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Original Article

Predictive role of CHA_2DS_2-VASc score in acute coronary syndrome patients and value of adding global longitudinal strain to CHA_2DS_2-VASc score

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ABSTRACT

Background: Future clinical management would be improved by accurate and early identification of ACS patients at high CV risk. In non-valvular atrial fibrillation patients, the prognostic risk of thromboembolism has been evaluated using CHA_2DS_2-VASc scores. It has recently been shown to assess the severity of CAD and foresee patient outcomes. Also, LV global longitudinal strain is an independent predictor of outcome. **Our study aimed** to determine the added value of LV longitudinal strain (GLS) to CHA_2DS_2-VASc in predicting the outcome and severity of CAD in patients with acute coronary syndrome (ACS).

Methods: A total of 577 patients with primary diagnosis of ACS were included between January and July 2021. All patients had evaluations based on history, clinical examination, 12-lead ECG, TTE, and coronary angiography. Six months follow-up had been provided to all patients.

Results: Syntax score was significantly higher among patients with high-risk CHA_2DS_2-VASc score (30.5 ± 6.1 **vs.** 17.34 ± 8.7 **vs.** 11.11 ± 8.2), *p*-value <0. 001. GLS was significantly lower among high SYNTAX score (−10.97 ± 2.68 vs. −12.61 ± 3.46 vs. −17.81 ± 2.89), *p*-value = 0.0001. There was a significant negative correlation between the CHA_2DS_2-VASc score and GLS. Moreover, adding GLS to CHA_2DS_2-VASc score significantly improved overall accuracy for the prediction of outcome and severity of CAD in ACS patients.

Conclusions: CHA_2DS_2-VASc score is an easy and simple parameter that can be used in predicting the severity of CAD & adverse clinical outcome in ACS patients and adding GLS to the CHA_2DS_2-VASc score significantly improved overall accuracy.

1. Introduction

One of the main reasons for death among cardiovascular disorders is CAD.[1] Severity of CAD and treatment strategies can be affected by many factors, such as the extent and distribution of the damaged vessels, stenosis degree, lesion features, or calcification of the vessels.[2] Also technical feasibility of percutaneous coronary intervention (PCI) and patient prognosis can be affected by these factors.[2] Scoring system Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) can help clinicians make decisions about the best course of therapy for high-risk patients, estimate their prognosis, and take proactive steps to prevent issues before they arise.[3] However validated, the widespread use of the SYNTAX score is restricted because it is an angiographic-based system that depends mainly on anatomical complexity rather than clinical variables or risk factor predictors.[4] Also, utilization of the SYNTAX score is unavailable in some clinical situations when emergent coronary angiography is not needed or when the angiography is not accessible due to limited resources.[5] So, an easy-to-use risk prediction tool could be beneficial in predicting the severity of CAD, especially in an emergency department.[5]

The original purpose of the CHA2DS2-VASc score was to evaluate thromboembolism risk and direct anticoagulation medication in patients with non-valvular atrial fibrillation.[6] Congestive heart failure (CHF), hypertension, advanced age (>65 years), diabetes mellitus (DM), female sex, stroke/transient ischemic attack (TIA), and vascular disease (history of myocardial infarct, peripheral arterial disease) are CHA_2DS_2-VASc score parameters.[7] The existence of CAD and the long-term prognosis of such patients can both be predicted by risk factors for thromboembolism comprised in the CHA_2DS_2-VASc score.[6] Also, LV global longitudinal strain is an independent predictor of outcome, better than LVEF, in patients with heart failure, myocardial infarction, and valvular heart disease.[8] Therefore, our objective was to evaluate the added value of LV longitudinal strain (GLS) to CHA_2DS_2-VASc score in

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Abbreviations

CAD	Coronary artery disease
LV	Left ventricle
MI	Myocardial infarction
CV	cardiovascular
PCI	Percutaneous coronary intervention
CABG	Coronary artery bypass graft
Crcl	Creatinine clearance
MACE	Major adverse cardiovascular events
ACS	Acute coronary syndrome
STEMI	ST-segment elevation myocardial infarction
GLS	Global longitudinal strain

predicting the outcome and severity of CAD in patients with the acute coronary syndrome.

2. Methods

2.1. Study design and overview

This single-center prospective study was conducted from January 2021 to July 2021. Informed consent papers were signed by each participant after the study received approval from the local ethical committee.

