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Added Value of CHA2DS2–VASc Score to Safe Contrast Volume for Contrast Induced Nephropathy Prediction after Percutaneous Coronary Intervention

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Abstract

Background: The CHA2DS2-VASc score is utilized to order the danger of embolization in atrial fibrillation (AF). Also, it has been assessed the worst clinical scenario in acute coronary syndrome patients, regardless of having AF. The study aimed to use the CHA2DS2-VASc score added to the safe contrast volume (Volume /CrCl) for contrast-induced nephropathy (CIN) early prediction post-PCI.

Patients and Methods: The study included two hundred fifty-nine patients who underwent percutaneous coronary intervention. For each patient, The CHA2DS2-VASc score and Volume /CrCl were evaluated. The patients in our study were divided, according to CIN development into two groups. CIN was identified as a rise in serum creatinine >0.5 mg/dl or >25% increase in baseline within 48 to 72 hours after PCI. Statistical analysis: the receiver operating characteristic analysis was used to detect the best cut-off values to predict CIN, and we concluded the predictors of CIN through multivariate logistic regression analysis. Results: There was a positive correlation between the Mehran score and the CHA2DS2-VASc score. Independent predictors of CIN were Mehran score, Volume/CrCl ratio>3.2 and CHA2DS2-VASc >3, CHF or EF < 40%, hypotension, anemia, primary PCI, and weight. If the patient had (CHA2DS2-VASc score>3 or Volume/CrCl >3.2), as a single predictor, we could predict CIN with (sensitivity 96.97 %, 95% CI 0.71 to 0.82).

Conclusion: The CHA2DS2-VASc score and Volume/CrCl ratio are new predictors of CIN, and we can use the CHA2DS2-VASc score, and safe contrast volume for early detection of CIN after PCI.

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Keywords: The CHA2DS2-VASc Score; safe contrast volume (Volume/Crl) Contrast Volume to Creatinine Clearance Ratio; Contrast-Induced Nephropathy(CIN); Percutaneous Coronary Intervention (PCI).

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Introduction

The (CIN) is a serious complication of coronary catheterization that might happen after contrast media usage causing acute kidney insult.[1] Despite the accuracy of multiple scoring models for detecting the risk of CIN, the complexity of assessing risk stratification limits their use.

The Mehran score allows early and accurate prediction of CIN occurrence and is widely used to predict CIN. The risk score is calculated using eight prognostic points: (1) hypotension; (2) intra-aortic balloon pump usage; (3) chronic heart failure; (4) age; (5) anemia; (6) diabetes mellitus; (7) contrast media volume; and (8) serum creatinine value.[2]

The CHA2DS2–VASc score was made as an indicator for embolic risk and anticoagulant treatment in non-valvular AF. It includes 1) Congestive heart failure or LV systolic dysfunction; 2) Hypertension; 3) The age of equal or more than seventy-five years; 4) diabetes mellitus; 5) previous cerebrovascular stroke or TIA; 5) vascular disease; 6) age between sixty-five and seventy-four years; and 7) female sex variables.[3] Although this score has been used lately to find out the risk of many cardiovascular diseases, only a few studies have explored its value for CIN early detection after PCI.

The aim of the work:

In this study, we tried to find a safe contrast volume through computing cut-off the value of the safe contrast volume (V/CrCL) and CHA2DS2-VASc score for early detection of CIN occurrence following PCI.

Patients and Methods:

