

Abstract:

CHA2DS2-Vasc Score as a Novel Predictor for Contrast-Induced Nephropathy, Irrespective to Atrial Fibrillation, after Percutaneous Coronary Intervention in Acute Coronary Syndrome

Saad M. Ammar, Mohamed A. Hamouda, Mohamed W. Abdelhamid, Shereen M. Ahmed

Department of cardiovascular medicine, Benha faculty of medicine, Benha University, Egypt.

Correspondence to: , Mohamed W. Abdelhamid, Department of cardiovascular medicine, Benha faculty of medicine, Benha University, Egypt.

Email:

m.wafik2@gmail.com Received: 18 August 2022 Accepted: 7 November 2022 Background: Patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) are at particularly high risk of contrast-induced nephropathy (CIN), which, when occurring, may be followed by persistent worsening of renal function. The aim of this work was to validate CHA₂DS₂-VASc score as a novel predictor for contrast-induced nephropathy. irrespective to atrial fibrillation, after percutaneous coronary intervention in acute coronary syndrome. Methods: This was a single center, prospective cohort, non-randomized, observational study. This study included 200 patients with acute coronary syndrome who were planned for percutaneous intervention referred to the Department of Cardiology, Universal medical insurance tertiary hospital, Port Said, in the period between September, 2021 to January 2022. These patients were divided into two groups as: Group 1 (with CIN) and Group 2 (without CIN). Results: The current study showed that, CIN cases were significantly associated with higher CHA₂DS₂-VASc score when compared to those with no CIN. The optimal cut off value was 4, sensitivity was 75%, specificity was 71.4%, PPV was 33.3%, NPV was 93.7%, and accuracy was 72%. For the presence of CHA_2DS_2 -VASc score <4, AUC for predicting CIN was 0.749 (sensitivity 62.5%, specificity 93.3%). For the presence of

CHA₂DS₂-VASc score \geq 4, AUC for predicting CIN was 0.807 (sensitivity 77.1%, specificity 86.8). Conclusion: CHA₂DS₂-VASc score has a positive predictive value being sensitive and specific for prediction of risk of CIN in population underwent PCI. Thus, CHA₂DS₂-VASc could be used easily in day-to-day clinical practice before PCI to give protective measures for patients at high risk.

Key words: CHA₂DS₂-VASc score; Novel predictor; Contrast-induced nephropathy; Percutaneous coronary intervention; Acute coronary syndrome

Introduction:

CHA₂DS₂-VASc is a composite scoring system comprising congestive heart failure/left dysfunction. ventricular diabetes hypertension, age≥75 years, mellitus, previous stroke, vascular disease, age 65–74 years, and sex(female). It has been traditionally used as a prediction tool for risk of stroke in patients with atrial fibrillation. These variables used in this score are risk factors for poor clinical outcomes in cardiovascular diseases. Studies have shown CHA₂DS₂-VASc score to have a good predictive value for adverse clinical outcomes in patients with coronary artery disease such as stable angina pectoris and acute coronary syndrome(ACS) with or without atrial fibrillation.⁽¹⁾

In patients with stable coronary artery disease(CAD) as well as ACS, who undergo percutaneous coronary intervention(PCI), contrast-induced nephropathy(CIN) is a known complication and is often associated with an increased in-hospital and long-term morbidity including chronic renal dysfunction and mortality. The incidence of CIN ranges from 7% to 25% in different population subgroups based on the risk status. Hence, risk stratification has an important bearing to provide the appropriate preventive therapies to these high-risk individuals even before contrast media exposure.⁽²⁾

In the past, several risk prediction models have been proposed to envisage the CIN incidence. *The study conducted in 2004* ⁽³⁾ proposed a scoring system comprising eight variables which correlated well with the CIN risk.

The aim of this work was to validate CHA₂DS₂-VASc score as a novel predictor for contrast-induced nephropathy, irrespective to atrial fibrillation, after percutaneous coronary intervention in acute coronary syndrome.

Patients and Methods:

<u>Study design:</u>

It was a single center, prospective cohort, non-randomized, observational study that was conducted at the Department of Cardiology, Universal medical insurance tertiary hospital, Port Said.

