The evaluation of the newly defined CHA2DS2-VASc-HSF score in the severity of coronary artery disease and short-term prognosis

CHA2DS2-VASc-HSF score and coronary artery disease

Sara Cetin Sanlialp1, Gokay Nar2
1Department of Cardiology, Servergazi State Hospital
2Department of Cardiology, Faculty of Medicine, Pamukkale University, Denizli, Turkey

Abstract
Aim: In this study, we aimed to evaluate the ability of the CHA2DS2-VASc-HSF score to predict short-term prognosis in acute coronary syndrome (ACS) patients.

Material and Methods: A total of 167 patients who underwent coronary angiography were included in this retrospective study. The patients were divided into two groups according to CHA2DS2-VASc-HSF: the low-score group (≤ 4 points) and the high score group (> 4 points). Primary and secondary endpoints were defined. CHA2DS2-VASc and GRACE scores were calculated, and the severity of coronary artery disease (CAD) was evaluated using SYNTAX I score (SSI).

Results: Patients in the high score group had increased CHA2DS2-VASc, GRACE scores and SSI. Also, in-hospital death and MACE within 30 days were more common in this group. There was a strong correlation between the CHA2DS2-VASc-HSF score and SSI (r=0.825, p<0.001). In the ROC analysis, CHA2DS2-VASc-HSF predicted in-hospital death and MACE within 30 days with cut off value 5.5 and 4.5, respectively (AUC= 0.803, p<0.001; AUC= 0.877, p<0.001). In multivariate binary logistic regression analysis, CHA2DS2-VASc-HSF, CHA2DS2-VASc, GRACE and age were independent predictors of short-term prognosis.

Discussion: We evaluated the role of the CHA2DS2-VASc-HSF score in CAD severity and short-prognosis, and we agree that this new score can be used to predict CAD severity and short-term prognosis in patients presenting with ACS.

Keywords
Cardiovascular disease; CHA2DS2-VASc-HSF Score; GRACE; Prognosis; SYNTAX I
Introduction
Acute coronary syndrome (ACS) including unstable angina (UA), ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI), is closely associated with morbidity and mortality [1]. Early risk stratification in ACS may be useful in predicting prognosis or in determining appropriate therapy options. Various risk scores have been developed to identify patients who may need more aggressive treatment and who may be at high risk for major adverse cardiovascular events (MACE). For risk stratification, the Global Registry of Acute Coronary Events (GRACE) or thrombolysis in myocardial infarction (TIMI) are generally preferred in clinical practice [2,3].

CHA2DS2 and CHA2DS2-VASc clinical scores for calculating the risk of cardioembolism in patients with non-valvular atrial fibrillation (NVAF). Also, these scores include traditional cardiovascular risk factors predisposing to coronary artery disease (CAD) [4,5]. Several studies have shown that these scores may predict the severity of CAD, peripheral artery disease (PAD) and the adverse cardiovascular outcomes in CAD patients [6,7]. In addition, Cetin et al. reported that a newly defined CHA2DS2-VASc-HS score, such as CHA2DS2, CHA2DS2-VASc, may indicate the CAD severity [8]. Recently, a new scoring system has been developed by adding hyperlipidemia, smoking, family history and, male gender instead of the female gender to the CHA2DS2-VASc score and has been shown to associate with CAD severity and complexity [9,10]. In addition, Kalyoncuoglu et al. showed that the performance of this score was successful in showing the long-term prognosis, similar to GRACE score, in NSTEMI patients [11]. However, to our knowledge, no studies have been reported on the relationship between CHA2DS2-VASc-HSF score and short-term prognosis, including in-hospital death and MACE within 30 days. Thus, in this study, we aimed to evaluate the role of the CHA2DS2-VASc-HSF score in determining CAD severity and short-term prognosis in patients with ACS.

Material and Methods
Study Design
In this retrospective observational study, medical records of 167 ACS patients who underwent coronary angiography with or without percutaneous coronary intervention (PCI) from January 2020 to July 2020 were analyzed using the hospital database. Malignancy, active infection, autoimmune disease, connective tissue disease, end-stage renal disease, coronary ectasia, myocardial bridging or vasospastic angina, severe liver disease and missing data in the analysis were determined as exclusion criteria. This study was approved by the Pamukkale University Faculty of Medicine Hospital Ethics Review Board in accordance with the Declaration of Helsinki, and all patients gave informed consent before enrolling in the study. (12/2020-24, protocol no: 10.150.1.90 /020-11760)

Data Analysis and Definitions
Each patient’s medical history, family pre-mature CAD history were reviewed. The physical examination, electrocardiographic findings, echocardiographic and laboratory data were analyzed. Medical history consisted of hypertension, diabetes, smoking history, chronic heart failure, stroke or transient ischemic attack (TIA), previous MI or CAD and PAD. The diagnosis of ACS was made in accordance with current clinical practice guidelines based on symptoms, electrocardiographic and imaging methods [12,13].