This study was done in the Zagazig Cardiac Catheterization Unit. This study included cases that have been treated with either primary or elective PCI. The patients with inappropriate coronary anatomy for primary PCI in the setting of acute STEMI were excluded; moreover, end-stage renal failure, which was defined as (CrCL) creatinine clearance less than fifteen mL/min, with or without pre-existing dialysis was excluded; and patients who underwent contrast within seven days or before also were not included in our study. The occurrence of CIN is defined as a decrease in renal functions (a rise in serum Cr by more than twenty-five percent above basal level or half mg/dl) occurring within 2- 3 days after the injection of contrast dye in the absence of other causes.[1] We subjected patients according to their history with special stress on; age, gender, chest pain, symptoms of pulmonary congestion, Symptoms of systemic congestion, and risk factors of Ischemic artery disease, e.g. diabetes mellitus, hypertension, and smoking. History of nephrotoxic drugs usage as NSAIDs, gentamycin, Risk factors for CIN as, renal disease (e.g., diabetic nephropathy); Recurrent contrast medium exposure within seven days, and reduced arterial volume (e.g., by diuretics). The physical examination was done with particular stress on the pulse, blood pressure, lower limb edema, and neck vein congestion. Before doing PCI, an ECG was done to detect ischemic insult. Echocardiography was done before elective PCI and before (if feasible) or after Primary PCI. The ejection fraction was assessed by the Simpson method. The level of serum creatinine was measured in the day before elective PCI or the setting of primary PCI and then 48 to 72 hours following the PCI procedure. Creatinine clearance (CrCL) was calculated on the day before elective PCI or on submitting in the setting of primary PCI using (Cockcroft- Gault formula): Creatinine clearance (CrCL (ml/ min) = (140-Age) X body weight (kg) ÷ 72 X Serum creatinine(Cr) (mg/dl) (X 0.85 for women). We gave isotonic saline 0.9% intravenously to all patients who were not in CHF and with creatinine equal to or more than 1.5 mg/dl, at a rate of one ml/ kg/hour, for 12 hours pre-elective PCI, and for 12 hours after the procedure (half ml/kg/hour in case of EF <40%). Nephrotoxic drugs were avoided, and the amount of dye was spotted. A non-ionic low-osmolality contrast dye was used in this procedure. All procedures were done via the femoral route, as a short sheath 6-8 F is put in the common femoral artery through the adjusted Seldinger technique, after the presenting of the guiding catheter, the coronary lesion is firstly crossed with a 0.014-inch diameter coronary wire, which works as a "rail" for coronary devices eg: balloons and stents. The stent is then transferred and distended either directly or following pre-dilatation with a balloon.[4] Moreover, CHA2DS2–VASc score was assessed through

the following scoring system: one point for (CHF) congestive heart failure, Hypertension (HTN), diabetes mellitus, age between sixty-five to seventy-four years, female gender and vascular disease; and two points for the age of more than or equal seventy-five years, stroke or transient ischemic attack (TIA) history.[5] We considered arterial hypertension if the patient was on anti-hypertensive treatment or systolic blood pressure of equal or more than one hundred and forty mm Hg or diastolic blood pressure of equal or more than ninety mm Hg. and considered DM if the patient was on anti-diabetic drugs or insulin, or fasting plasma glucose of equal or more than one hundred and twenty-six mg/dL. Vascular disease was defined as the occurrence of a previous MI, revascularization, peripheral artery disease (PAD)-related amputation, or presence of peripheral artery disease evidence angiographically.We computed Mehran risk score which includes eight prognostic variables: (1) Hypotension (five points if systolic blood pressure is less than eighty mmHg for at least one hour needing inotropes); (2) intra-aortic balloon pump usage (five points); (3) CHF (five points, if NYHA class III/IV or history of pulmonary edema); (4) age (four points, if more than seventy-five years); (5) anemia (three points, if hematocrit < 39% for men and <36% for women); 6) Diabetes mellitus (three points); (7) Contrast media volume (one point per one hundred ml); 8) and creatinine level more than 1.5 (four points). Mehran et al.[7] also estimated four categories of CIN risk as follows: Low: less than five points; Moderate: sex to ten points; High: eleven to fifteen points; and Very high: more than fifteen points.

Table 1. The comparison of Clinical, laboratory, and angiographic data between the two groups according to CIN occurrence.