Patient selection:

This study included 200 patients with acute coronary syndrome who were planned for percutaneous intervention referred to the Department of Cardiology, Universal medical insurance tertiary hospital, Port Said, in the period between September,2021 to January 2022.

• All patients were prescribed a loading dose of aspirin 300 mg and clopidogrel 300 mg prior to the procedure. A dose of 70-100 U/kg of unfractionated heparin was given during the procedure and the use of glycoprotein IIb/IIIa receptor inhibitor and the type of stents was based on the physician's discretion ⁽⁵⁾.

These patients were divided into **<u>two groups</u>** as:

Group 1 (with contrast induced nephropathy (CIN)) and Group 2(without CIN).

<u>Contrast induced nephropathy</u> was defined as increase in serum creatinine level $\geq 0.5 \text{ mg/dL}$ or $\geq 25\%$ increase from baseline within 48 h after PCI. ⁽⁶⁾

Inclusion criteria :

Patients (of both genders) who was admitted with acute coronary syndrome, including both ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (non-STEMI) who were planned for percutaneous intervention at Universal medical insurance tertiary hospital.

Exclusion criteria :

• Patients<18 ys old & >75 ys old.

• Patients with an estimated glomerular filtration rate (eGFR) < 30 mL/min, either with or without pre-existing dialysis, shock, acute renal failure, acute or chronic infection/inflammatory conditions, recent exposure to radio-graphic contrast media (within 10 days of enrollment), or having contraindications for PCI.

• Patients whose procedure was complicated by perforation or dissection.

• Patients who unfortunately died during or early after procedure or lack of data on serum creatinine during the 48 h after the procedure.

Methodology:

All patients were subjected to the following:

- Complete personal history including: Name, age, sex, occupation, special habits and risk factors for ischemic heart disease (smoking, diabetes, hypertension), family history of CAD, previous history of CAD or coronary artery bypass graft, previous atherosclerotic cerebrovascular events and current medical therapy.
- Complete physical examination, including:
- **A.** Weight (in kg), height (in cm), body surface area $(BSA)^{(7)}$ in m².

BSA=[(height (in cm)+weight (in Kg)-60)]/100

- **B.** Vital signs including body temperature, heart rate, respiratory rate and systolic and diastolic blood pressure.
- C. Killip class at time of presentation.
- Killip classification is widely used in patients presenting with acute MI for the purpose of risk stratification, as follows⁽⁸⁾:
- Killip class I includes individuals with no clinical signs of heart failure
- Killip class II includes individuals with rales or crackles in the lungs, S_3 gallop, and elevated jugular venous pressure
- Killip class III describes individuals with frank acute pulmonary edema
- Killip class IV describes individuals in cardiogenic shock or hypotension (measured as systolic blood pressure <90 mmHg), and evidence of low cardiac output (oliguria, cyanosis, or impaired mental status).

• The following laboratory tests:

- A. Serum Creatinine, and eGFR was calculated using Cockcrofte Gault method: (9)
- [140-age(years) × weight (kg)/72 × serum creatinine(mg/dl) [× 0.85 for female subjects]

Baseline serum creatinine was determined upon admission and was monitored for 48 hrs. and 7 days after the procedure to determine the occurrence of CIN.

B. Routine work up:

- Complete blood count, blood urea, random blood sugar, glycated hemoglobin, serum sodium, potassium and fasting lipid profiles.
- <u>Electrocardiography</u>: 12 lead surface ECG was done for each patient.
- <u>Echocardiography</u>: Left ventricular ejection fraction was estimated by 2D echocardiography at admission using Simpson method ejection fraction
- Calculating <u>CHA₂DS₂-VASc score</u> for each patient as follows: ⁽¹⁰⁾.
- C for Congestive heart failure 1 point.
- H for Hypertension or high blood pressure 1 point
- A for Age greater than or equal to 75 years 2 points
- D for Diabetes mellitus or type 2 diabetes 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 1 point

The maximum score for a CHA₂DS₂-VASc is nine.

Ethical consideration

This study gained the approval of the institutional ethic committee at faculty of medicine, Benha University no.#000125

Statistical analysis:

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Normality of data

• Kolmogorov Smerinov test was done to test the normality of data distribution.