HT was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or under medical treatment. Diabetes was defined as fasting blood glucose ≥126 mg/dL or blood glucose at any time ≥200 mg/dL or antidiabetic drug use. Hyperlipidemia was defined as increased LDL-C level or lipid-lowering drug use according to the recommendations of the National Cholesterol Education Program-3. Family history was defined as the presence of a diagnosis of CAD in the first degree relative of a patient before age 65 years in women and 55 years in men. The ischemic cerebrovascular event was defined as TIA or ischemic stroke. Vascular disease was defined as a history of revascularization or MI, amputation or angiographic evidence of PAD. Chronic heart failure (HF) was defined as verification of identified signs and symptoms of HF using objective evidence of cardiac dysfunction. Current smoking was defined as >10 cigarettes per day for at least 1 year without any cessation attempt.

Risk Scoring and the evaluation of CAD severity
The patients were evaluated in terms of GRACE, CHA2DS2-VASc and CHA2DS2-VASc-HSF scores. The GRACE score, consisting of age, heart rate, systolic blood pressure, creatinine level, Killip class, ST deviation, cardiac biomarker, and cardiac arrest was measured for each patient. The CHA2DS2-VASc score was the sum of 1 point each for chronic HF, hypertension, diabetes, and vascular disease, 1 point for 65–74 years old, 2 points for >75 years old and prior stroke or TIA, and 1 point for the female gender. Compared to the CHA2DS2-VASc score, hyperlipidemia, smoking, family history of CAD and, male gender instead of female in the gender category were added to the newly defined CHA2DS2-VASc-HSF score, and these risk factors were scored as 1 point. Then the patients were divided into two groups as CHA2DS2-VASc-HSF score >4 points and score ≤4 points. Diagnostic angiogram views, previously recorded on digital media, were analyzed by experienced clinicians who were blind to the patients’ clinical and laboratory data. Significant CAD was defined as >50% narrowing of the lumen diameter in any of the main epicardial coronary arteries. CAD severity was evaluated using the SYNTAX I score (SSI). To calculate SSI, the online calculator (www.syntaxscore.com) was used for each lesion with ≥ 50% diameter stenosis in vessels ≥ 1.5 mm in diameter [14].

Study Endpoints
The primary endpoint of the study was in-hospital death and the secondary endpoint was MACE, including all-cause mortality, objective findings of coronary ischemia, recurrent MI, or unplanned revascularization in 30 days.

Statistical Analysis
SPSS v.17.0 for Windows (SPSS, Inc., Chicago, Ill., USA) was used for data analysis. Qualitative variables were shown as percentages (numbers), and quantitative variables were presented as mean ± SD. The Kolmogorov-Smirnov test was used to determine the normal distribution. Variables were evaluated based on normality distribution using Student’s t-test.
or Mann-Whitney U test. Categorical variables were compared using the x² test. The relationship between the variables was analyzed using the Pearson or Spearman correlation. Receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of the CHA2DS2-VASC-HSF score in predicting in-hospital mortality and MACE within 30 days. Multivariate binary logistic regression analysis was used to examine independent factors for clinical endpoints, and p<0.05 was considered statistically significant.

**Results**

The study population consisted of 118 patients with low scores (≤ 4) and 49 patients with high scores (>4) according to the CHA2DS2-VASC-HSF scoring model. Baseline characteristics and the clinical data, including laboratory, echocardiographic and angiographic parameters of the patients are listed in Table 1. Patients in the high score group were older and involved a higher percentage of the male gender, compared with the patients in the low-score group (for all p<0.05). Hypertension, diabetes, dyslipidemia, smoking, a history of any vascular disease, stroke or TIA, and heart failure were more common in the patients with high scores (for all p<0.05). However, the type of ACS did not differ between the groups.

In laboratory parameters, patients with a high score showed significantly increased levels of fasting glucose, creatinine and hemoglobin, however there were no significant differences in lipid parameters and white blood cell counts between the groups. LVEF was significantly lower in patients with high scores (p=0.008).