	CIN		P value
	No (N=226)	YES (N=33)	
Age (years)	57(32-80)	66 (42-78)	<0.001
Weight (Kg)	79.5 ± 9.9	83.4 ± 8.9	0.02
Male, n (%)	152 (67.3%)	23 (69.7%)	0.85
CHF OR EF<40%	60 (26.5%)	23 (69.7%)	<0.001
History of hypertension	146 (64.6%)	20 (60.6%)	0.69
History of diabetes	90 (39.8%)	24 (72.7%)	0.001
History of stroke or TIA	25 (11.1%)	8 (24.2%)	0.04
Vascular disease	100 (44.2%)	12 (36.4%)	0.46
Hypotension	17 (7.5%)	16 (48.5%)	<0.001
Anemia	83 (36.7%)	19 (57.6%)	0.03
Smoking	101 (44.7%)	13 (39.4%)	0.71
Family history of CAD	87 (38.5%)	11 (33.3%)	0.70
Dye volume in ml	177 (50-410)	220 (120-400)	<0.001
Creatinine before in mg/dl	1 ± 0.3	1.4 ± 0.6	<0.001
Creatinine after in mg/dl	1 ± 0.3	2.3 ± 1.1	<0.001
Creatinine Clearance before in ml/min	92 ± 26.1	67.3 ± 29.3	<0.001
CHA2DS2-VASc	2 (0-7)	4 (1-7)	<0.001
Mehran score	5 (0-19)	15 (7-26)	<0.001
Volume /creatinine clearance	2.1 (0.4-10.9)	4 (1.3-10.7)	<0.001
PCI	149 (65.9%)	10 (30.3%)	<0.001
	77 (34.1%)	23 (69.7%)	
eGFR>60ml/min	226 (87.26%)		
eGFR <60 ml/min		33(12.74%)	

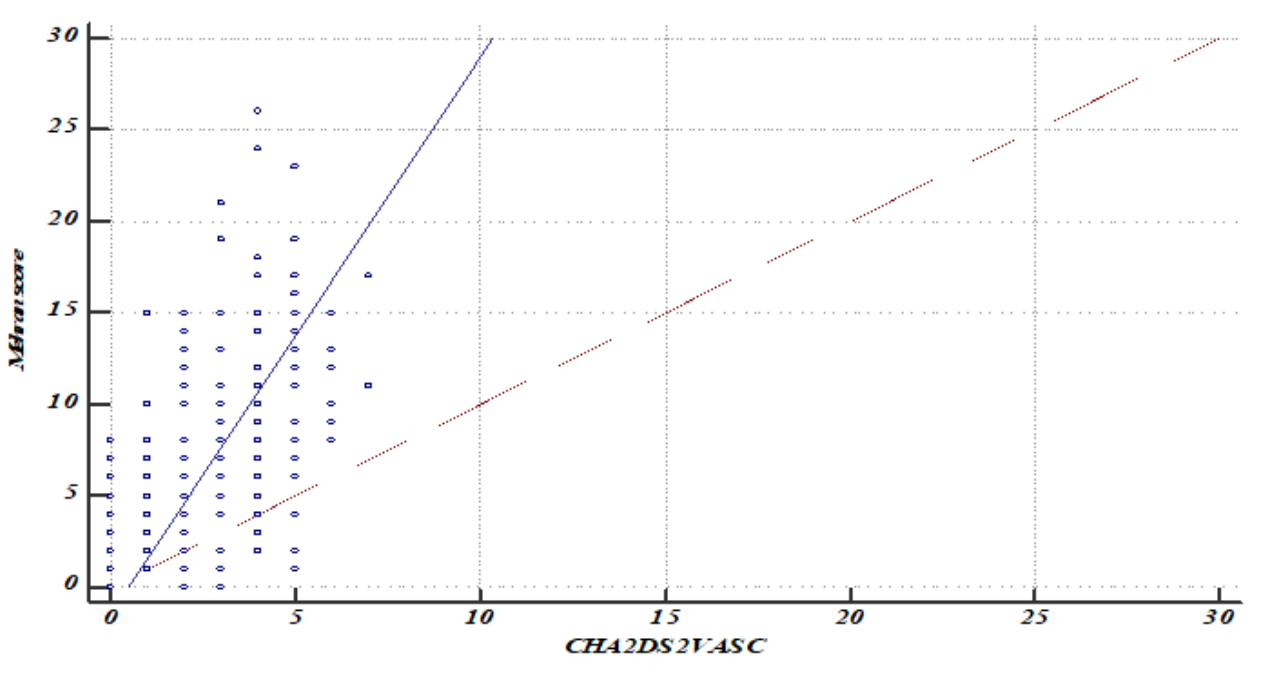

Figure 1. the correlation between CHADS-VASC score and Mehran score .(r= 0.61,p <0.001). 0.966). .

