovascular disease: systematic review. *BMJ* 2012;**344**:e3318.
- [20]. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation* 2008;**117**:743e753.
- [21]. Gautam Naik, Saritha Sekhar, Mukund Prabhu, Gurpreet Singh, Aniketh Vijay, Muthiah Subrahmanian, K U Natarajan. Comparison of CHA2DS2-VASc-HS Score and Gensini Score to Predict Severity of Coronary Artery Disease. *Journal of Clinical and Diagnostic Research*. 2018 Jul, Vol-12(7): IC01-IC04

- [22]. Alaa Nabil Al-shorbagy, Montaser Mostafa Al-Cekelly, Ashraf Al-said Dwedar, Mohamed Hassan Soliman. The Predictive Value of Newly Defined CHA2DS2-VASC-HSF Score for Severity of Coronary Artery Disease in Non ST Segment Elevation Myocardial Infarction. Z.U.M.J. Vol. 24; No.4 July.;2018
- [23]. Poci D, Hartford M, Karlsson T, Herlitz J, Edvardsson N, Caidahl K. Role of the CHADS2 score in acute coronary syndromes: risk of subsequent death or stroke in patients with and without atrial fibrillation. *Chest*. 2012;141(6):1431-1440.
- [24]. Kim KH, Kim W, Hwang SH, Kang WY, Cho SC, Kim W, Jeong MH ; Other Korean Working Group in Myocardial Infarction Registry Investigators. The CHA2DS2- VASc score can be used to stratify the prognosis of acute myocardial infarction patients irrespective of presence of atrial fibrillation. *J Cardiol*. 2015;65(2):121-127
- [25]. Bozbay M, Uyarel H, Cicek G, Oz A, Keskin M, Murat A, Yildirim E, Karaca G, Ergelen M, Eren M. CHA2DS2-VASc score predicts in-hospital and long-term clinical outcomes in patients with st-segment elevation myocardial infarction who were undergoing primary percutaneous coronary intervention. *Clin Appl Thromb Hemost*. 2017;**23(2)**:132-138
- [26]. Shafiq A, Jang JS, Kureshi F, Fendler TJ, Gosch K, Jones PG, Cohen DJ, Bach R, Spertus JA. Predicting Likelihood for Coronary Artery Bypass Grafting After Non-ST-Elevation Myocardial Infarction: Finding the Best Prediction Model. *Ann Thorac Surg*. 2016 Oct;**102(4)**:1304-11.