Patients: 577 patients in total with primary diagnosis of ACS were hospitalized in the coronary care unit. and were followed up after hospital discharge for 6 months. All patients' CHA2DS2-VASc and syntax scores were computed. **CHA_2DS_2-VASc scores were divided into 3 tertiles;** low (1), intermediate (2–4), and high ($\geq$5) scores.

Inclusion criteria: patients with primary diagnosis of ACS who underwent coronary angiography.

Exclusion criteria: patients with previous CABG or PCI, patients presented with cardiogenic shock or cardiac arrest, patients that did not undergo coronary angiography, patients that dropped out in follow up, hepatic and renal failure with Crcl <15 ml/min, and those with Rheumatic heart disease or prosthetic valve. Patients who refused to sign an informed consent form (or the designated authoritative family member on their behalf) were also excluded.

2.2. Study variables

2.2.1. Clinical and laboratory data

- Complete history with special emphasis on age, sex, history of CAD, risk factors including (hypertension, DM, smoking, dyslipidemia, history of previous TIA or stroke, vascular diseases, and family history of ischemic heart disease). Physical examination (Full general and local examination, with particular focus on pulse rate, rhythm, blood pressure, and Killip class). Patients who have unstable angina, a myocardial infarction (MI) with or without ST elevation, or both, are diagnosed with ACS.[9]
- Calculation of CHA_2DS_2-VASc score; C for Congestive heart failure (1 point). H for Hypertension (1 point). A for Age $\geq$75 years (2 points). D for Diabetes mellitus (1 point). S for prior Stroke or TIA (2 points). V for Vascular disease (1 point). A for Age between 65 and 74 years (1 point) S for female Sex add (1 point).[10]
- Blood samples were taken for cardiac enzymes (Troponin I > 1 ng/ml considered positive"), Random blood glucose level & renal and liver function tests.
- Twelve-lead electrocardiogram at 25 mm/s speed and 1.0 mV/10 mm calibration was registered to detect the presence of ischemic changes as ST segment deviation (Elevation, Transient elevation, or depression and T wave changes (flattening or inversion).

2.2.2. Echocardiography

Within three days of their admission to the hospital, all patients had thorough transthoracic echocardiograms done utilizing a Philips Epic 7C machine equipped with a 5.5 X transducer S5-1 probe and an accompanying ECG signal. In the left lateral decubitus posture, patients were evaluated. All echocardiograms were acquired and recorded in an offline manner.

2D conventional echocardiography: LV end-diastolic and end-systolic volumes were employed to compute left ventricular ejection fraction (LVEF) using modified biplane Simpson's method in the apical four-chamber and apical two-chamber views.[11] All patients were examined to detect wall motions abnormalities by wall motion score index, using 17 segments model by the American Society of Echocardiography, a semi-quantitative scoring method was used to evaluate each segment (1 = normo-kinetic, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic) and an index of the global wall motion score was calculated as the average of regional score divided by the number of segments.[11]

2D speckle tracking echocardiography: assess all LV myocardium in the 3 standard apical views (4-, 2-, and long-axis view) at a frame rate between 60 and 100 fps. The closing of the aortic valve in the apical long-axis view was employed to specify end-systole. The endocardial borders were manually drawn in the apical views at end-systole to identify the regions of interest. Each LV apical view had its peak systolic longitudinal myocardial strain automatically calculated across the myocardium, reported circumferentially in a polar plot map, and reported spatially from base to apex using a color-coded parametric representation. The GLS was calculated by averaging the peak systolic segmental strain values from the three standard apical views. Three consecutive cardiac cycles were used to average longitudinal peak strain values.[11]

2.2.3. Coronary angiography

Performed on all patients to evaluate the number of vessels, segments affected & the severity of the stenotic lesion and calculate the syntax score.

2.2.4. In-hospital outcomes

The in-hospital outcomes were recorded. Outcome variables include heart failure, cardiogenic shock, stroke, hemorrhage & significant arrhythmia, and death.

2.2.5. Follow up

6 months follow-up to detect adverse events that occurred after hospital discharge and during 6 months of follow-up (irrespective of those recorded during hospital admission) as re-ischemia, stroke, heart failure, and death. 6 months follow up was done by telephonic calls and outpatients clinic visit. Patients who developed heart failure and stroke were admitted to our hospital.

