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CHA2DS2-VASC Score as A Novel Predictor for Contrast Associated Nephropathy After Percutaneous Coronary Intervention in Acute Coronary Syndrome in Beni-Suef Governorate – Egypt

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Abstract:

Objective: Promising results of CHA2DS2-VASc score have been reported for the prediction of contrast-induced acute kidney injury (CI-AKI) after percutaneous coronary intervention (PCI). Therefore, in this study, we have assessed predictive value of CHA2DS2-VASc score for CI-AKI after primary PCI and comparing this score with both Mehran and GRACE scores.

Methods: This analytical cross-sectional study was conducted between October 2020 and September 2021 at Beni-suef hospitals. A total of 648 patients with ACS who had undergone primary PCI were included in the current study, Using ROC curve analysis, the sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores were compared and either a 25% or 0.5 mg/dL increase in post procedure serum creatinine level as compared to baseline level was categorized as CI-AKI.

Results: CHA2DS2-VASc showed the highest specificity prediction (100%) among the three studied scores, while GRACE score showed the highest sensitivity prediction (60%). From the calculated R2 for the three scores, the highest goodness of fit is for the combination of CHA2DS2-VASc and GRACE Score for CIN prediction.

Conclusion: CHA2DS2-VASc and GRACE scores have a good predictive value for the prediction of CI-AKI after primary PCI.

Keywords: ST elevation myocardial infarction, STEMI, Acute coronary syndrome, percutaneous coronary intervention, primary PCI.

1. Introduction

On the description and management of contrast induced nephropathy (CIN), there is no agreement universally. In the present concept of CIN, renal injury is defined as either an increase in serum creatinine of 25% from baseline or an elevation in serum creatinine level of 0.5 mg/dL within 48–72 hours after intravascular contrast injection **(Moro AB et al.,2021).**

Acute kidney injury associated with contrast injection often appears after two to three days. However, if renal injury happens up to seven days after contrast and is not linked to any other kidney failure causes, CIN should be considered. So, a temporal relation is suggested. After contrast exposure, serum creatinine levels peak two to five days later and usually return to baseline in 14 days **(Elserafy AS et al., 2018).**

Iodine contrast medium is essential for both invasive and interventional cardiac procedures. Due to an increase in coronary angiography and coronary interventional procedures, an increase in the use of contrast media, and an increase in the number of invasive cardiac procedures performed in high-risk patients with chronic kidney disease, diabetes mellitus, hypertension, and kidney failure from contrast-induced nephropathy continue to be growing concerns. A sudden change in kidney function is primarily caused by contrast-induced nephropathy, or acute kidney injury during coronary angiography or percutaneous coronary intervention **(Ul Abideen Z et al., 2018).**

Patients and methods:

Type and Site of the study:

Iodinated contrast material was voluntarily used in patients undergoing coronary angiography in a prospective observational cross-sectional study in Beni-suef hospitals in Egypt, and the incidence of contrast-induced nephropathy in these patients was determined.

Study population:

Total of 648 patients without age restrictions undergoing elective and urgent coronary angiography using non-ionic iodinated contrast media (Omnipaque) were included in the study.

Patients under the study:

History taking: Symptomatology, the presence of common cardiovascular risk factors (smoking, diabetes, and hypertension), a family history of coronary artery disease (CAD), a history of CAD or a coronary artery bypass graft, a history of prior atherosclerotic cerebrovascular events, and current medical treatment are all included.

Clinical examination:

Complete cardiac examination was done in addition to searching for signs of volume overload.

Laboratory Investigation: The serum creatinine collected at admission to determine the e-GFR using The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Serum creatinie level was assessed 48-72 hours after exposure to contrast. Initial examinations included random plasma

sugar levels and complete blood counts. At the time of admission, Simpson's approach was used to determine the left ventricular ejection fraction (LVEF) using 2D echocardiography. CHA2DS2-VASc score was calculated for each patient by giving a score of 1 to each of these variables: (i) CHF or left ventricular systolic dysfunction EF ≤ 40%, (ii) hypertension, (iii) age 65- 74 years, (iv) diabetes mellitus, (v) vascular disease, and (vi) female gender and 2 points for (vii) age 75 years or older, and (viii) previous stroke or transient ischemic attack each. Each patient received a minimum score of 1 because they had experienced a CAD episode brought on by vascular atherosclerosis. The goal is to determine whether or not a CHA2DS2-VASc score of less than 4 may accurately predict contrast-induced nephropathy by comparing it to Mehran and GRACE scores.

