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Study of the CHA2DS2-VASc score in acute coronary syndrome

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Introduction

Coronary artery disease (CAD), with its variable presentations, was the commonest cause of death (13.3%) in 2010, increasing by 26–35% from 1990 to 2010 (1).

Acute coronary syndrome (ACS), an acute presentation of CAD, always carries the highest risk of adverse cardiovascular events. Good management, based on early risk stratification, can lead to better outcomes. Scoring systems, including the Global Registry of Acute Coronary Events (GRACE) (2), and thrombolysis in myocardial infarction (TIMI) (3), were developed to identify patients with the highest risk for worse outcomes and to treat them early and successfully.

Coronary artery anatomy can be detected using coronary angiography (CAG), and CAD severity can be evaluated using the SYNTAX and Gensini scores (4).

The CHA2DS2-VASc score is utilized to predict the risk of embolic stroke in non-valvular atrial fibrillation (AF) (5). It has likewise been utilized as a tool to predict reperfusion failure in myocardial infarction (MI) and risk of stroke during ACS (4).

Because the CHA2DS2-VASc scoring scheme is easily remembered and can be applied by physicians at the bedside, its ability to predict CAD severity was investigated by Cetin et al., in stable CAD patients (6) and by Chua et al, in the ACS setting (7).

In the present study, we aimed to validate the CHA2DS2-VASc score within the ACS setting in terms of CAD severity as well as short-term and long-term clinical events.

Methods

Study population

A total of 125 consecutive patients admitted for ACS in specialized medical hospital in Egypt between December 2016 and June 2017 were enrolled in the present prospective observational

study. Mean patient age was 57.78 (± 9.5) y, and 78.4% of them were male. Of these, 81 patients (64.8%) underwent CAG and 89 patients (71.2%) were followed-up for six months.

Ethics statement

All procedures were performed as recommended by the ethical committee of the Faculty of Medicine, and were conducted according to the principles stated in the Declaration of Helsinki. Data were analyzed anonymously. The study was explained to all patients and they gave oral informed consent.

Methodology

We included ACS patients with ST segment elevation MI (STEMI) or non-ST segment elevation MI (NSTEMI) receiving invasive or noninvasive management.

All patients underwent history assessment, full general, local examinations; and 12-lead electrocardiography (ECG) and CAG.

Variable definitions

ACS was defined based on the ECG and biomarkers of cardiac necrosis in patients with acute ischemic chest pain (≥20 minute). STEMI & NSTEMI were defined based on the third universal definition and ESC guidelines (8, 9).

Hypertension was defined as increased systolic blood pressure (BP) above140 mmHg, and diastolic above 90 mmHg, or use of antihypertensive medication (10).

Diabetes Mellitus (DM) was identified as Fasting Blood Sugar ≥126 mg/dl, Random Blood Sugar >200 mg/dl, or use of hypoglycemic drugs (11).

In-hospital outcomes were adverse events including MI, stroke, and death occurring during hospitalization (7).

Six-month outcomes were adverse events including MI, stroke, and death occurring six months after the first attack (7).

Follow-up was done during patient hospital visits or via telephone (12).

The CHA2DS2-VASc score represents congestive heart failure (HF) (C), hypertension (H), age≥ 75 years (A2), DM (D), stroke (S2), vascular disease (V), age ≥65 to 74 years (A), and female as a gender category (Sc). It was calculated as previously described.

We categorized patients into two groups based on the cutoff point ≥2 and < 2 (9, 12).

Coronary angiography

All patients underwent CAG within 48 hours after admission; CAG with multiple projections were performed using different coronary catheters. Severity of coronary lesions was defined as follows; >50% stenosis diameter was considered significant, and presence of >2 major epicedial coronary vessels was referred to as multivessel disease (MVD) (12). Left main (LM) CAD was characterized as ≥50% narrowing in the LM artery (6).

Coronary artery severity scores

The SYNTAX score was used to assess CAD severity by evaluating the number of coronary vessels affected, the dominance and location of lesions, the complexity including calcifications, tortuosity, bifurcation, disease, long lesions, and the presence of thrombus. We calculated SYNTAX score using the online tool http://www.syntaxscore.com (13) and categorized it into three tertiles; the first, <22; the second, 22–32; and the third, ≥32.