2.3. Statistical analysis

SPSS version 25 was utilized for data administration and statistical analysis. (IBM, Armonk, New York, United States). With the help of the Kolmogorov–Smirnov test and direct data visualization techniques, quantitative data were examined for normality. Means and standard deviations of numerical data served as a summary. Numbers and percentages served as a summary of categorical data. An independent *t*-test was employed to compare quantitative data between research groups. The chi-square test or Fisher's exact test, as necessary, was employed to contrast categorical data. To predict in-hospital outcomes, ROC analysis was performed on CHA_2DS_2-VASc. Calculations were made to determine the Area Under Curve (AUC), the optimal cut-off point, and diagnostic indices. Spearman's correlation was employed to perform the

correlations. There are two sides to every single statistical test. Significant *p* values were categorized as those below 0.05.[12]

3. Results

3.1. Patient demographics and clinical risk factors

In the period from January 2021 to July 2021, we incorporated a total number of 577 patients with ACS. 6months follow-up was done to 567 patients as ten patients died during hospital admission. The mean age of studied patients was 58.4 ± 11.5 years old, and most patients were males (65.2 %). 277 patients (48.4 %) were hypertensive, 233 patients (40.4 %) had DM, 59 patients (10.2 %) had CHF and 16 patients (2.8 %) had previous strokes or TIA.

3.2. Clinical presentation and 2D echocardiography data

According to clinical presentation; 195 patients (33.8 %) presented with unstable angina, 107 patients (18.7 %) with non-STEMI, and 277 patients (48.5 %) with STEMI.

Regarding 2D echocardiography 414 patients (71.7 %) had regional wall mobility abnormality, 227 patients (39.3 %) had Mild MR, 69 patients (12 %) had moderate MR, and 75 patients (13 %) had severe MR. The mean LV ejection fraction was 54.5 ± 11 %.

3.3. In-hospital outcomes

Regarding in-hospital outcomes, 69 patients (11.9 %) developed in-hospital heart failure. Only 8 patients (1.4 %) had a cardiogenic shock, 4 patients (1.4 %) developed stroke, 2 patients (1.4 %) developed hemorrhage and the in-hospital mortality rate was 1.7 %, as 10 patients died during their hospital stay (all died after coronary angiography was done).

Patients were divided according to CHA_2DS_2-VASc score into 251 (43.5 %) patients with a low-risk score (1), 288 (49.9 %) patients with an intermediate-risk score (2–4), and 38 (6.6 %) patients with a high-risk score (>5). Also according to syntax score; patients were divided into 40 patients (6.9 %) with high syntax score ≥33 and 537 patients (93.1 %) with mild to intermediate score <33. Regarding revascularization: 473 of the included patients underwent revascularization; 52 of them underwent CABG and 421 patients underwent PCI.

3.4. Outcomes of 6 months follow up

Regarding 6-month follow-up outcomes, a total of 567 patients; 58 patients (10.2 %) had re-ischemia {27 patients (46.6 %) with low vs. 26 patients (44.8 %) with intermediate vs. 5 patients (8.6 %) with high CHA_2DS_2-VASc score}, ten patients (1.8 %) developed stroke {4 patients (40 %) with intermediate vs. 6 patients (60 %) with high CHA_2DS_2-VASc score}, and 21 patients (3.7 %) developed heart failure {1patients (4.8 %) with low vs. 11 patients (52.3 %) with intermediate vs. 9 patients (42.9 %) with high CHA_2DS_2-VASc score}. The 6-month mortality rate was 1.06 %, as 6 patients died during the 6 months post-hospital discharge and during the period of follow-up {2 patients (33.3 %) with intermediate vs. 4 patients (66.7 %) with high CHA_2DS_2-VASc score}.

3.5. Correlation between CHA_2DS_2-VASc score and severity CAD

Syntax score was significantly higher among patients with high-risk CHA_2DS_2-VASc score, *p*-value <0.001.Table 1.

ROC curve was employed to test the diagnostic value (overall accuracy) of CHA_2DS_2-VASc score in predicting the severity of CAD in ACS patients. A cutoff value of 2 was shown to have the best diagnostic accuracy with a sensitivity of 92.5 %, specificity of 68.5 %, AUC 0.829, and *p*-value = 0.0001. Fig. 1.

