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The Predictive Value of Newly Defined Cha_2ds_2-Vasc-Hsf Score for Severity of Coronary Artery Disease.

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ABSTRACT

CHADS2 and CHA2DS2-VASc scores have been proven to be effective for assessing prognostic risk of thromboembolism in non-valvular atrial fibrillation patients. A new score CHA2DS2-VASc-HSF was formulated to assess the risk of CAD. We evaluated these scores as multivariable risk assessment tools to determine the severity of CAD in all patients undergoing coronary angiography. To study the relation between CHA2DS2-VASC-HSF Score and severity of coronary artery diseases assessed by Syntax score. Across sectional study on two hundred patients with coronary artery disease who were underwent coronary angiography was included in the study between September 2017 and March 2018. This included fifty patients with chronic stable angina, fifty patients with unstable angina, fifty patients with non-ST segment elevation myocardial infarction (NSTEMI), and fifty patients with ST segment elevation myocardial infarction (STEMI). They were further divided into 2 groups according to Syntax score of severity (below or equal 22 and above 22).Cha2ds2-Vasc-Hsf Score was applied to all patients. This study showed a statistically high significant positive correlation between CHA2DS2-VASC-HSF score and Syntax score I of patients in the 4 groups ($r = 0.48, 0.45, 0.33, 0.47$, respectively; $p < 0.05$). Our study also showed a statistically significant negative correlation between CHA2DS2-VASC-HSF score and ejection fraction (EF %) of patients in the 4 groups ($r = -0.39, -2.4, -0.31, -0.38$, respectively, $p < 0.05$). There is a statistically significant positive correlation between CHA2DS2-VASC-HSF score and serum cholesterol levels of patients in the 4 groups ($r = 0.34, 0.52, 0.22, 0.28$, respectively; $P < 0.01$). A statistically highly significant positive correlation between CHA2DS2-VASC-HSF score and serum low density lipoprotein (LDL) levels of patients in the 4 groups ($r = 0.48, 0.6, 0.48, 0.48$, respectively; $p < 0.05$). CHA2DS2-VASC-HSF score predicts the severity of atherosclerosis in patients with coronary artery disease, is correlated with cholesterol and LDL levels, and inversely related to ejection fraction.

Keywords: CHA2DS2-VASC-HSF, severity, syntax, coronary, score, predictive.

Core tip: This is a cross sectional study of CHA2DS2-VASC-HSF score on two hundred patients with coronary artery disease who were underwent coronary angiography. Patients with chronic stable angina, unstable angina, non-ST segment elevation myocardial infarction, and ST segment elevation myocardial infarction are equally distributed. It showed a statistically significant positive correlation between CHA2DS2-VASC-HSF score and Syntax score I of patients. It also showed a negative correlation between CHA2DS2-VASC-HSF score and ejection fraction, and a positive correlation with serum cholesterol and serum LDL levels of patients.

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in the present world[1]. CAD was known for a long time as related to the luminal diameter of the epicardial coronary arteries. The main aim of research is to promote the capabilities of current medical practice in early detection, prevention and treatment of CAD [2]. The clinical presentation and assessment of the CAD is a corner stone in assessment of the critical patients[3]. Stable angina and acute myocardial ischemia are two face of the same coin of atherosclerosis but still have different outcomes[4].

Differentiation between isolated unstable angina and unstable angina with NSTEMI depends on levels of myocardial band (MB) fraction of serum creatine kinase (CK-MB). Although CK-MB is considered to be a fairly sensitive and specific marker for myocardial ischemia [5], it is not routinely measured in cases of unstable angina [4]. However, CK-MB could not achieve the desired accuracy [6]. The introduction of cardiac-specific troponin I [7] and cardiac specific troponin T [8] allow for more accuracy in clinical diagnosis and assessment [9].