The Gensini score was used for coronary artery stenosis assessment. Reductions in coronary lumen were categorized as 25%, 50%, 75%, 90%, 99%, or 100% (complete occlusion); these percentages were respectively numbered 1, 2, 4, 8, 16, and 32. The number was then multiplied with a coefficient based on artery type and segment (14).

The GRACE risk score was calculated from age, heart rate, Killip classification, deviation of ST-segment, systolic BP, elevated cardiac biomarkers, cardiac arrest at admission, and elevated creatinine (2) while giving two points for age > 75 years and past stroke (15).

Exclusion criteria

Coronary artery bypass graft surgery (CABG) patients, decompensated liver diseases, renal failure on replacement therapy, or malignant hematological disorders were excluded from the study.

Statistical analysis

Data were processed using software SPSS version 21. The data normality was first tested with a one-sample Kolmogorov-Smirnov test. We calculated the required sample size in relation to the city population based on expected effect size principle and found it to be 73; however, we continued to enroll patients till the end of the six- month period.

Qualitative data were described using number and percentage. The association between categorical variables was tested using the Chi-square test. Continuous variables were presented as mean ± SD (standard deviation) for parametric data and median for non-parametric data. The two groups were compared using the Student's t test (parametric data) and the Mann–Whitney test (non-parametric data). The Spearman correlation was used to correlate non-parametric data.

Significant variables were entered into the logistic regression model, utilizing the forward Wald statistical technique, to predict the most significant determinants and to control for possible interactions and confounding effects.

In all the above statistical tests, the significance threshold was fixed at 5% level (p-value). The results were considered non-significant when the probability of error was more than 5% ($p>0.05$); significant when the probability of error was less than 5% ($p < 0.05$); and highly significant when the probability of error was less than 0.1% ($p < 0.001$). The smaller the p-value obtained, the more significant the results.

Receiver operating characteristic (ROC) curves were used to compare CHA2DS2-VASc score with the SYNTAX, Gensini, and GRACE scores.

Based on the univariate analysis results, we selected significant variables and analyzed them using multivariate regression analysis after adjusting for confounding factors to predict six-month mortality.

Results

Patients were divided into 2 groups in relation to their CHA2DS2-VASc score with the cutoff point as 2; we analyzed the associations of CHA2DS2-VASc risk score with CAD and adverse clinical outcomes.

A comparison of demographic data between the 2 groups are shown in Table 1.

Table 1. Average and baseline demographic results of the study population

	No	%	Mean	±SD
Age (Mean ± SD)			57.78	±9.5
Male	98	78.4%		
Killip class I	87	69.6%		
II	28	22.4%		
III	6	4.8%		
IV	4	3.2%		
Smoker	65	52.0%		
Hypertension	76	60.8%		
DM	59	47.2%		
Dyslipidemia	40	32.0%		
Family History	24	19.2%		
Previous MI	19	15.2%		
Total cholesterol			201.57	±59.9
LDL			133.44	±28.8
CHA2DS2-VASC score ≥ 2	84	67.2%		
SYNTAX score			20.12	±14.5
Gensini score			43.12	±33.1
Obstructive MVD	25	3.9%		
LM affected	8	9.9%		
In-hospital death	10	8.0%		
Six-month death	17	19.3%		

SD: Standard Deviation, DM: Diabetes mellitus, MI: myocardial Infarction, LDL: low density lipoprotein, LM: left main, MVD: multivessel disease

Higher CHA2DS2-VASc score patients had significantly lower percutaneous procedures, while the number of patients needing emergency CABG after ACS was significantly higher when CHA2DS2-VASC score was ≥2 (p=0.028) (Table 2).