3.6. Correlation between CHA_2DS_2-VASc score and in-hospital &6-months follow-up outcome

Both in hospital & 6-months follow-up complications were significantly associated with higher CHA_2DS_2-VASc scores, *p*-value <0.05. Table 2.

ROC curve was employed to test the diagnostic accuracy of the CHA_2DS_2-VASc score in predicting in-hospital and 6-month mortality in ACS patients. Using cutoff value 3 displayed a sensitivity of 93 % and specificity of 87.2 % in predicting in-hospital & 6-month mortality with a *p*-value of 0.0001 and AUC of 0.95. Fig. 1

3.7. Correlation between GLS and severity CAD& mortality

GLS was significantly lower among high SYNTAX score (−10.97 ± 2.68 vs. −12.61 ± 3.46 vs. −17.81 ± 2.89) with a *p*-value of 0.0001. ROC curve was used to test the diagnostic accuracy of GLS in predicting CAD severity and outcome in ACS patients. Using cutoff values −13.85 and −11.55 for both severity and mortality with AUC of 0.891 & 0.906; respectively (*p*-value <0.001). Fig. 1

3.8. Correlation between CHA_2DS_2-VASc score and GLS

There was a significant negative correlation between CHADVASC score and GLS score. Fig. 2.

3.9. Added value of GLS to CHA_2DS_2-VASc score

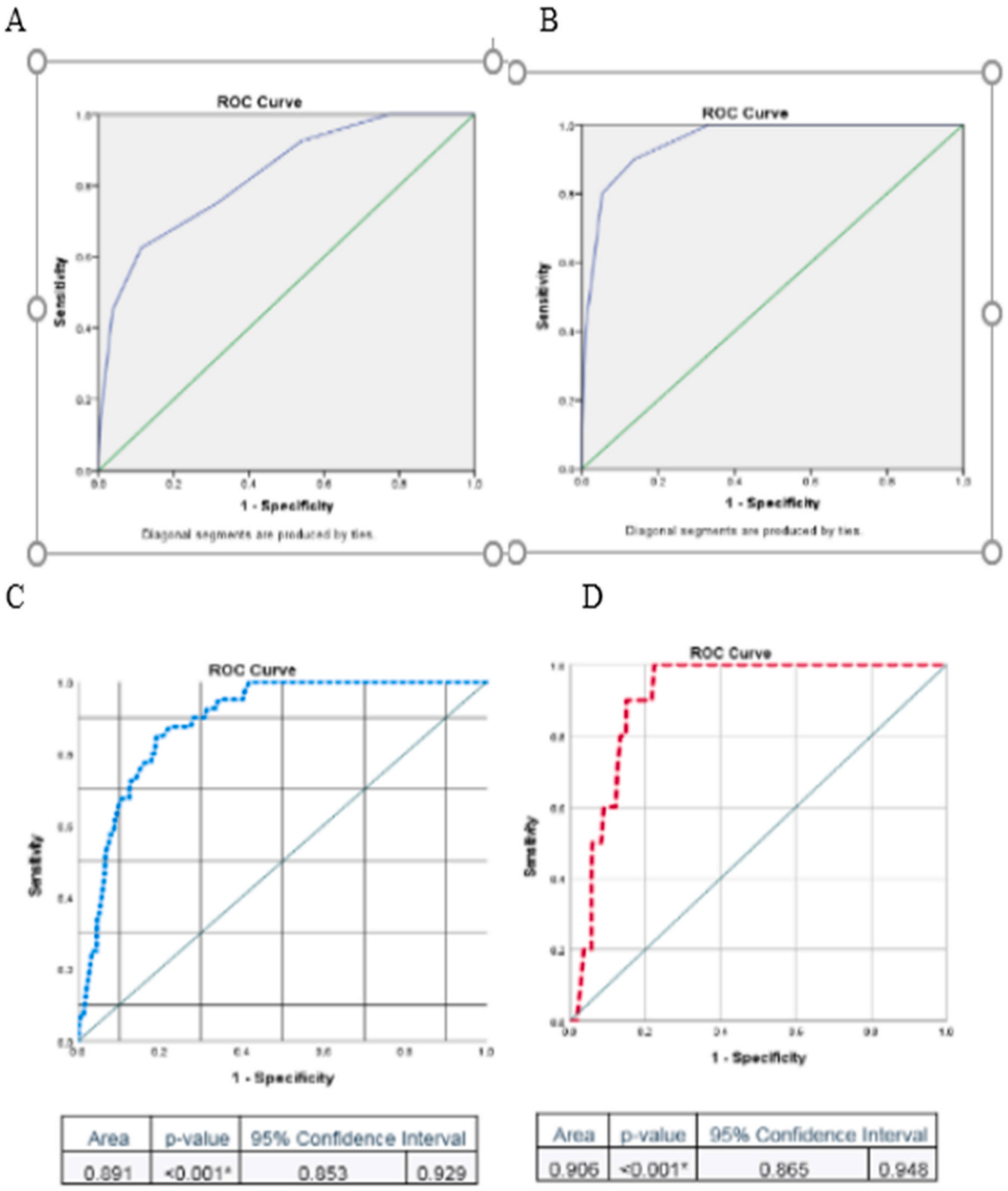
Of the 206 patients with CHA_2DS_2-VASc score ≥2(cutoff value for the severity of CAD); 37 patients had severe CAD. Of the 142 patients with GLS ≥13.85(cutoff value for the severity of CAD); 34 patients had severe CAD. However, sensitivity didn't change but the specificity and overall accuracy increased when combing GLS with the CHA_2DS_2-VASc score for the prediction of the severity of CAD (Overall accuracy with CHA_2DS_2-VASc score was 70.2& with GLS was 80.2 while with combined CHA_2DS_2-VASc score and GLS was 92) Table 3.