Inclusion criteria:

Between October 2020 and September 2021, a total of 648 patients who presented with acute coronary syndrome (ACS) and had PCI were initially recruited. These ACS patients included subgroups with unstable angina, ST elevation myocardial infarction (STEMI), and non-ST-elevation myocardial infarction who were scheduled for PCI. According to the task force's definition, all of these patients' diagnoses were based on their histories, physical exam findings,

electrocardiographic standards, and assessments of their cardiac biomarkers.

Exclusion criteria: End stage renal disease patients receiving regular hemodialysis, shock, acute renal failure, acute or chronic infection or inflammation, recent exposure to radiographic contrast media (within 10 days of enrollment), or PCI contraindications were among the exclusion criteria. The study eliminated patients who passed away during the surgery, did so shortly after, or for whom there was insufficient information regarding serum creatinine 48 hours later.

Ethical considerations: By fully disclosing the study to participants and obtaining their signed informed consent, our study complies with ethical standards. The Human Research Ethics Committee at Beni-suef University Hospitals will be consulted for ethical permission.

Sample size justification: It was assumed that contrast induced nephropathy may affect 7 to 25% of patients. This assumption associated with uncertainty allowing the calculation of maximum sample size. The sample size was calculated using “Epi Info 7, StatCalc, Center for Disease Control (CDC), WHO” depending on the following criteria:

- CIN impact= 7 - 25%

- Confidence level = 90%

- Margin of error = 5%

- Loss to follow up = 10%

So sample size of 648 patients at 0 day fulfills the above criteria.

Results

1. Baseline demographic, clinical, and angiographic characteristics of overall study population.

Participants were (399 males, 61.6%), most of them were less than 65 years old (427, 65.9%), Most of the enrolled participants had BMI <25 (416, 64.2%), smoking was reported by (298, 46%) of the studied participants.

Table (1): Demographic data and special habits among studied population:

		Frequency	Percent
Age	**<65**	427	65.9
	65-74	126	19.4
	>75	95	14.7
Sex	**Male**	399	61.6
	Female	249	38.4
BMI	**BMI <25**	416	64.2
	BMI ≥ 25	232	35.8
SMOKING	**No**	350	54.0
	Yes	298	46.0

Data presented as frequency and percentage.

2. Incidence of Contrast-induced nephropathy (CIN) in the current study:

As shown in table (2), contrast-induced nephropathy (CIN) occurred in 210/648 (32.4 %) patients. Based on the presence or absence of CIN, the enrolled participants were divided into Group 1 (No-CIN) and Group 2 (CIN).

Table (2): Incidence of Contrast-induced nephropathy (CIN) in the current study:

		Frequency	Percent
CIN	**No-CIN**	438	67.6
	CIN	210	32.4
	Total	648	100.0

Table (3): CHA2DS2-VASc, Mehran and GRACE scores were significantly higher among CIN patients' group as compared to non—CIN.

		CIN		**p-value**
		No-CIN N= 438	**CIN N= 210**	
CHA2DS2-VASc	**Mean ±SD**	1.4 ±0.6	5.1 ±1.3	<0.001*
	Minimum – maximum	1 - 3	1 – 8	
Mehran Score	**Mean ±SD**	3.5 ±2.3	11.0 ±4.2	<0.001*
	Minimum – maximum	1 - 13	1 – 19	
GRACE score	**Mean ±SD**	104.2 ±15.5	134.3 ±23.8	<0.001*
	Minimum – maximum	73 - 156	82 – 171	

3. Multivariate analysis for prediction of CIN:

Multivariate analysis reported that sex, diabetes, hypertension, stroke, TIA, thromboembolism, PVD, CHF, EF%, smoking, anemia and albumin were independent predictors for CIN.

Table (4): Independent predictors of CIN in multivariate regression analysis:

	p-value	**Odds ratio**	**95% C.I. for Odds ratio**

			Lower	Upper
Sex (female patient)	0.001	0.068	0.015	0.312
Diabetes (positive)	0.000	0.004	0.001	0.020
HYPERTENSION (positive)	0.000	0.018	0.005	0.070
stroke, TIA, Thromboembolism (positive)	0.000	0.004	0.000	0.031
CHF; (positive)	0.000	0.021	0.003	0.133
EF %	0.016	0.901	0.827	0.980
SMOKING; (positive)	0.028	5.700	1.208	26.896
Anemia; (positive)	0.000	0.035	0.007	0.185
Albumin	0.242	3.587	0.423	30.433

4. Sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores in CIN prediction

Using ROC curve analysis, the sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores for prediction of CIN among studied patients was evaluated

The area under the curve (AUC) of CHA2DS2-VASc for prediction of CIN with was (AUC = 0.990, SE = 0.006, 95% CI: 0.979-1.000). A CHA2DS2-VASc of ≥4.50 could predict CIN with a sensitivity of 59.5% (true positive cases) and a specificity of 100% (true negative cases).