Table 2. Association between CHA2DS2-VASc score and Percutaneous Procedures or CABG

Intervention	Group (1) <2 (n=31)		Group (2) ≥2 (n=50)		p-value
	No	%	No	%	

Diagnostic angiography	14	34.1	13	15.5	
PCI	16	39.0	28	33.3	0.028*
CABG	1	2.4	9	10.7	

* Significant p <0.05, PCI: Percutaneous Intervention, CABG: Coronary artery Bypass Graft

LM and MVD were observed mostly in patients in the higher CHA2DS2-VASc score group (LM, p=0.021; MVD, p=0.031)

Further, totally occluded, bifurcational, or long lesions were more commonly in higher CHA2DS2-VASc score patients, while focal lesions were more common in the lower score group (p< 0.001)

Significantly higher SYNTAX & Gensini scores were seen in higher CHA2DS2-VASc scores patients (p<0.001) (Table 3).

Table 3. Association between CHA2DS2-VASc score and SYNTAX score with significantly higher Syntax and Gensini Scores in Patients with CHA2DS2-VASc score > 2

SYNTAX Tretile	Group (1) <2 (n=31)		Group (2) ≥2 (n=50)		p-value
Up to 22	27	87.1	21	42.0	
Up to 32	3	9.7	9	18.0	<.001**
More than 32	1	3.2	20	40.0	
SYNTAX	9 (0-35)		25.7 (0-60)		<.001**
GENSINI Median (Min-Max)	20 (0.0-80)		51 (0.0-196)		<.001**

**** Highly significant p<0.001**

ROC curves were generated to compare the effectiveness of the CHA2DS2-VASc score, SYNTAX score, and Gensini score in anticipating CAD severity. The cutoff value of the CHA2DS2-VASC score (>2.0) in predicting MVD had 76% sensitivity and 76.8% specificity, that of the SYNTAX score (>25) had 84% sensitivity and 98.9% specificity, and that of the Gensini score (>50) had 84% sensitivity and 85.7% specificity (**Fig. 1**)

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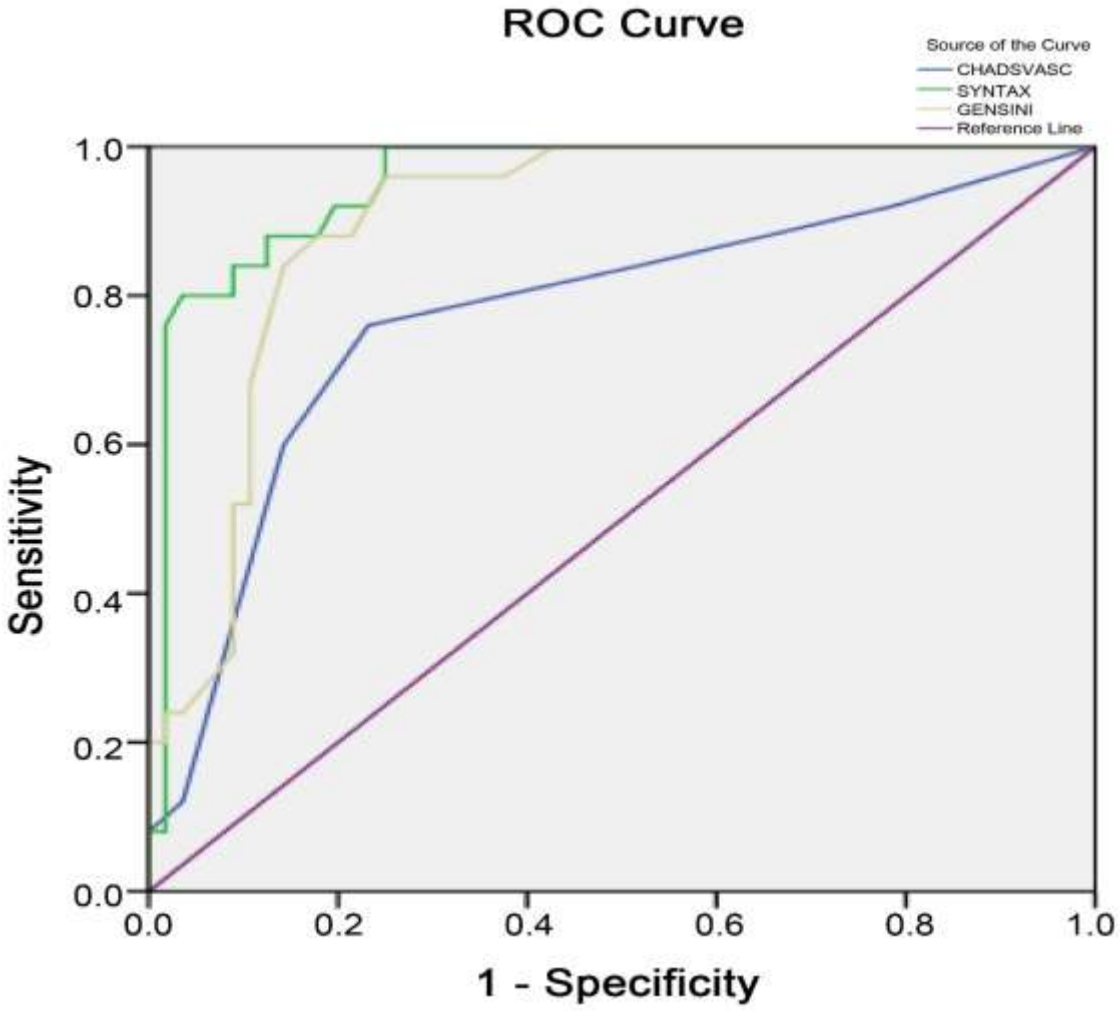