Of the 87 patients with a CHA_2DS_2-VASc score ≥3(cutoff value for mortality); 15 patients died & of the 94 patients with GLS ≥11.55(cutoff value for mortality); 14 patients died. Sensitivity, specificity, and overall accuracy increased when combing GLS with the CHA_2DS_2-VASc score for the prediction of mortality in ACS patients (Overall accuracy with CHA_2DS_2-VASc score was 87.3& with GLS was 85.9 while with combined CHA_2DS_2-VASc score and GLS was 91.9). Table 4.

Table 1
Correlation between CHA_2DS_2-VASc score and severity CAD.

	CHA_2DS_2-VASc grade						*p* value
	Low risk		Intermediate risk		High risk		
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	
SYNTAX Score	11.11 ± 8.2	0–38	17.34 ± 8.7	0–43	30.5 ± 6.1	18–41.5	<0.001

[1] Data are presented as mean ± SD. *p*-values significant <0.05.



Area	p-value	95% Confidence Interval	
0.891	<0.001*	0.853	0.929

Area	p-value	95% Confidence Interval	
0.906	<0.001*	0.865	0.948

Fig. 1. A) ROC curve analysis of CHA_2DS_2-VASc score in the prediction of severe CAD in ACS patients. B) ROC curve analysis of CHA_2DS_2-VASc score in the prediction of in-hospital and 6-month mortality. C) ROC curve analysis of GLS in the prediction of severe CAD in ACS patients. D)ROC curve analysis of GLS in the prediction of in-hospital and 6-month mortality. [5] ACS: Acute coronary syndrome, CAD: Coronary artery disease, GLS: Global longitudinal strain, ROC curve: Receiver operating characteristic curve.

4. Discussion

The decrease in mortality rates in ACS patients is likely related to the prediction of potential complications. Though the CHA_2DS_2-VASc score was recommended to foresee cerebrovascular events in atrial fibrillation patients, recent studies have detected its value in the assessment of high-risk ACS patients.[13]

The present study comprised 577 patients with ACS divided according to CHADSVASC score into 3 groups low, intermediate, and high (0–1,2-4, ≥5; respectively). We demonstrated a statistically significant association between the CHA_2DS_2-VASc score and the severity of CAD (by syntax score) and the CHA_2DS_2-VASc score cutoff value of 2 was shown to have the best diagnostic accuracy in foreseeing the severity of CAD in ACS patients. This was consistent with **Akboga et al**[4] who discovered a greater CHA_2DS_2-VASc score in patients with higher SYNTAX scores. Also, **Alhaithami et al**[14] **showed** significant positive associations of CHA_2DS_2-VASc score with both SYNTAX and Gensini scores with CHA_2DS_2-VASc cut-off value > 2 in predicting multivessel CAD. However, concerning the cutoff value, Elmenshawy et al[15] found that the best cutoff point was a score >4 with 87 % sensitivity, 57.1 %