The area under the curve (AUC) of Mehran score for prediction of CIN with was (AUC = 0.941, SE = 0.009, 95% CI: 0.922-0.960). A Mehran score of ≥10.50 could predict CIN with a sensitivity of 52.4% (true positive cases) and a specificity of 98.4% (true negative cases).

The area under the curve (AUC) of GRACE score for prediction of CIN with was (AUC = 0.845, SE = 0.017, 95% CI: 0.810-0.879). A GRACE score of ≥127.50 could predict CIN with a sensitivity of 60% (true positive cases) and a specificity of 90.6% (true negative cases).

CHA2DS2-VASc showed the highest specificity prediction (100%) among the three studied scores, while GRACE score showed the highest sensitivity prediction (60%).

Table (5): results of ROC curve analysis for sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores for prediction of CIN among studied population:

	AUC	SE	p-value	95% CI of AUC		Cut-off	Sensitivity	Specificity
				Lower Bound	Upper Bound			
CHA2DS2=VASc	0.990	0.006	<0.001*	0.979	1.000	≥4.50	59.5%	100%
Mehran Score	0.941	0.009	<0.001*	0.922	0.960	≥10.50	52.4%	98.4%
GRACE score	0.845	0.017	<0.001*	0.810	0.879	≥127.50	60%	90.6%

AUC: Area under the curve, **CI:** Asymptotic 95% Confidence Interval of AUC.

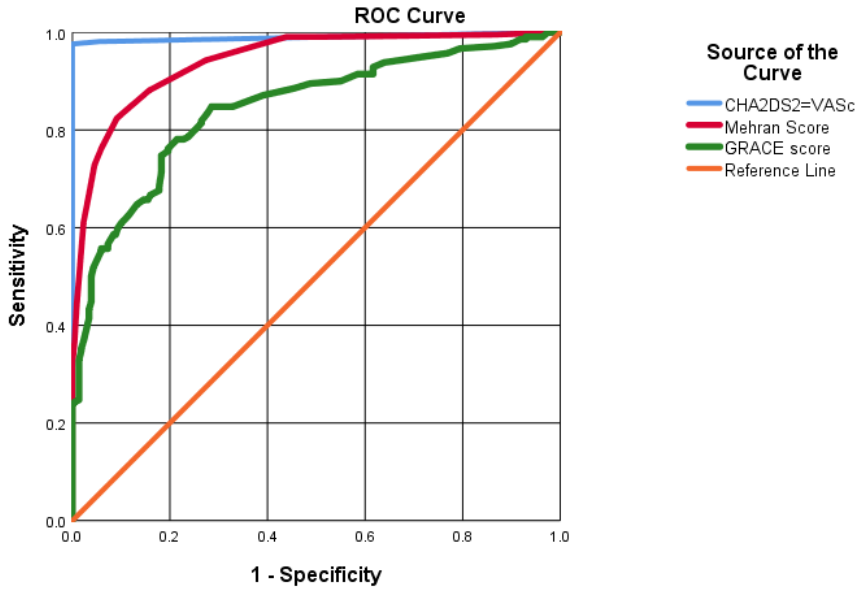

Figure (1): results of ROC curve analysis for sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores for prediction of CIN among studied population.

Regression analysis for predictive ability of CHA2DS2-VASc and GRACE score for CIN (Prediction Analysis)

Tables (6), (7) and (8) demonstrate the results of linear regression analysis of CHA2DS2-VASc, GRACE, and combined CHA2DS2-VASc with GRACE for estimation of CIN.

Table (6): Linear regression analysis of predictive ability of CHA2DS2-VASc for CIN:

	Unstandardized Coefficients		**Standardized Coefficients**	**t-test**	**p-value**	**95.0% Confidence Interval for B**	
	B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	-0.226	0.014		-16.518	<0.001*	-0.253	-0.199
CHA2DS2=VASc	0.216	0.004	0.893	50.508	<0.001*	0.207	0.224

R^2 of the model= 0.893

CHA2DS2-VASc can predict CIN by the following equation:

CIN= -0.226 + (0.216 * CHA2DS2-VASc)

Table (7): Linear regression analysis of predictive ability of GRACE score for CIN:

	Unstandardized Coefficients		**Standardized Coefficients**	**t-test**	**p-value**	**95.0% Confidence Interval for B**	
	B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	-1.058	.073		-14.459-	.000	-1.202-	-.915-
GRACE Score	0.012	.001	.604	19.277	.000	.011	.013