Figure 1. ROC curves for assessing prediction of Multivessel CAD using CHA2DS2-VASC score, SYNTAX score, and Gensini score. Cutoff values of the CHA2DS2-VASC score (>2.0) had 76% sensitivity and 76.8% specificity, that of the SYNTAX score (>25) had 84% sensitivity and 98.9% specificity, and that of the Gensini score (>50) had 84% sensitivity and 85.7% specificity

Regarding in-hospital outcomes, we observed higher in-hospital death and complications with higher CHA2DS2-VASc score patients (p=0.031 for mortality)**.** HF, cardiogenic shock, renal impairment, and AF were more commonly observed in higher CHA2DS2-VASc score patients (≥2) with no significant increase in re-infarction or stroke. (**Fig. 2**)

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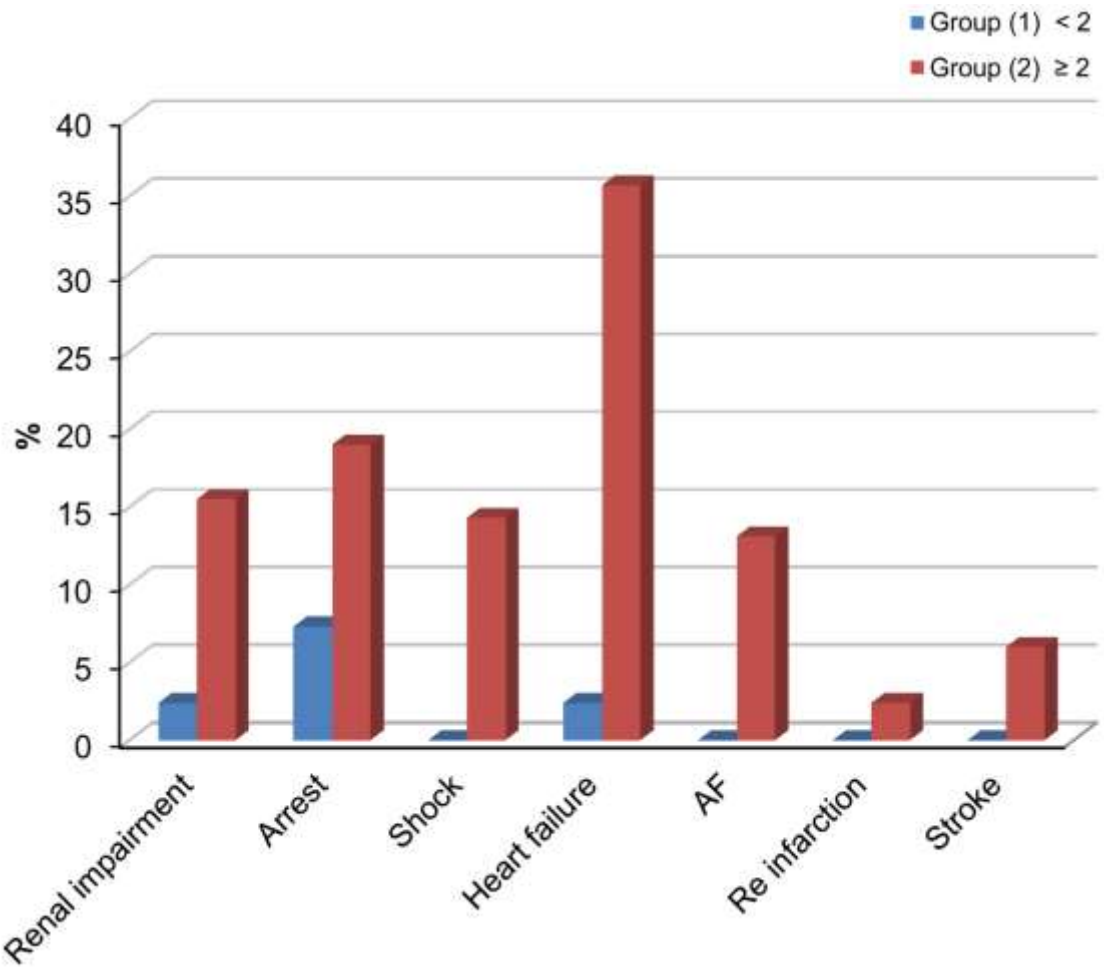