Descriptive statistics:

 Mean, Standard deviation for parametric numerical data, while Median and range for non-parametric numerical data. Frequency and percentage of non-numerical data. Analytical statistics:

- Student T Test
- Mann Whitney Test (U test)
- Chi-Square test
- Fisher's exact test
- Correlation analysis
- The ROC Curve (receiver operating characteristic)

Regression analysis

A p value is considered significant if <0.05 at confidence interval 95%.

Results:

Mean age of studied cases was 57.6 years; they were 116 males(58%)and 84 females(42%). Among them, 38.5% were smokers. 35.5% had DM. 49% had hypertension, 14.5% had CAD, 2% had renal diseases, 7.5% had PAD, 3.5% had S/P CABG and 4% had S/P CVA; 18.5% had KILLIP class>II (**Table 1**).

Contrast—induced nephropathy occurred in 32/200(16%) patients.

nephropathy Contrast—induced was significantly associated with higher frequency of DM(46.9% versus 29.2%), hypertension(68.8% 45.2%), versus CAD(31.3%) versus 11.3%), renal diseases(12.5% 0%), killip versus class>II(21.9% versus 17.9%) (p=0.049, 0.015, 0.003, <0.001, 0.592 respectively). Otherwise, no significant association was found regarding baseline demographic, history and clinical data of studied cases according to presence or absence of CIN (p>0.05 for each)(**Table 2**).

Table 3 shows that no significant differences

 were found regarding anthropometric

measures of studied cases according to presence or absence of CIN (p>0.05 for each).

Contrast-induced nephropathy cases were significantly associated with higher **RBS**(185.6 versus 15.7.6. p=0.032), HbA1C(8.2 versus 7, p=0.031), LDL(106.3 versus 82.7, p<0.001), TG(140.5 versus 124.2, p<0.001), lower eGFR pre-PCI (62.8 versus 93.2, p<0.001), serum creatinine 48 hrs.(1.5 versus 0.9, p<0.001) and serum creatinine 7 days after contrast(1.3 versus 1.1, p < 0.01), when compared to those with no CIN. Otherwise, no significant differences were found regarding laboratory parameters of studied cases according to presence or absence of CIN (Table 4).

Contrast—induced nephropathy cases were significantly associated with lower LVEF when compared to those with no CIN $(57.2\pm7.4 \text{ versus } 50.3\pm7.2, p<0.001).$

No significant differences were found between both groups regarding STEMI and NSTEMI

(Table 5).

Table 6 shows that CIN cases were significantly associated with higher contrast For the presence of CHA_2DS_2 -VASc score ≥ 4 , AUC for predicting CIN was 0.807

volume (mean=170.8 \pm 45.5 ml vs 134.6 \pm 20.2 ml, p<0.001) and number of stents (median(min-max)= $^{7}.5(1-3)$ vs $^{7}(0-3)$, p<0.001) when compared to those with no CIN.

Contrast—induced nephropathy cases were significantly associated with higher CHA_2DS_2 -VASc score when compared to those with no CIN(median(min-max)=5(1-7)) versus 3(1-7) respectively, p<0.001)(**Table 7**).

Table 8 shows the receiver operatingcharacteristic(ROC)curve of CHA2DS2-VASc score that was conducted forprediction of CIN.

Among all studied cases, CHA_2DS_2 -VASc score showed moderate accuracy AUC (AUC=0.784). The optimal cut off value was 4, sensitivity was 75%, specificity was 71.4%, PPV was 33.3%, NPV was 93.7%, and accuracy was 72%.

For the presence of CHA₂DS₂-VASc score <4, AUC for predicting CIN was 0.749 (sensitivity 62.5%, specificity 93.3%) (**Figure 1**).

(sensitivity 77.1%, specificity 86.8) (Figure 2).