R^2 of the model= 0.604

GRACE Score can predict CIN by the following equation:

CIN= -1.058 + (0.012* GRACE Score)

Table (8): Linear regression analysis of predictive ability for combined CHA2DS2-VASc and GRACE Score for CIN:

	Unstandardized Coefficients		**Standardized Coefficients**	**t-test**	**p-value**	**95.0% Confidence Interval for B**	
	B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	-0.110	.048		-2.279-	0.023*	-.205-	-.015-

CHA2DS2=VASc	0.226	.006	.938	37.431	<0.001*	.214	.238
GRACE score	-0.001	.001	-.063-	-2.500-	0.013*	-.002-	.000

R^2 of the model= 0.899

CHA2DS2-VASc with GRACE both can predict CIN by the following equation:

CIN= -0.110+ (0.226* CHA2DS2=VASc) + (-0.001* GRACE)

From the calculated R^2 for the three above models, the highest goodness of fit is for the combination of CHA2DS2-VASc and GRACE Score for CIN prediction (R^2= 0.899, followed by prediction by CHA2DS2-VASc alone (R^2= 893).

Discussion

In this research in the current study, 648 ACS patients in total were enrolled. Participants were mostly under 65 (427, 65.9%), with 399 of them being men (61.6%).

Using ROC curve analysis, the sensitivity and specificity of CHA2DS2-VASc, Mehran and GRACE scores for prediction of CIN among studied patients.

The area under the curve (AUC) of CHA2DS2-VASc for prediction of CIN with was (AUC = 0.990, SE = 0.006, 95% CI: 0.979-1.000). A CHA2DS2-VASc of ≥4.50 could predict CIN with a sensitivity of 59.5% (true positive cases) and a specificity of 100% (true negative cases).

The area under the curve (AUC) of Mehran score for prediction of CIN with was (AUC = 0.941, SE = 0.009, 95% CI: 0.922-0.960). A Mehran score of ≥10.50 could predict CIN with a sensitivity of 52.4% (true positive cases) and a specificity of 98.4% (true negative cases).

The area under the curve (AUC) of GRACE score for prediction of CIN with was (AUC = 0.845, SE = 0.017, 95% CI: 0.810-0.879). A GRACE score of ≥127.50 could predict CIN with a sensitivity of 60% (true positive cases) and a specificity of 90.6% (true negative cases).

From the calculated R^2 for the three scores, the highest goodness of fit is for the combination of CHA2DS2-VASc and GRACE Score for CIN prediction (R^2= 0.899, followed by prediction by CHA2DS2-VASc alone (R^2= 893)

CHA2DS2-VASc showed the highest specificity prediction (100%) among the three studied scores, while GRACE score showed the highest sensitivity prediction (60%).

Agreeing with our study results: A study comprised three hundred consecutive PCI-treated ACS patients. The CHA2DS2-VASc score of every subject was ascertained. These patients were divided into two groups: Group 1 (those with CIN) and Group 2 (those without CIN). After performing a receiver operating characteristic curve analysis, the study population was split into two groups once more: Group A receives a CHA2DS2-VASc value of less than three, whereas Group B receives a score of four or higher. A total of 41 individuals (13.6%) had CIN. ROC analysis revealed that the CHA2DS2-VASc score for CIN had a good predictive value. Patients with a

CHA2DS2-VASc score of 4 or higher had a higher frequency of CIN (56.8% vs. 4.8%; p 14 0.0001), and multivariate analysis revealed that a score of 4 or higher is an independent predictor of CIN **(Chaudhary A K et al., 2019)**.

In a 2014 study, Liu, Y.H., et al. shown that in patients with STEMI prior to primary PCI, GRACE risk score (>160) is an independent and substantial predictor of CI-AKI.

200 consecutive patients who were diagnosed with IHD and underwent PCI between January 2019 and January 2020 at **Tanta City's Almogama Alteby Hospital** were divided into two groups: Group I consisted of those who developed CIN 48 hours after PCI (28%) and Group II consisted of those who did not (72%). We computed the CHA2DS2-VASc score for every patient. Before and 48 hours after PCI, the serum creatinine level and estimated glomerular filtration rate were determined for each patient. Fifty-six individuals, or 28 percent, had CIN. In addition to having lower baseline estimated glomerular filtration rates and left ventricular ejection fractions, patients with CIN also exhibited greater rates of diabetes mellitus and hypertension. The CIN group's average CHA2DS2-VASc score was noticeably greater than the non-CIN group's **(S. Abd-Allah et al., 2020)**.