Ethical:

Written Informed consent was taken from all patients and approval was obtained from the Institutional Review Board (IRB) at Zagazig University, Egypt

Statistical analysis:

The analysis of data was done using the (SPSS) program version twenty (SPSS 20: Chicago, USA). Mean and standard deviation expressed continuous variables. The Independent T-test was used to calculate the difference between quantitative variables in the two groups for the parametric variables and the Mann-Whitney test was used for non-parametric variables. To find the independent predictors of CIN, we did univariate and multivariate logistic regressions. We used Pearson's product-moment coefficient of correlation (r) to examine the statistical correlation between continuous variables. The P-value < 0.05 indicates significance. For detection of the cut-off values in the prediction of CIN development, we used (ROC) receiver operating characteristic curve analysis.

Results:

This study included 259 patients who underwent PCI and classified them into two groups; the Group without CIN which had 226 patients (87.26%) and the group with CIN which had 33 patients (12.74%). **(Table 1)** As regards the age, weight, DM, EF<40%, history of stroke or TIA, the presence of peri-operative hypotension, anemia, and primary PCI were higher in patients with contrast-induced nephropathy group. Also, The patients with (CIN) had higher dye volume, creatinine before and after the procedure, CHA2DS2-VASc score, Mehran score, and dye volume/CrCL ratio. In our study, there was a significant positive correlation between the CHA2DS2-VASc score and the Mehran score (r =-0.608, p < 0.001) **(Figure 1)**. The ROC curve analysis showed that the dye volume / Cr CL ratio has the best cut-off value to predict CIN if it is greater than 3.2 (81.82% sensitivity, 78.32 % specificity, 95% CI 0.776 - 0.871). It also shows that the Mehran score has the best cut-off value to predict CIN if it is greater than 8 (93.94 % sensitivity, 76.55 % specificity, 95% CI 0.904). As regards the CHA2DS2-VASc score, the best cut-off value to detect CIN if it is greater than 3 (66.67 % sensitivity, 69.91% specificity

Table 2. The best cut off value of CHA2DS2-VASc score and Volume /creatinine clearance ratio as a predictor for development of CIN.

	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	**NPV % (95% CI)**	**AUC (95% CI)**	**P value**
CHA2DS2-VASc .score >3 Or V/CrCl >3.2	96.97 (84.24-99.92)	56.19 (49.46-62.77)	2.21 (1.89 - 2.60)	0.05 (0.01 - 0.37)	0.77 (0.71 - 0.82)	<0.001
CHA2DS2-VASc .score >3 + V/CrCl >3.2	51.52 (33.54-69.20)	92.04 (87.70-95.21)	6.47 (3.72 - 11.25)	0.53 (0.37 - 0.75)	0.72 (0.66 -0.77)	<0.001

95% CI 0.67- 0.78). The addition of CHA2DS2-VASc score to Volume /creatinine clearance showed that if the patient had (CHA2DS2-VASc score>3 or V/CrCl >3.2), as a single predictor, we could predict CIN with (sensitivity 96.97 %, specificity56.19 %, 95% CI 0.71 to 0.82). **(Table 2)**. When we compared patients with CHA2DS2-VASC score ≤3 (169 patients) versus those with CHA2DS2-VASc score >3 (90 patients); we found that CIN developed in only 11 patients in cases with CHA2DS2-VASc score ≤3 (6.5%) while in cases with CHA2DS2-VASc score >3, 22 patients developed CIN (24.4%). The statistical analysis showed a highly significant difference between these two groups (x=3.9, p<0.001). On multivariate analysis, VOL/CrCl >3.2 (OR 4.03 ; p = 0.001), CHA2DS2VASc.score >3(OR 15.0; p < 0.001), CHF or EF < 40 %(OR 0.065; p = 0.002), primary PCI (OR 4.464 ; p = 0.03), weight(OR 1.086; p = 0.007), and Mehran score(OR 2.492; p < 0.001), were the independent predictors of CIN after PCI **(Table 3)**.