Figure 2. In-hospital complications in the CHA2DS2-VASc score groups

In addition, regarding six-month adverse events, we observed a significantly higher mortality with higher CHA2DS2-VASc scores. (**Fig. 3**).

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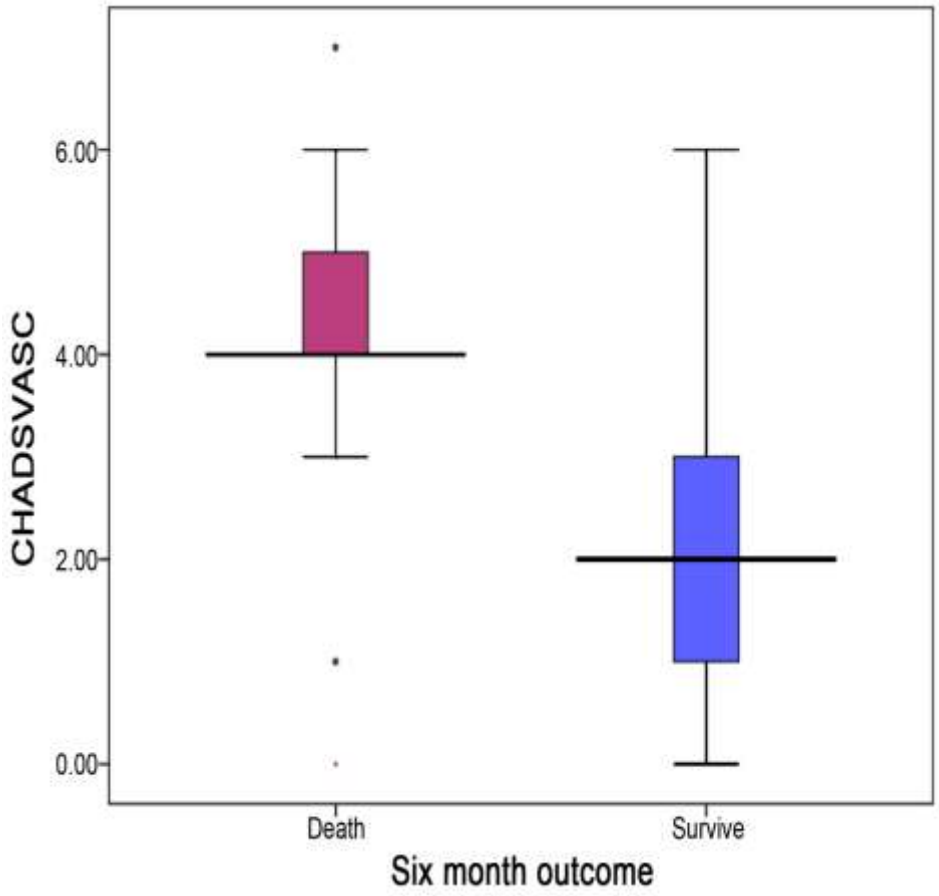