CHADS2 score is a clinical tool that was proved to assess the risk, as well as to guide the treatment strategy, of stroke in cases of non-valvular atrial fibrillation. This score is proven to have a prognostic value for thromboembolic events in these cases. The update of CHA2DS2-VASc score adds finer stratification for low risk patients [2]. However, further update with more variables; i.e. hyperlipidemia (H), smoking (S) and family history of CAD(F), so-called CHA2DS2-VASc-HSF score, is considered for more refining of the assessment of patients at risk for CAD as regard the significant contribution of these factors in the risk of cardiovascular events [10].

These scores are widely used clinically. Their significance is related to predictionof risk of cardiac thromboembolism[11], risk of stroke or death after coronary artery bypass grafting (CABG) [12], risk of stroke and death in patients with stable CAD [13], risk of stroke and death in acute coronary syndrome [14], and risk of death after stroke [1].They also can help guide anti-thrombotic therapy [11]. The CHADS2, CHA2DS2-VASc, and CHA2DS2-VASc-HS scores can predict CAD severity using the Gensini score in patients who underwent diagnostic coronary angiography[15].

This study aim to investigate the association of CHA2DS2-VASc-HSF score with severity of coronary artery disease as assessed by Syntax Score (SxS) in patients with ischemic heart disease.

MATERIAL AND METHODS

Ethical consideration

Patients' data are manipulated confidentially. The formal consent was taken from all participants. The study was conducted under acceptance of the research ethics committee of College Of Medicine, Zagazig University.

Recruitment of participants

Two hundred patients who were undergoing coronary angiographyat Cardiology Department, Zagazig University Hospitals, since September 2017 to March 2018. Patients who had ischemic heart disease were included in this study. Patients with history of coronary artery bypass graft (CABG) surgery, severe renal or liver disease, infectious or inflammatory disease, previous or current neoplasm and hematological disorders are excluded. The sample was divided into 4 groups; group I: chronic stable angina, group II: unstable angina, group III: NSTEMI, and group IV: STEMI.

Data collection

The data collected include: complete history taking with special emphasis on age, sex, history of CAD, hypertension, diabetes mellitus, smoking, dyslipidemia, history of previous TIA or stroke, vascular diseases and family history of ischemic heart disease. Full general and local examination was done, with special emphasis on pulse rate, rhythm and blood pressure. Echocardiography was done. Fasting & random blood glucose level,

lipid profile (cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides (TG)) and coronary angiography.

The CHA2DS2-VASc-HSF score

The CHA2DS2-VASc-HSF score was formulated as follow, with maximum score of 12 points[10]:

- Heart failure (C) (1 point) (signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction).
- Hypertension (H) (1 point) (defined as measurements of systolic and diastolic blood pressure ≥ 140/90 mm Hg or having antihypertensive medications).
- Age; more than 75 years (A2)(2 points), from 65 to 74 years (A) (1 point).
- Diabetes mellitus (D) (1 point); defined as a fasting blood glucose level > 126 mg/dL or blood glucose ≥ 200 mg/dL or using hypoglycemic drugs.
- Previous ischemic stroke or transient ischemic attack (S2) (2 points).
- Vascular disease (V)(1 point); defined as myocardial infarction [MI] and peripheral artery disease including prior revascularization, amputation or angiographic evidence or aortic plaque.
- Female sex (Sc) (1 point).
- Hyperlipidemia (H)(1 point); defined as increased level of low density lipoprotein cholesterol (LDL-C) according to the National Cholesterol Education Program-3 recommendations and history of using lipid lowering medications.
- Smoking status (S)(1 point);defined as smoking > 10 cigarettes a day for at least one year without a quit attempt.
- Family history of CAD (F) (1 point); defined as MI before 55 years of age for men or 65 years of age for women in first-degree relatives**[10].**

Statistical analysis

Level of significance for all tests done, the threshold of significance was fixed as 5% level student t-test (t) and the probability (*P* value): P value of > 0.05 indicates non-significant results, P value of < 0.05 indicates significant results, P value of < 0.01 indicates highly significant results and P value of < 0.001 indicates very highly significant results.