Discussion:

The main goal of our study in real life is to find a way to reduce the suffering of people or to prevent the occurrence of CIN. The current evidence showed an association between CIN and prolonged hospitalization, increased expenses, as well as increased morbidity and mortality.[8,9] Many models for the prediction of CIN were created in an attempt to prevent this annoying complication, in Mehran's model is the most trusted one.[10] This score has the disadvantage of its complexity and difficulty to be applied and its limited predictive value for CIN until completing the procedure, so early treatment of CIN may be delayed.[11] The CHA2DS2-VASc score can be assessed quickly, without any difficulty, and remembered easily. So, it is a valuable predictive score.[6] We found that there was no significant difference between the two groups regarding gender. This result was in agreement with Lian et al.[11] and Kocas et al.[12] studies. However, different results were detected by Cicek and Yıldırım,[6] Kurtul et al.[13] and Ji et al.[10] who found a significant difference statistically between CIN group and no CIN group patients regarding gender and stated that the patients in the CIN group were more to be females compared with patients in no CIN group. Our study was in agreement with Cicek and Yıldırım,[6] Kurtul et al.[13] and Ji et al.[10] studies that show a significant difference between both groups regarding the age of patients. Diminished GFR and tubular secretion may justify this and concentrating ability and changes in renal function with advanced age. The prevalence of multi-vessel disease in ischemic heart disease combined with calcification and tortuosity of the vessels increases the needed amount of CM and this increases the risk of CIN in the elderly.[14] However, there is a contradiction between our study and Kocas et al.[12] study that had not a significant difference between both groups regarding the age of patients. Regarding hypertension, our study showed no significant difference between both groups. This result was in agreement with the Lian et al.[11] study. However, there is a contradiction between our study and Cicek and Yıldırım,[6] Kurtul et al.[13] and Ji et al.[10] studies that found a significant difference between both groups. The low sample size may explain this in our study.Regarding Diabetes mellitus, our study showed a significant difference between both groups. This was