Logistic regression analysis was conducted for prediction of CIN susceptibility using age, gender, DM, hypertension, KILLIP, eGFR, metformin, ACEI/ARB use, contrast volume and CHA₂DS₂-VASc score as confounders. Presence of DM, hypertension, KILLIP>2, use of metformin, ACE inhibitor/ARB, lower eGFR, higher contrast volume, CHA₂DS₂-VASc score were associated with risk of CIN in univariable analysis. However, in multivariable analysis, only KILLIP>2, higher contrast volume, CHA₂DS₂-VASc score were considered independent predictors of CIN susceptibility (**Table 9**).

		Cases (n=200)
Age (years)	mean±SD	57.6±6.7
Males	N (%)	116(58%)
Females	N (%)	84(42%)
Smoking	N (%)	77(38.5%)
Diabetes mellitus	N (%)	71(35.5%)
Hypertension	N (%)	98(49%)
CAD	N (%)	29(14.5%)
Renal diseases	N (%)	4(2%)
PAD	N (%)	۱°(7.5%)
S/P CABG	N (%)	٧(3.5%)
S/P CVA	N (%)	^(4%)
KILLIP class > II	N (%)	37(18.5%)

Table (1). Baseline demographic, history and clinical data of studied cases.

SD: Standard deviation; CAD: Coronary artery disease; PAD: Peripheral arterial disease; S/P CABG: Status post coronary artery bypass graft; S/P CVA: Status post cerebrovascular accident

CHA2DS2-VASc score as a novel predictor for CIN, 2022

		Group 1 (CIN) n=32	Group 2 (No CIN) n=168	р	
Age (years)	mean±SD	57.6±6.1	57.6±6.8	0.991	
Males	N (%)	18(56.3%)	98(58.3%)	0.007	
Females	N (%)	14(43.8%)	70(41.7%)	0.827	
Smoking	N (%)	13(40.6%)	64(38.1%)	0.788	
Diabetes mellitus	N (%)	15(46.9%)	49(29.2%)	0.049	
Hypertension	N (%)	22(68.8%)	76(45.2%)	0.015	
CAD	N (%)	10(31.3%)	19(11.3%)	0.003	
Renal diseases	N (%)	4(12.5%)	0(0%)	<0.001	
PAD	N (%)	(3.1%)	14(8.3%)	0.473	
S/P CABG	N (%)	٣(9.4%)	4(2.4%)	0.083	
S/P CVA	N (%)	۲(6.3%)	6(3.6%)	0.617	
KILLIP class > II	N (%)	7(21.9%)	30(17.9%)	0.592	

SD: standard deviation; CAD: coronary artery disease; PAD: peripheral arterial disease; S/P CABG: Status post coronary artery bypass graft; S/P CVA: status post cerebrovascular accident

Table (3). Comparison	of anthropometric measure	es of studied cases according to	presence or absence of CIN.

		Group 1 (CIN)		Group 2 (No CIN)			р	
		n=32			n=168			
BMI (kg/m ²)	mean±SD	26.3	±	4.2	28.0	±	4.8	0.069
SBP (mmHg)	mean±SD	119.7	±	25.2	125.4	±	24.7	0.235
DBP (mmHg)	mean±SD	75.0	±	14.6	76.2	±	13.6	0.645

SD: Standard deviation; BMI: Body mass index; RR: Respiratory rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: Heart rate

		Group	1 (CI	N)	Group	2 (No	CIN)	р
		n=32			n=168			
Hemoglobin (g/dL)	mean±SD	13.0	±	2.0	12.8	±	1.7	0.617
RBS (mg/dL)	mean±SD	185.6	±	57.1	157.6	±	50.3	0.032
HbA1C (%)	mean±SD	8.2	±	1.9	7	±	1.6	0.031
TC (mg/dL)	mean±SD	216.5	±	36.7	211.0	±	33.4	0.539
HDL (mg/dL)	mean±SD	38.6	±	7.8	39.2	±	6.4	0.683
LDL (mg/dL)	mean±SD	106.3	±	11.7	82.7	±	11.2	<0.001
TG (mg/dL)	mean±SD	140.5	±	21.4	124.2	±	18.2	<0.001
CH/HDL	mean±SD	5.6	±	0.8	5.6	±	0.7	0.704
eGFR pre-PCI (ml/min)	mean±SD	62.8	±	5.9	93.2	±	19.7	<0.001
Serum Creatinine before contrast (mg/dL)	mean±SD	1.0	±	0.2	1.1	±	0.2	0.287
Serum Creatinine 48 after contrast (mg/dL)	mean±SD	1.5	±	0.4	0.9	±	0.1	<0.001
Serum Creatinine 7 days after contrast (mg/dL)	mean±SD	1.3	±	0.2	1.1	±	0.2	<0.001

Table (4). Comparison of labo	oratory parameters of studied cas	ses according to presence	e or absence of CIN.