RESULTS

Demographics of the study groups were homogenous. The mean (± SD) age of groups I, II, III, IV were 54.9 ± 9.2, 57.8 ± 7.0, 57.9 ± 7.7 and 54.6 ± 10.0 years respectively, with no significant difference in-between(P > 0.05). Male to female ratio was nearly matched. As males were presented by 56%, 64%, 74% and 80% in groups I, II, III and IV, respectively, without significant difference (P > 0.05).

In our study, cardiac signs and symptoms belong to CHA2DS2-VASc-HSF score is represented in (Table 1). The mean SYNTAX score of each group is shown in (Table 2), and the mean (± SD) of CHA2DS2-VASc-HSF score at each group is demonstrated in (Table 3). The ranges of CHA2DS2-VASc-HSF score at each group are also shown.

By calculating correlation coefficient (r) between CHA2DS2-VASc-HSF score and SYNTAX score (Table 4), it showed positive relation in all groups and with all SYNTAX subcategories. However, the strength of correlation is variable. There is statistically significant correlation between CHA2DS2-VASc-HSF score with SYNTAX score I (Figure 1) and score II for PCI in all groups ($p < 0.05$). With SYNTAX score II for CABG;therelation is significant in group IV only ($p < 0.05$).

This study showed statistically significant negative correlation (Figure 2) between CHA2DS2-VASc-HSF score and ejection fraction (Table 5) ($p < 0.05$ in groups II and III, $p < 0.01$ in groups I and IV).

Regarding the lipid profile, CHA2DS2-VASc-HSF score showed positive correlation with levels of cholesterol (Figure 3), triglycerides and LDL, and negative correlation with levels of HDL, in all groups (Table 6).

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All relations were statistically significant ($p < 0.05$) except with serum HDLin groups II, and with serum triglyceride in groups III ($p > 0.05$).

Table 1: Cardiac signs & symptoms belong to CHA_2DS_2-VASc-HSF score

Cardiac signs and symptoms	Group I (n=50)		Group II (n=50)		Group III (n=50)		Group IV (n=50)	
	No.	%	No.	%	No.	%	No.	%
CHF or reduced EF%	5	10.0	2	4.0	6	12.0	11	22.0
Hypertension	24	48.0	35	70.0	29	58.0	26	52.0
Diabetes	20	40.0	25	50.0	21	42.0	23	46.0
Stroke or TIA	3	6.0	5	10.0	3	6.0	1	2.0
Vascular diseases	2	4.0	5	10.0	32	64.0	36	72.0
Hyperlipidemia	23	46.0	34	68.0	29	58.0	28	56.0
Smoking	15	30.0	21	42.0	30	60.0	35	70.0
Family history	20	40.0	16	32.0	29	58.0	19	38.0

Table 2: Cardiac risk according to SYNTAX score in the studied groups

Syntax	Group I		Group II		Group III		Group IV	
	> 22	≤ 22	> 22	≤ 22	> 22	≤ 22	> 22	≤ 22
I	12	38	14	36	19	31	20	30
II for PCI	21	29	20	30	31	19	27	23
II for CABG	9	41	10	40	12	38	13	37

[a]SYNTAX > 22 = high risk, Syntax ≤ 22 = low risk

Table 3: The mean ± SD of CHA_2DS_2-VASc-HSF score in the studied groups

Total score	Group I (n = 50)	Group II (n = 50)	Group III (n = 50)	Group IV (n = 50)
Mean ± SD	2.86 ± 1.25	3.36 ± 1.19	4.3 ± 1.055	4.28 ± 1.07
Range	1 - 6	1 - 6	2 - 6	3 – 7

Table 4: Correlation coefficient (r) between CHA_2DS_2-VASc-HSF score and Syntax score

Syntax score	Group I	Group II	Group III	Group IV
Syntax score I	0.4811	0.4454	0.3326	0.4669
Syntax score II for PCI	0.6866	0.3186	0.3869	0.5778
Syntax score II for CABG	0.0894	0.1487	0.1015	0.4041

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Table 5: Correlation coefficient (r) between CHA_2DS_2-VASc-HSF score and EF%

EF%	Group I	Group II	Group III	Group IV
Correlation coefficient (r)	-0.3919	-0.2433	-0.3072	-0.3825
P value	P <0.01	P <0.05	P <0.05	P <0.01