The medians of CHA2DS2-VASC and CHA2DS2-VASC-HSF in the patients with low and high scores were 2 vs 4 and 3.5 vs 6, respectively (for all p<0.001). In additional, there was a significant difference in the GRACE scores in the groups (110 vs 151, p<0.001). Hospital deaths occurred in 2% of patients with low score and in 14% of patients with high score (p<0.001). MACE within 30 days occurred in 3% and 22% of the patients with low and high scores, respectively (p<0.001). In the ROC analysis, the

---

**Table 1. Basic characteristics and clinical data of the study population divided into low-risk (≤ 4) and high-risk (> 4) groups based on the CHA2DS2 -VASC-HSF score**

| Variables | Low-score group (n=118) | High-score group (n=49) | p-value |
|-----------|-------------------------|-------------------------|---------|
| Age (median) | 63.50 | 78.00 | <0.001 |
| Male gender, n (%) | 74 (63) | 41 (84) | 0.006 |
| Hypertension, n (%) | 53 (45) | 37 (76) | <0.001 |
| Diabetes, n (%) | 36 (31) | 28 (57) | <0.001 |
| Dyslipidemia, n (%) | 16 (14) | 24 (49) | <0.001 |
| Smoking, n (%) | 33 (28) | 22 (45) | 0.034 |
| Family history, n (%) | 15 (13) | 15 (30) | 0.006 |
| Vascular disease history, n (%) | 7 (6) | 16 (33) | <0.001 |
| Stroke/TIA history, n (%) | 1 (0.8) | 5 (10) | <0.001 |
| Heart failure history, n (%) | 8 (7) | 16 (33) | <0.001 |
| UA, n (%) | 26 (22) | 8 (16) | 0.397 |
| NSTEMI, n (%) | 46 (39) | 21 (43) | 0.642 |
| STEMI, n (%) | 46 (39) | 20 (41) | 0.825 |
| GRACE (median) | 110.00 | 151.00 | <0.001 |
| CHA2DS2-VASC (median) | 2.00 | 4.00 | <0.001 |
| CHA2DS2-VASC-HSF (median) | 3.50 | 6.00 | <0.001 |
| In-hospital mortality, n (%) | 2 (2) | 7 (14) | <0.001 |
| MACE within 30 days, n (%) | 4 (3) | 11 (22) | <0.001 |
| Fasting glucose, mg/dL (median) | 123.50 | 175.00 | <0.001 |
| Creatinine, mg/dL (median) | 0.85 | 1.01 | <0.001 |
| TG, mg/dL (median) | 113.00 | 124.00 | 0.457 |
| TC, mg/dL (median) | 162.00 | 172.00 | 0.255 |
| HDL-C, mg/dL (median) | 106.84±31.47 | 118.61±26.23 | 0.475 |
| LDL-C, mg/dL (median) | 41.00 | 39.00 | 0.217 |
| Hemoglobin, g/dL (median) | 13.25 | 12.40 | 0.005 |
| WBC, cells/μL (median) | 9.43 | 10.08 | 0.111 |
| LVEF % (median) | 50.00 | 40.00 | 0.008 |
| SSI 20.24±12.38 | 28.46±9.67 | <0.001 |

**Figure 1.** Receiver operating characteristic (ROC) curves in predicting in-hospital mortality and MACE within 30 days
The cut-off value for in-hospital death was 5.5 with 88% specificity and 66% sensitivity, and the cut-off value for MACE within 30 days was 4.5 with 83% specificity and 80% sensitivity (AUC = 0.803, p<0.001; AUC= 0.877, p<0.001) (Figure 1).

The CAD severity was evaluated using SSI, and SSI more increased in the patients with CHA2DS2-VASc-HSF>4 (20.24±12.38 vs 28.46±9.67, p<0.001). When the patients were divided into three groups according to SSI; CHA2DS2-VASc-HSF, CHA2DS2-VASc and GRACE scores differed between low and intermediate tertile and low and high tertile. However, all scores were similar between intermediate and high tertile (Table 2, Figure 2). In addition, there was a strong correlation between CHA2DS2-VASc-HSF and SSI (r= 0.825, p<0.001) (Figure 2). In a binary multivariate logistic regression analysis, CHA2DS2-VASc-HSF, CHA2DS2-VASc, GRACE, age were found to be independent predictors for primary and secondary clinical endpoints (for all p<0.05). However, SSI score and LVEF were only independent predictors for in-hospital death (Table 3).