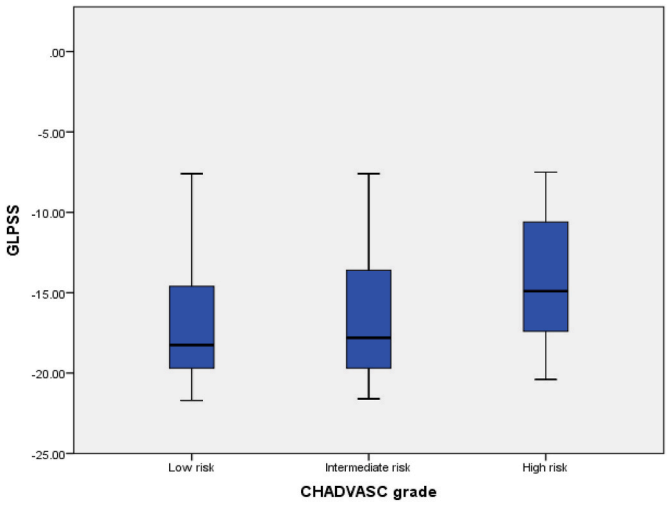


Fig. 2. Box plot showing difference of GLS score based on CHA_2DS_2-VASc grading.[6] GLPSS: Global longitudinal peak systolic strain. CHA_2DS_2-VASc grade; low risk (1), intermediate risk (2–4), and high risk (≥5) scores.

specificity, and AUC of 81.5 %, which was discordant with our result and may be due to a different study population (ACS vs. STEMI patients only).

We found that incidence of in-hospital complications (including heart failure, cardiogenic shock & stroke, and in-hospital mortality) were significantly associated with higher CHA_2DS_2-VASc scores. CHA_2DS_2-VASc cutoff value 3 had the best diagnostic accuracy in predicting the incidence of in-hospital mortality. **Węgiel et al**[16] concluded that Patients with acute MI receiving primary PCI are more likely to have a poorer in-hospital and post-discharge prognosis if their CHA_2DS_2-VASc score value is > 3. In addition, patients with low CHA_2DS_2-VASc scores experience a positive result and a low incidence of post-discharge complications.

We followed patients for up to 6 months and the incidence of complications (heart failure, stroke, and mortality) was more common in higher CHA_2DS_2-VASc scores. CHA_2DS_2-VASc cutoff value ≥ 3 had the best diagnostic accuracy in predicting 6-month mortality. This was similar to prior work by **Bozbay et al**[17] who showed that in patients with ST-segment elevation MI, a CHA_2DS_2-VASc score >2 was linked with cardiogenic shock, a high Killip class, a low LVEF, fatal reinfarction, and both in-hospital and long-term mortality. Also, **Alhaithami et al**[14] noticed that higher CHA_2DS_2-VASc scores cutoff value (>3) and GRACE scores were independent predictors of mortality at six months. The incidence of in-hospital and 6-months MACE (cardiogenic shock, stroke, death, and hemorrhage) was significantly higher as the CHA_2DS_2-VASc score was raised. Our results are in agreement with **Peng et al**[18] who concluded that The CHA_2DS_2-VASc score was an independent predictor of subsequent MACE and the very high-risk score group displayed a 3.8-fold higher risk of MACE than the group with low-risk scores.

Table 2
Association between in-hospital & 6-months complications and CHA_2DS_2-VASc score among the included patients.

		CHA_2DS_2-VASc grade						*p* value
		0–1		2–4		≥5		
		Count	Row N %	Count	Row N %	Count	Row N %	
In-hospital complications	HF	11	15.9 %	37	53.6 %	21	30.4 %	**0.0001**
	Death	0	0.0 %	2	20.0 %	8	80.0 %	**0.0001**
	Stroke	1	25.0 %	1	25.0 %	2	50.0 %	**0.002**
	Hemorrhage	0	0.0 %	2	100.0 %	0	0.0 %	0.36
6-month complications	re- ischemia	27	46.6 %	26	44.8 %	5	8.6 %	0.64
	Stroke	0	0.0 %	4	40 %	6	60 %	**0.0001**
	HF	1	4.8 %	11	52.3 %	9	42.9 %	**0.0001**
	Mortality	0	0.0 %	2	33.3 %	4	66.7 %	**0.0001**

Significant *p*-values are marked in bold. HF= Heart failure.