Table 6: Correlation coefficient (r) between CHA2DS2-VASc-HSF score and serum lipids

Serum lipids	Group I	Group II	Group III	Group IV
Cholesterol	0.3412	0.5208	0.2179	0.2837
Triglyceride	0.3460	0.0489	0.1204	0.2915
HDL	-0.6093	-0.2323	-0.5244	-0.4231
LDL	0.4834	0.5954	0.4826	0.48197

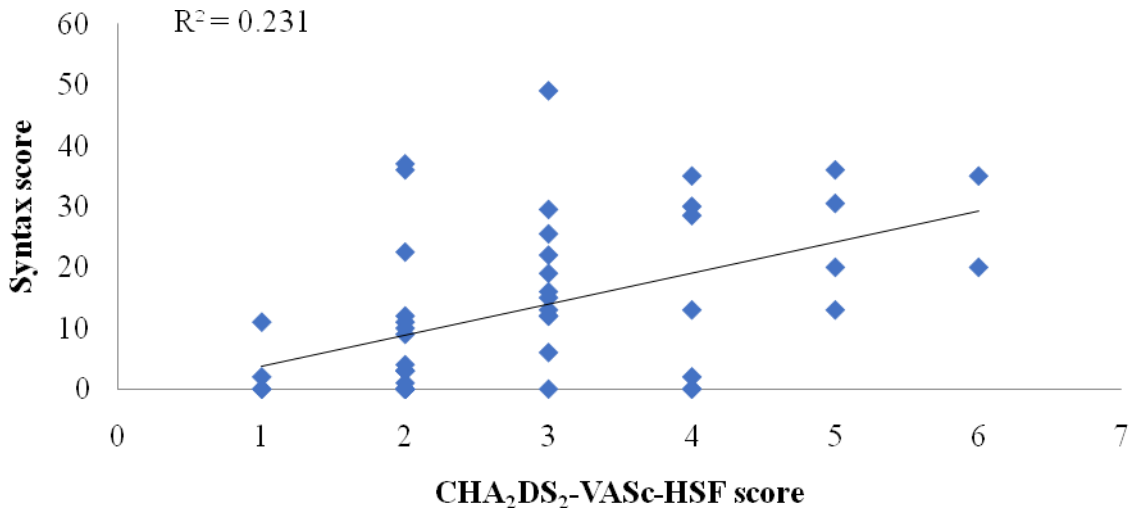

Fig 1: Correlation coefficient (r) between CHA_2DS_2-VASc-HSF score and Syntax score I of patients in group I (r = 0.4811, P <0.01).

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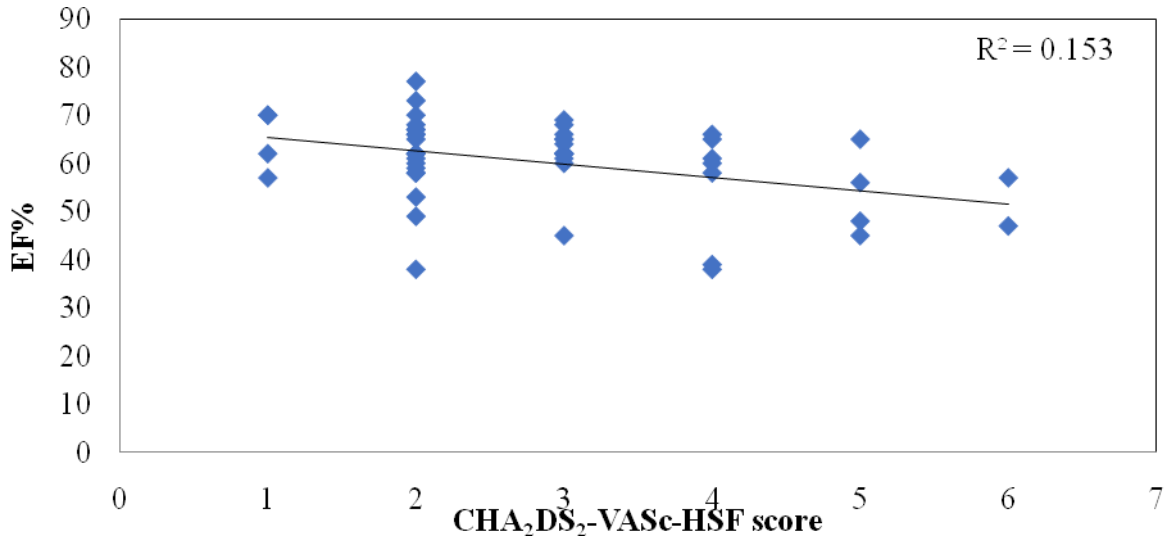