Figure 3. Six-month mortality in the CHA2DS2-VASc score groups

Multivariate regression analysis showed that higher CHA2DS2-VASc scores and GRACE scores were independent predictors of death at six months; we found a significantly increased risk of mortality with higher CHA2DS2-VASs score (OR 2.28; p<0.001) and higher Grace score (OR 1.07; p<0.001) (Table 4).

Table 4. Multivariate regression analysis for using CHA2DS2-VASc score and GRACE score as independable predictors of death at six months

Independent predictors	β	P - value	OR	95%CI
CHA2DS2-VASC score	0.826	<0.001	2.28	(1.47-3.53)
GRACE score	0.064	<0.001	1.07	(1.03-1.09)

OR: odds ratio, CI: confidence interval

A ROC curve was generated to compare the effectiveness of the CHA2DS2-VASc and the GRACE scores in predicting six-month mortality. The CHA2DS2-VASc score >2 had 88% sensitivity and 65.3% specificity in predicting six-month mortality, which were comparable to the established GRACE score cutoff value (**Fig. 4**).

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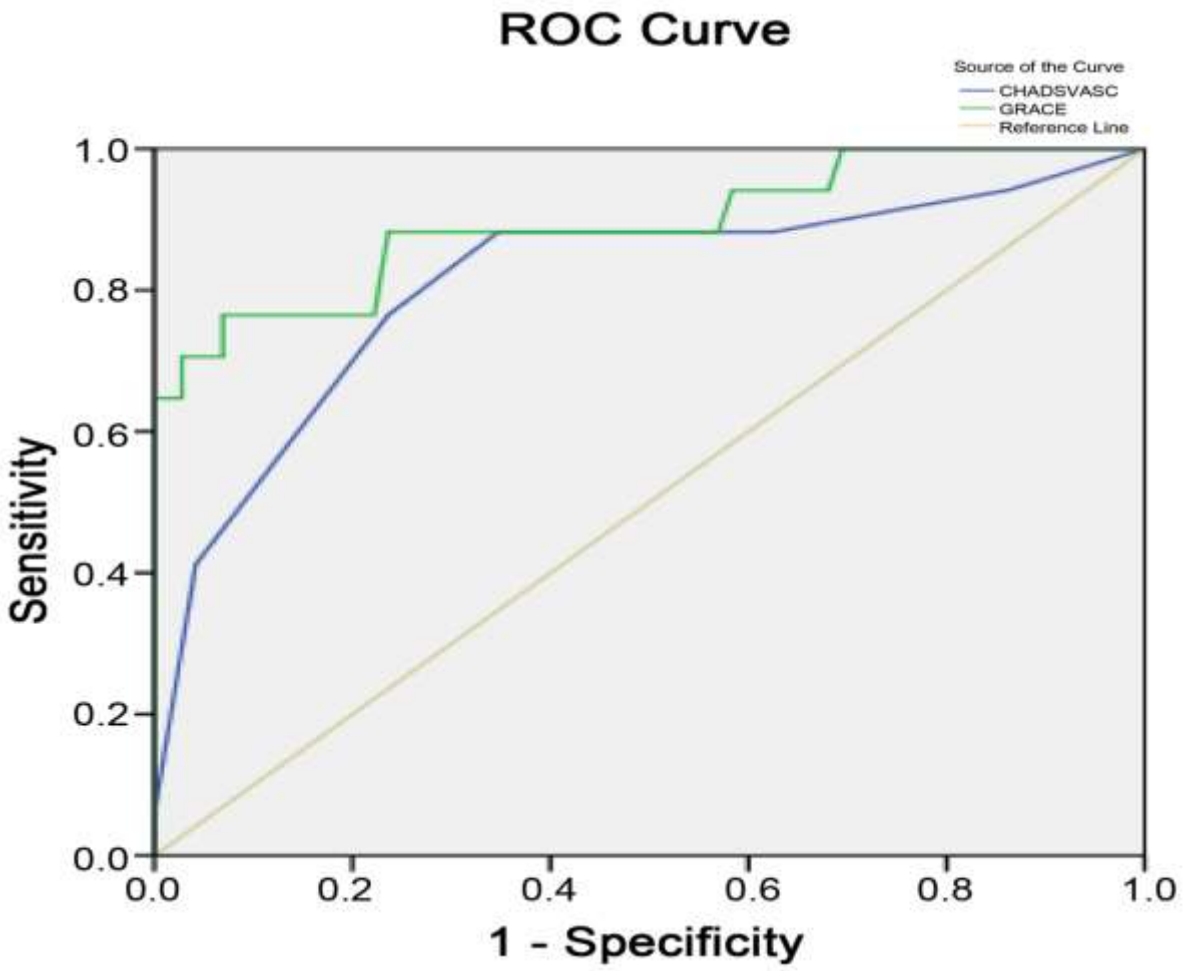