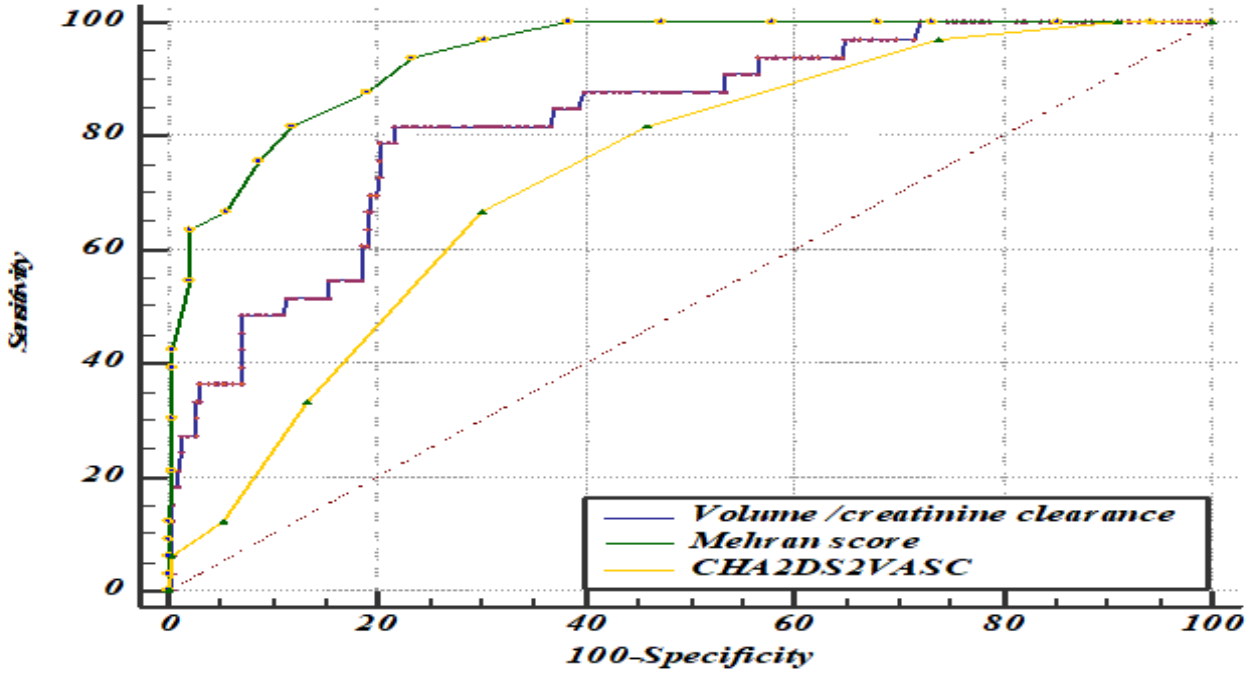

Figure 2. ROC curve analysis to determine best Cut off values for of CHADSVASc score, Mehran score and Volume of the dye /creatinine clearance for prediction of CIN.

in agreement with Cicek and Yıldırım,[6] Kurtul et al.[13] and Rahman et al.[15] studies.[16] Regarding CHF and hypotension, our study showed a significant difference between both groups.This was in agreement with Cicek and Yıldırım,[6] Kurtul et al.[13] and Lian et al.[11] Studies. Also, this result agrees with Senoo et al.[17] who identified Congestive heart failure (CHF) as an independent risk factor for CIN. ours explain that radio-contrast causes vasoconstriction of renal arteries and hypoxia to the medulla, and this may explain the cause of CIN. These circumstances of the decreased effective volume of circulation lead to a rise in sympathetic work, increased vasopressin in circulation, and renin-angiotensin system activation, which all share in medullary hypoxia.[18] The present study discovered a significant increase in the prevalence of anemia in the CIN group compared to no CIN one.These findings were in agreement with Li et al.[19] who found that patients with CIN group exhibited a higher frequency of anemic patients. This may be due to reduced renal blood flow by the direct effect of contrast media on the kidney as known in the pathophysiology of CIN. On the contrary, Lian et al.[11] showed in their study that there was no significant difference between CIN and no CIN patients regarding anemia. our explain that the selected patients where a low prevalence of anemia.The weight in this study was found as a new independent risk predictor for CIN. It is a fact that many diseases of the cardiovascular system can be caused by obesity which is better identified by BMI and CIN may occur through the effect of obesity on the glomerular structure and function.[20] Moreover, the incidence of CIN related to contrast medium use after a coronary angiogram is 10-15%[21] and agrees with our study which showed an incidence of 12.7%.It is recognized that the volume of the dye and basal kidney functions are strong predictors of CIN. We investigated the value of the addition CHA2DS2VASc score which is simple and easily calculated pre-procedure, to the V/CrCl ratio for raising CIN prediction following PCI. In our study, a CHA2DS2-VASc score of more than three was an independent predictor of Contrast-induced nephropathy occurrence in cases who were treated by PCI which agrees with Kurtul et al.[13] study, that indicated the risk of CIN significantly increases when CHA2DS2-VASc score > 3 in patients with STEMI. Nevertheless, Cicek and Yıldırım[6] study showed that a CHA2DS2-VASc score ≥ 3 is an independent predictor of CIN in ACS patients who are treated with urgent

Table 3. Univariate & Multivariate logistic regression analysis to detect independent predictors of CIN.

	Univariate Analysis				Multivariate Analysis			
		95% C.I.				**95% C.I.**		
	OR	Lower	Upper	Sig.	OR	Lower	Upper	**Sig.**
VOL/CrCl >3.2	16.26	6.35	41.59	<0.001	4.03	1.71	9.53	0.001
CHA2DS2-VASc score >3	4.65	2.14	10.11	<0.001	15.00	5.74	39.17	<0.001
CHF OR EF<40%	6.36	2.86	14.15	<0.001	0.065	0.011	0.379	0.002
Hypotension	1.61	1.36	1.90	<0.001	0.686	0.456	1.033	0.071
Anemia	1.33	1.04	1.70	0.03	0.609	0.364	1.02	0.06
PCI (primary)	4.45	2.02	9.82	<0.001	4.446	1.16	17.04	0.03
Weight in kg	1.04	1.00	1.08	0.004	1.086	1.022	1.154	0.007
Mehran	1.65	1.41	1.92	<0.001	2.492	1.744	3.561	<0.001

Table 4. The validity of CHA2DS2_VASC, Mehran score and Volume/creatinine clearance as predictors for development of CIN.