Fig 2: Correlation coefficient (r) between CHA_2DS_2-VASc-HSF score and EF% of patients in group I (r = -0.3919, P <0.01).

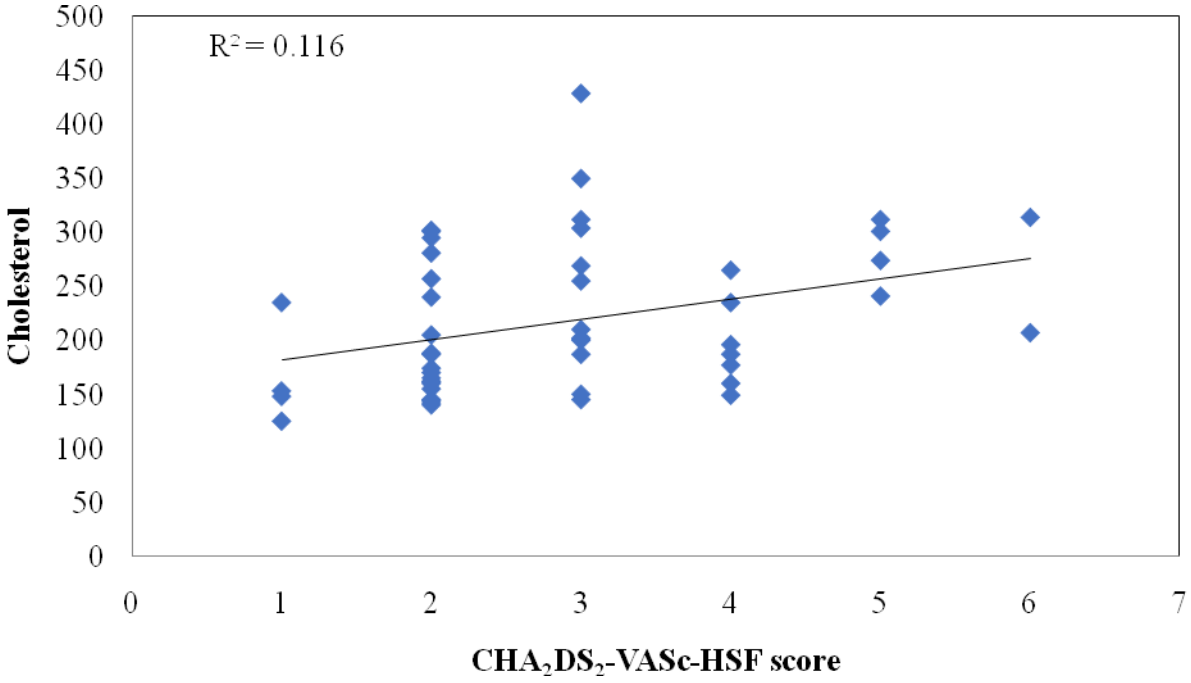

Fig 3: Correlation coefficient (r) between CHA2DS2-VASc-HSF score and serum cholesterol levels of patients in group I (r = 0.3412, P <0.01).

DISCUSSION

Key findings

Acute myocardial infarction is the leading cause of death world wise. However, 80% of myocardial infarction death rate belongs to developing countries**.** The need for good diagnostic and prognostic tools for morbidity and mortality related to acute coronary disease is mandatory [16].