Figure 4. ROC curves for assessing prediction of six-month outcomes using the CHA2DS2-VASC score and the GRACE score. The CHA2DS2-VASc score cutoff value (>2) had 88% sensitivity and 65.3% specificity, and the GRACE score cutoff (≥140) had 88% sensitivity and 76.4% specificity

Discussion

ACS is the leading cause of mortality globally and is associated with serious adverse outcomes. Risk assessment to predict these serious adverse events, based on clinical features, is challenging (16).

The GRACE score is used to predict in-hospital and six-month outcomes while the TIMI score can predict in-hospital outcomes of ACS (17).

CAD severity can be evaluated using anatomic scores including SYNTAX and Gensini scores (14,18).

In our study, we utilized CHA2DS2-VASc score to risk stratify ACS as regard CAD severity and adverse clinical outcomes. We found a higher CHA2DS2-VASc score (≥2) was associated with a significant decrease in percutaneous procedures, but a significant rise in the number of patients needing emergency CABG as the findings of a previous study by Chau et al., which reported a lower rate of percutaneous intervention and more emergency CABG in ACS patients with CHA2DS2-VASc scores ≥2 (7).

Bobazy et al. found an increased history of CABG among patients with acute MI with CHA2DS2-VASc scores ≥2 (12). Less percutaneous procedures and the need for emergency CABG among patients with higher CHA2DS2-VASc scores can be explained by the deteriorated clinical conditions, more advanced and complex CAD and higher comorbidity in such patients.

We also observed a positive association between CAD severity in ACS patients and higher CHA2DS2-VASc scores. We found positive associations between CHA2DS2-VASc score and different CAD assessment scores, including the SYNTAX and Gensini scores.

MVD and LM lesions are considered important issues reflecting CAD severity (19). Among our patients who underwent CAG, MVD and LM disease were significantly presented in higher CHA2DS2-VASc scores patients (≥2), similar to findings of a previous study by Scudiero et al., which reported increased MVD presentation among ACS patients with higher CHA2DS2-VASc scores (20). Bozbay et al. found higher MVD in STEMI patients with CHA2DS2-VASc scores ≥2 (12), and Hioki et al. found a significant correlation between increased CHA2DS2-VASc scores and the presence of MVD and LM disease in stable CAD (21).

Totally occluded, bifurcational, and long lesions are considered coronary artery complexities (18), and we found significant increased coronary complexity associated with higher CHA2DS2-VASc scores (≥2). This was supported by the findings of Hioki et al., which showed increased prevalence of bifurcational lesions in ACS and stable CAD patients with higher CHA2DS2-VASc scores (21).

We found a significantly higher median SYNTAX score with higher CHA2DS2-VASc score (≥2)**;** this significant association demonstrates the important of using the CHA2DS2-VASc score to predict CAD severity. Consistent with our findings, Uysal et al. identified an association between increased CHA2DS2-VASc scores and increased syntax scores in STEMI patients (22), and Hioki et al. reported similar results in patients with stable CAD (22).

Further, we observed higher Gensini scores in association with CHA2DS2-VASc score ≥2, related to the findings of Cetin et al. and Modi et al. who reported significant association of both scores in predicting CAD severity in stable CAD patients (6, 23).