Table 3
Sensitivity statistics of high CHA_2DS_2-VASc Score (>2), impaired GLS (<13.85) and of both combined for prediction of severity of CAD.

Severity of CAD (Syntax score)	CHA_2DS_2-VASc Score >2		GLS<13.85		CHA_2DS_2-VASc Score >2 and/or GLS<13.85	
	YES (206 patients)	No (371 patients)	YES (142 patients)	No (371 patients)	YES (80 patients)	No (497 patients)
Severe (40 patients)	37(92.5 %)	3(7.5 %)	34(85 %)	6(15 %)	37(92.5 %)	3(7.5 %)
Not severe (537 patients)	169(31.5 %)	368(68.5 %)	108(20 %)	429(80 %)	43(8 %)	494(92 %)
Sensitivity	37/(37 + 3)	92.5	37/(37 + 3)	85	37/(37 + 3)	92.5
Specificity	368/(368 + 169)	68.5	432/(432 + 105)	80.	494/(494 + 43)	91.9
Overall accuracy	TP + TN/Total n.	70.2	TP + TN/Total n.	80.2	TP + TN/Total n.	92

[3] CAD= Coronary artery disease, GLS = Global longitudinal strain, TN = True negative, TP = True positive.

Table 4
Sensitivity statistics of high CHA_2DS_2-VASc Score (>3), impaired GLS (<11.55) and of both combined for prediction of mortality.

Mortality	CHA_2DS_2-VASc Score >3		GLS <11.55		CHA_2DS_2-VASc Score >3 and/or GLS<11.55	
	YES (87 patients)	No (490 patients)	YES (94 patients)	No (483 patients)	YES (63 patients)	YES (514 patients)
Yes (16 patients)	15(93.7 %)	1(6.3 %)	14(87.5 %)	2(12.5 %)	16(100 %)	0 (0 %)
No (561 patients)	72(12.8 %)	489(87.2 %)	80(14.3 %)	481(85.7 %)	47(8.4 %)	514(91.6 %)
Sensitivity	15/(15 + 1)	93	14/(14 + 2)	87.5	16/(16 + 0)	100
Specificity	489/(489 + 72)	87.2	481/(481 + 80)	85.7	514/(514 + 47)	91.6
Overall accuracy	TP + TN/Total n.	87.3	TP + TN/Total n.	85.9	TP + TN/Total n.	91.9

[4]GLS = Global longitudinal strain, TN = True negative, TP = True positive.

In this study, there was a significant negative correlation between the CHA_2DS_2-VASc score and GLS. Moreover, when added GLS to CHA_2DS_2-VASc score significantly improved overall accuracy for the prediction of outcome and severity of CAD in ACS patients.

To the best of our knowledge and till the time of preparing this manuscript, there is no similar study to have examined the role of GLS in the literature that is publicly accessible.

5. Study limitation

The main limitation is a single-center study, Patients presented with cardiogenic shock and those who underwent revascularization by PCI/CABG were excluded from this study so we excluded an important sub-population of ACS patients. We need multi-center research with larger sample sizes using other predictive scores such as CHA_2DS_2-VASc HSF score to further support our findings.

6. Conclusions

In patients with ACS, the CHA_2DS_2-VASc score is a simple-to-calculate measurement that is employable to predict the severity and likelihood of unfavorable in-hospital & 6-month clinical outcomes. Adding GLS to the CHA_2DS_2-VASc score significantly improved overall accuracy.

7. Key questions of the study

1. What is already known on this subject?

CHA_2DS_2-VASc score, a traditional scoring system, is recommended to evaluate thromboembolism risk and direct anticoagulation medication in patients with non-valvular atrial fibrillation.

2. What does this study add?

In patients with ACS, CHA_2DS_2-VASc score of 3 or more correlated with the severity of CAD and worse in-hospital & 6-months outcome. Also, overall accuracy increased when adding GLS value to the CHA_2DS_2-VASc score.

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Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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