Agreeing also with our studyA total of 1,408 patients were involved in the study. The CHA2DS2-VASC score of every subject was ascertained. The receiver operating characteristic analysis was used to divide the study population into two groups: the CHA2DS2-VASC score 3 group (n = 944) and the CHA2DS2-VASC score 4 group (n = 464). The patients were then split into two groups according to the presence or absence of CIN. CIN was defined as a rise in serum creatinine of more than 0.5 mg/dl or a 25% increase over baseline within 72 hours following PCI. 159 occurrences (11.3%) of CIN were found overall. A study on the receiver operating characteristic curve revealed that the CHA2DS2-VASC score had a good diagnostic value for predicting CIN. When comparing patients with high scores on the CHA2DS2-VASC scale to those with low scores, the former showed a higher prevalence of CIN (23.9% vs 5.1%; p 0.001), and the latter was found to be an independent predictor of CIN by multivariate analysis. Patients with ACS who received immediate PCI can now predict CIN using the new, simple-to-use CHA2DS2-VASC score (**Kurtul A et al.,2017)**.

500 acute STEMI patients who presented consecutively to two PCI clinics in Egypt were included in a recent study. Cardiogenic shock, known severe renal impairment (baseline serum creatinine ≥ 3 mg/dL), and hemodialysis indications—both past and present—were excluded criteria. Baseline estimated glomerular filtration rate (eGFR), Mehran's score, CHA2DS2VASC score, and contrast media volume. The predictive accuracy of CHA2DS2VASC and Mehran's scores, as well as post-PCI CIN (defined as a 0.5 mg/dL absolute rise or a 25% relative increase in serum creatinine from baseline), were assessed. 35 (7%) of the study group experienced CIN. values for Mehran's score and the CHA2DS2VASC score. It was discovered that the CHA2DS2VASC score and Mehran's score were independent predictors of CIN ($P < 0.001$ for all). CHA2DS2VASC ≥ 4 demonstrated an excellent predictive ability for post-pPCI CIN, similar to Mehran's score, according to ROC curve research **(Samir A., et al.,2023)**.

What was against our study results in the study, The Mehran Risk Score (MRS) was compared with three widely used scoring systems, namely the CHA2DS2-VASc score, the Canada Acute Coronary Syndrome Risk Score (C-ACS), and the Thrombolysis in Myocardial Infarction risk

index (TRI), in order to predict the contrast-induced acute kidney injury (CI-AKI) following primary percutaneous coronary intervention (PCI) **(Kumar R et al.,2021)**.

In this study, consecutive primary PCI patients were included. Patients with chronic kidney illness, those in Killip class IV at presentation, and those who had recently used the contrast agent were excluded. Along with the three risk scores—CHA2DS2-VASc, C-ACS, and TRI—MRS was evaluated for each patient. A rise in post-procedure blood creatinine of either 0.5 mg/dL or 25% relative was considered CI-AKI **(Kumar R et al.,2021)**.

The MRS has proven to have greater discriminating power than CHA2DS2-VASc, C-ACS, and TRI. Nevertheless, the TRI can be helpful in clinical practice because to its high sensitivity and ease of use in identifying patients at higher risk of CI-AKI following initial PCI **(Kumar R et al.,2021)**.

According to **Salama et al. (2019),** patients with STEMI who received PCI had an independent correlation between the formation of CIN and a CHA2DS2-VASC score of >3. The higher the CHADS2-VASC score, the higher the chance of developing CIN following PCI.

On **2014**, A study included 422 consecutive patients treated with primary PCI for STEMI. For each patient, Mehran, Gao, Chen, (Age, Glomerular Filtration Rate, and Ejection Fraction (AGEF)); (Age, Creatinine, and Ejection Fraction (ACEF)); and GRACE risk scores were computed. Major adverse clinical events, in-hospital and 3-year all-cause mortality, and the predictive accuracy of the six CIN scores The majority of these six risk scores showed satisfactory calibration and a reasonably strong predictive value for CIN-narrow (C statistic range: 0.746 to 0.873). When compared to other risk scores, the ACEF and AGEF risk scores exhibit superior calibration and discrimination for CIN-narrow, in-hospital outcomes **(Liu Y et al.,2016).**

Conclusion

CHA2DS2-VASc showed the highest specificity prediction (100%) among the three studied scores, while GRACE score showed the highest sensitivity prediction (60%). The highest goodness of fit is for the combination of CHA2DS2-VASc and GRACE Score for CIN prediction (R2= 0.899, followed by prediction by CHA2DS2-VASc alone (R2= 893). So both scores can be used as independent predictors for CIN.

Recommendations: Further studies with a large scale of patients are needed to support our findings. CHA2DS2-VASc and GRACE Scores can be used as independent predictors for CIN.

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