	Cut-off	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	AUC (95% CI)	**P**
Volume /creatinine clearance	>3.2	81.82 (64.5 - 93.0)	78.32 (72.4 - 83.5)	35.5 (24.9 - 47.3)	96.7 (93.0 - 98.8)	0.83(0.78 - 0.87)	<0.001
Mehran score	>8	93.94 (79.8 - 99.3)	76.55 (70.5 - 81.9)	36.9 (26.6 - 48.1)	98.9 (95.9 - 99.9)	0.94(0.90 - 0.97	<0.001
CHA2DS2_VASC	>3	66.67 (48.2 - 82.0)	69.91 (63.5 - 75.8)	24.4 (16.0 - 34.6)	93.5 (88.7 - 96.7)	0.73(0.67- 0.79	<0.001

The 95%CI: 95% confidence interval, Positive predictive value (PPV) and negative predictive value (NPV), Area under the ROC curve (AUC)

PCI. To our knowledge, our study was the only study that included both primary and elective PCI. Many cut-off values for safe contrast volume have been produced, yet the Volume /crCl ratio identifies the complexity of dosage and kidney function. Along these lines, this index must be more precise in anticipating the safety degree of contrast media than the absolute contrast media volume alone, particularly regarding the risk of CIN.[22] Positively, the V/CrCl proportion, a simple technique that can be utilized in practice for the assurance of the most noteworthy safe contrast volume, has been used to predict CIN following coronary catheterization.[23] Laskey et al.[23] found that a Volume /CrCl ratio of more than 3.7 with ideal for CIN detection. Nevertheless, these studies mostly followed the effects of contrast media according to the Serum Creatinine levels on the first day (rather than within three days), and just 6.8% had 24 and 48 hours Serum Creatinine level measurements in their studies, so they underestimated the incidence of CIN. In Our study, the sampling of serum Cr level within 48 to 72 hours after the procedure detected that the Volume /CrCl ratio was an

independent predictor of CIN. A study has identified that the cut-off value for the V/CrCl proportion was 2.6 in cases of known diabetics experiencing elective PCI.[24] Another research included 1020 elderly patients (age over sixty-five years) with relatively accepted renal function (the baseline creatinine less than 1.5 mg/dL) treated with PCI. (ROC) the curve used to detect the cut-off value of Volume /CrCl for predicting CIN that was 2.74.[22] Nevertheless, our study revealed that the best cut-off value for the Volume /CrCl ratio was (3.2) in patients treated with PCI procedure. The difference in cut-off values for the V/CrCl ratio and CIN incidence in the previous studies can be justified by the use of many definitions of CIN (24 or 48–72 hours) and the different numbers of patients with STEMI, DM, and CKD. Our study confirmed the value of adding CHADSVASc score to V /CrCl, as we concluded that if the patient had (CHADS-VASc score > three plus Volume /CrCl > 3.2), as a single predictor, we can predict CIN with specificity (92.04%) and sensitivity (51.52%). Also if the patient had (CHADS-VASc score > 3 or Vol /CrCl > 3.2) as a single predictor, we could predict CIN with sensitivity (96.97 %) and specificity (56.19%).

Limitation:

The fact that the patients were from the same geographic area and a single medical center with a limited number of patient subgroups were significant limitations of this study.

Conclusion:

In our study, there was a statistically significant correlation between the CHADVASC score and the incidence of CIN, and we can use the CHA2DS2-VASc score, and safe contrast volume for early detection of CIN after PCI.

Recommendation:

Use of CHA2DS2VASc score and Volume /CrCl ratio in early detection and management of contrast-induced nephropathy post-PCI.

Acknowledgments:

We thank all the clinicians and patients for their cooperation in the study.

Conflicts of interest:

No conflict of interest.

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