Scores based on clinical data have had a role in prevention and treatment of coronary artery diseases, in comparison to SYNTAX score that depends mainly on angiography for grading the anatomic severity of coronary artery disease. The use of CHADS2 and CHA2DS2-VASc scores is proved to be useful to assess risk of thromboembolism in cases of non-valvular atrial fibrillation. The CHA2DS2-VASc-HS and CHA2DS2-VASc-HSF scorescan be used to predict the severity of coronary artery disease[17].

However, there were no statistical differences in-between ratio of male and females in the sample groups, and ANOVA test showed to significant contribution to the outcome of the study, it is important to mention that gender is associated with different risks of coronary artery disease [18]. In other words, females have higher risk for coronary artery disease, due to different remodeling of cardiac muscle in response to pressure overload, i.e. more hypertrophy than dilation. Furthermore, the protective role of estrogen against myocyte loss[19]. That was also observed in predominance of females (55%) in cases of acute heart failure.

The cardiovascular risk is also affected by co-morbid conditions. Family history of premature coronary artery disease (male first-degree relative < 55 years or female first-degree relative < 65 years), metabolic syndrome and subclinical atherosclerosis are important co-players that add to the cumulative risk of cardiovascular event[20].So, this adds to the significance of including hyperlipidemia, smoking and family history to the assessment of cardiology patients, i.e. using CHA2DS2-VASc-HSF scores rather than older ones.

The anatomical grade of the coronary artery disease assessed angiographically via SYNTAX score have a correlation with age and associated co-morbidities. It was shown that patients with SYNTAX score more 22 are older and have higher rate of co-morbidities, namely, diabetes, hyperlipidemia and smoking[21]. That is matched with our observation about significant positive correlation between CHA2DS2-VASc-HSF scores of patients and levels of cholesterol triglycerides and LDL, and negative correlation with serum levels of HDL. The rate of hyperlipidemia in population is affected by gender, race, co-morbid disorders, chronic drug intake, and obesity [22].

We observed that in patients undergoing coronary angiography, the CHA2DS2-VASc-HSF score is positively correlated with the SYNTAX score I and II for PCI, but not always correlated with score II for CABG (only in patients with STEMI). That can be extrapolated to be used as a predictor for angiographic severity of CAD within similar groups of patients (Table 4).

The correlation with SYNTAX score is valuable as regarding that SYNTAX score can help assign patients with multi-vessel or left main CAD to either CABG or PCI and can anticipate the technical difficulty of PCI [23].

From diagnostic point of view, we observed a statistically significant negative relation between CHA2DS2-VASc-HSF score and ejection fraction. This finding increases the value of the score in clinical use, especially in situations where echocardiography is not feasible in time or place.

Strengths and Weakness of study

The study sample included four groups of coronary artery disease that can cover a wide range of the clinical presentation of atherosclerosis related disease. The CHA2DS2-VASc-HSF score provides wider range of associated factors that affect the risk and severity of coronary artery disease, than its ancestors; CHADS2 and CHA2DS2-VASc scores.

However, all existing scoring systems have some common disadvantages[2]: (1) lack of validation studies in daily medical practice. (2) the scores are more to be applied on short-term risks (within 10 years) more than long-term, (3) in some centers with high volume, it may need a digital system to calculate and record the score immediately, and (4) some factors like race, and interview factors that can affect the score and affect its validity [2].

Comparison to other tools

CHA2DS2-VASc-HSF score is clinically based tool that can be calculated within the context of patient clinical assessment and can predict the finding of more complex assessment tools like lipid profile, patient

echocardiography and SYNTAX score. In other hand, this score include more risk factors than its older ancestors (CHADS2 and CHA2DS2-VASc scores).

CONCLUSION

CHA2DS2-VASc-HSF scores can be considered a predictor of the risk and severity of CAD in comparison with SYNTAX score in patients with ischemic heart disease undergoing coronary angiography. The risk scoring systems may play an important role as predictive models because they are simple and can be easily applied by physicians without any additional costs in routine practice.

Limitations of the study

Sample size of 200 cases, each studied group included 50 cases only. That's why we recommend having much more sample size in another study to enhance our results.

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