When we compared CHA2DS2-VASc, SYNTAX, and the Gensini scores in predicting CAD severity, we found a significant linear association between all of them, with the SYNTAX score showing the best result. This reflects the helpfulness of the CHA2DS2-VASC score compared to well-established CAD assessment scores, and is probably because the classic CAD risk variables are included in the CHA2DS2-VASc score.

HF is the most common in-hospital complication of ACS (24). In our work, we observed a significantly higher incidence of in-hospital HF and higher incidence of cardiogenic shock (14.3%) in the CHA2DS2-VASc score group ≥2. Bozbay et al. reported similar results showing higher incidences of in-hospital cardiogenic shock in MI patients (9.5%) with CHA2DS2-VASc score ≥2 (12).

In-hospital stroke and re-infarction in our patients were non- significantly increased with a CHA2DS2-VASc score ≥2, similar to the findings of Bozbay et al. (12). These non-significant results may be related to the low number of study patients.

In-hospital death in our study was associated significantly with CHA2DS2-VASc scores ≥ 2, and this was similar to the results of Bazaby et al. (12) and Ipek et al., which revealed that a higher score was correlated with increased in-hospital mortality in acute MI. (25). Another study by Kurtul et al. on ACS patients reported that a significantly higher rate of in-hospital mortality was associated with a higher CHA2DS2-VASc score (26).

After six-month follow-up, we found significantly higher mortality in CHA2DS2-VASc score ≥2 group. Chua et al. also found higher long-term mortality in ACS patients with scores ≥2 (7). When we compared the CHA2DS2-VASc and GRACE risk scores in predicting six-month mortality, we observed a significant linear association between them, demonstrating the importance of the CHA2DS2-VASc score in predicting six-month outcomes ($p<0.001$). It is noteworthy that the CHA2DS2VASC score calculation is easier and could be quickly obtained at bedside as compared with GRACE risk score.

The use of the GRACE and the CHA2DS2-VASc scores in anticipating adverse outcomes in ACS was reported by Álvarez-álvarez et al. (27). The CHA2DS2-VASc score can also predict long-term adverse outcomes as reported by Hioki et al. in stable CAD (21).

When we compared the GRACE risk score and the CHA2DS2-VASc score using ROC curves, we found a significant prediction of six-month mortality using both scores; the cutoff CHA2DS2-VASc score (>2) in predicting mortality had 88% similar sensitivity and 65.3% limited specificity compared to GRACE score cutoff (≥140), similar to the findings of Chua S-K et al., who reported a significant association of the GRACE score with the CHA2DS2-VASc score in predicting adverse cardiovascular adverse events (7).

Finally, multivariate regression analysis identified the CHA2DS2-VASc score to be an independent predictor of six-month mortality**.**

We had several limitations in our study. First, data collection was from a single center with a small number of patients. Second, undiagnosed peripheral arterial diseases present at the time of presentation may have affected evaluation of the CHA2DS2-VASc scores. Third, cardiac biomarkers were not introduced in the CHA2DS2-VASc score; these need to be included in another study. Fourth, we lost contact with some of our patients during follow-up. Fifth, the results cannot be extrapolated or generalized to other populations. Thus, CHA2DS2-VASc score risk stratification performances should be validated in different and larger study populations

Conclusion

Higher CHA2DS2-VASc score was associated with more comorbidity, more severe and complex coronary artery anatomy, and higher adverse cardiovascular in-hospital and six- month outcome in ACS. The CHA2DS2-VASc score cutoff of ≥2 is a simple and quick tool for risk assessment by clinicians in the setting of ACS

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Ethic Committee:
This study was approved by the Institutional Review Board of Mansoura Faculty of Medicine (IRB code MS 16.11.08). This study was carried out in accordance with the rules of the Helsinki Declaration. Informed written consent was obtained from all the participants

Conflict of Interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article"

Authors Contribution:
1st Author MW: Analysis and interpretation of data, Paper Editing
2nd Author MY: Design of the work
3rd Author AW: Revision of the data, Paper Editing
4th Author AA: Data Collection, Paper formulation

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