Discussion

The main findings of our study were as follows: (1) Patients with CHA2DS2-VASc-HSF score >4 had more common cardiovascular risk factors or a history of CVD. Also, LVEF was lower and CHA2DS2-VASc, GRACE scores were higher in this group; (2) CHA2DS2-VASc-HSF was strongly correlated with CAD severity identified by SSI; (3) Patients in the high CHA2DS2-VASc-HSF group showed a significant increase in in-hospital death and MACE within 30 days; (4) The cut-off values of CHA2DS2-VASc-HSF were 5.5 and 4.5 in hospital deaths and MACE within 30 days, respectively; (5) In a binary multivariate logistic regression analysis, CHA2DS2-VASc-HSF score was an independent predictor of in-hospital death and MACE within 30 days.

ACS may be fatal if undiagnosed early and is associated with a poor prognosis. Although coronary angiography is the gold standard to diagnose, unfortunately, the lack of angiography units in developing countries makes it difficult to access patients. Hence, easy-to-use and inexpensive assessment tools are needed in clinical practice to determine cardiovascular risk profiles in the patients and to modify risk factors [15,16]. The CHA2DS2-VASc score, which is used to stratify the risk for stroke in NVAF patients, includes risk factors that trigger atherosclerosis, such as hypertension, diabetes, and increasing age [8]. Studies have reported that increased CHA2DS2-VASc score may indicate the severity of CAD and may be associated with acute stent thrombosis [17,18]. Recently, CHA2DS2-VASc-HS and CHA2DS2-VASc-HSF scores, including hyperlipidemia, smoking, female gender instead of male gender and family story have been developed for more reliable determination of the severity of CAD [19]. In a study involving 2976 people in Northern India, CHADS2, CHA2DS2-VASc, CHA2DS2-VASc-HS and CHA2DS2-VASc-HSF scores were associated with increased GENSINI score and number of diseased vessels. In another study, there was a significant relationship between SSI with CHA2DS2-VASc and CHA2DS2-VASc-HSF in patients with STEMI [9,20]. In our study, patients with CHA2DS2-VASc-HSF score>4 had a high SSI score and had a strong correlation with the severity of CAD as assessed by SSI similar to these studies. Especially, when patients were divided into three groups according to SSI, there was a remarkable difference in CHADS2-VASc and CHA2DS2-VASc-HSF among those with medium and high SSI and those with low SSI.

The prognostic value of CHA2DS2-VASc has been evaluated in several studies in patients with CAD. Rozenbaum et al. showed that the increase of CHA2DS2-VASc was associated with in-hospital death, MACE within 30 days and increased 1-year all-cause mortality [21]. In another study, Bozbay et al.

| Variables | Low tertile | Intermediate tertile | High tertile | p-value |
|-----------|-------------|---------------------|-------------|---------|
| Variables | SSI<22 | 22<SSI<32 | SSI>32 |         |
| GRACE | 1.038 | 0.981 | 1.019 | 0.018 | 1.120 | 0.012 |
| CHA2DS2-VASc | 1.156 | 0.985 | 1.356 | 0.039 | 0.703 | 0.028 |
| CHA2DS2-VASc-HSF | 1.150 | 0.723 | 1.728 | 0.026 | 1.109 | 0.019 |
| SYNTAX I | 1.032 | 0.902 | 1.195 | 0.048 | 0.980 | 0.278 |
| Age | 0.998 | 0.919 | 1.062 | 0.035 | 0.946 | 0.037 |
| Fasting blood glucose | 1.003 | 0.998 | 1.009 | 0.266 | 1.005 | 0.634 |
| Creatinine | 0.203 | 0.44 | 0.941 | 0.223 | 7.038 | 0.536 |
| Hemogram | 0.855 | 0.591 | 1.235 | 0.641 | 1.527 | 0.793 |
| LVEF | 0.960 | 0.897 | 1.027 | 0.046 | 0.971 | 0.195 |

Table 2. Comparison of CHA2DS2-VASc, CHA2DS2-VASc-HSF, GRACE scores of the study population grouped based on SYNTAX I score

Table 3. Multivariate binary logistic analysis to predict in-hospital death and MACE within 30 days

LVEF, left ventricular ejection fraction
showed more in-hospital death occurred in patients with high CHA2DS2-VASc score, and CHA2DS2-VASc was an independent predictor of long-term cardiovascular mortality [17]. To our knowledge, the relationship between the CHA2DS2-VASc-HSF score and the short-term prognosis has not been previously evaluated. Similar to these studies, increased CHA2DS2-VASc and CHA2DS2-VASc-HSF scores were associated with in-hospital mortality and MACE in the first 30 days in our study, and this relationship remained after multivariate regression analysis. Recently Kalyoncuoğlu et al. reported that in-hospital death, one-year mortality and one-year adverse cardiovascular outcomes were significantly higher in patients with a CHA2DS2-VASc-HSF score> 4 compared to low-risk patients in NSTEMI [11]. In addition, the high-risk patients in this study showed an increased GRACE score similar to our study. But they emphasized that in-hospital mortality results were not certain due to the small number of patient deaths, and did not provide information about the first 30-days prognosis in this study. Moreover, they showed that one-year mortality and adverse cardiovascular events were higher in patients with high SSI. Although we found that high SSI was an independent predictor for in-hospital death, a significant correlation was not observed between SSI and MACE within 30 days, unlike this study. The difference between the study results may be due to the type of ACS, the characteristics of the study population, the number of patients treated with PCI, the heterogeneity in aggressive treatment options, and duration of follow-up. However, in a study in which NSTEMI patients were evaluated with CHA2DS2-VASc-HS, demonstrating severe CAD and an increase of in-hospital mortality in patients with high scores supports our study [22].

**Study Limitations**

There were several limitations in this study, such as a retrospective single-center design and a relatively small sample. However, the real-world unselected population was evaluated. Visual X-ray coronary angiogram was performed for SSI calculation based on luminal stenosis, and advanced imaging methods enabling a more detailed evaluation of CAD were not used. In addition, we aimed to investigate the short-term prognostic significance of the CHA2DS2-VASc-HSF score, so...
The CHA2DS2-VASc-HSF score was correlated with CAD severity and may be used to predict short-term prognosis. Using the CHA2DS2-VASc-HSF score, patients at high risk can be identified and more aggressive treatment strategies can be followed to reduce death and adverse cardiovascular events. In addition, multi-center prospective large-scale studies should be performed to clearly demonstrate the prognostic significance of the CHA2DS2-VASc-HSF score.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References
1. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. Eur Heart J. 2014;35(42):2950-9.
2. Fox KA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de Weer F, et al. Prediction of risk of death and myocardial infarction in the six months following presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ 2006;333(7578):1091.
3. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. JAMA. 2000;284(7):835-42.
4. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285(22):2864-70.
5. Lip GV, Nieuwlaat R, Pisters R, Lane AD, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. Chest. 2010;137(2):263-72.
6. Korkmaz L, Adar A, Erkan H, Agar MT, Acar Z, Kurt IH, et al. Ankle-brachial index and coronary artery lesion complexity in patients with acute coronary syndromes. Angiology. 2012;63(7):495-9.
7. Paci D, Hartford M, Karlsson T, Heritz J, Edvardsson N, Caldhoff K. Role of the CHA2DS2 score in acute coronary syndromes: risk of subsequent death or stroke in patients with and without atrial fibrillation. Chest. 2012;141(1):431-40.
8. Cetin M, Cakici M, Zencir C, Tasolar H, Baykal E, Balli M, et al. Prediction of coronary artery disease severity using CHADS2 and CHA2DS2-VASC and a newly defined CHA2DS2-VASc-HS Score. Am J Cardiol. 2014;114(6):950-6.
9. Modri R, Pietted SV, Halkati PC, Parwal S, Sammar S, Mr P et al. CHA2 DS -VASC HS score- New predictor of severity of coronary artery disease in 2976 patients. Int J Cardiol. 2017;228(1):1002-6.
10. Uysal OK, Turkoglu C, Duran M, Kayar MG, Sabih DY, Gur M, et al. Predictive value of newly defined CHA2 DS2 -VASC-HSF score for severity of coronary artery disease in ST segment elevation myocardial infarction. Kardiol Pol. 2016;74:954-60.
11. Kalysaonagouli M, Durmas G, Belen E, Can MM. Predictive Accuracy of the CHA2DS2-VASc-HSF Score in Determining One-Year Cardiovascular Outcomes in Patients with Non-ST-Elevation Acute Coronary Syndrome: A Retrospective Study. Kosyapuol Heart J. 2020;23(1):27-37.
12. Raffi M, Patrons C, Collet JP, Mueller C, Valimgiloni M, Andreotti F, et al. ESC Scientific Document Group. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2016;37(3):267-331.
13. Steg G, James SK, Atar D, Badano LP, Blom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33(20):2569-619.
14. Sianos G, Morel MA, Kappelet AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005;1(2):219-27.
15. Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. Lancet. 1999;353(9147):89-92.