SD: Standard deviation; RBS: Random blood sugar; TC: Total cholesterol; HDL: High-density lipoprotein; TG: Triglycerides; LDL: Low-density lipoprotein; eGFR: Estimated glomerular filtration rate; INR: International normalized ratio

Table (5). Comparison of ECG and echo results of studied cases according to presence or absence of CIN.

		Group 1 (CIN)	Group 2 (No CIN)		
		n=32	n=168	р	
STEMI	N (%)	15(46.9%)	65(38.7%)	0.296	
NSTEMI	N (%)	17(53.1%)	103(61.3%)	0.386	
LVEF (%)	mean±SD	50.3±7.2	57.2±7.4	<0.001	

STEMI: ST elevation myocardial infarction; NSTEMI: Non-ST elevation myocardial infarction; LVEF: Left ventricular ejection fraction; SD: Standard deviation

		Group 1 (CIN)	Group 2 (No CIN)	р
		n=32	n=168	
Contrast volume (ml)	Mean ± SD	170.8±45.5	134.6±20.2	<0.001
Number of stents	median (minimum- maximum)	۲.5(1-3)	۲(0-3)	<0.001
	SD	0.07	0.8	

Table (6).	Comparison	of PCI data	of studied cases	s according to p	resence or absence of CIN.

SD: Standard deviation

Table (7). Comparison of CHA₂DS₂-VASc score of studied cases according to presence or absence of CIN.

		Group 1 (CIN)	Group 2 (No CIN)	
		n=32	n=168	<i>p</i>
CHA ₂ DS ₂ -VASc score	median (minimum- maximum)	5(1-7)	3(1-7)	<0.001
	SD	1.7	1.2	

SD: Standard deviation

Table (8). ROC curve for CHA₂DS₂-VASc score for prediction of CIN.

	CHA ₂ DS ₂ -VASc score	CHA ₂ DS ₂ -VASc score <4	CHA ₂ DS ₂ -VASc score ≥4
AUC	0.784	0.749	0.807
Sensitivity (%)	75%	62.5	75
Specificity (%)	71.4%	93.3	77.1
PPV (%)	33.3%	99.3	86.8
NPV (%)	93.7%	14.2	60.7
Accuracy (%)	72%	64.4	75.7

AUC: area under ROC; ROC: receiver operating curve; PPV: positive predictive value; NPV: negative predictive value.

	Univari	Univariable			Multivari	Multivariable		
	р	OR	95% CI		p	OR	95% CI	
Age	0.996	1.002	0.969	1.032				
Gender	0.798	1.057	0.692	1.613				
Diabetes mellitus	0.014	1.365	1.190	2.093	0.136	0.496	0.197	1.247
Hypertension	0.017	1.699	1.102	2.621	0.746	0.872	0.380	2.000
KILLIP class > II	0.004	1.474	1.195	1.984	0.036	1.387	1.129	1.928
eGFR pre-PCI	<0.001	0.820	0.710	0.929	0.283	0.809	0.758	1.493
Metformin	0.018	1.784	1.103	2.886	0.633	1.225	0.533	2.816
ACEi/ARB	0.018	1.784	1.103	2.886	0.247	1.011	0.993	1.029
Contrast volume	<0.001	1.023	1.014	1.032	<0.001	1.035	1.020	1.051
CHA ₂ DS ₂ -VASc score	<0.001	1.562	1.340	1.822	<0.001	1.577	1.238	2.008

Table (9). Regression analysis for prediction of CIN susceptibility.

eGFR: estimated glomerular filtration rate; ACEi: Angiotension converting enzyme inhibitor; ARB: Angiotension receptor blocker; OR: odds ratio; CI: confidence interval. Logistic regression test was used.

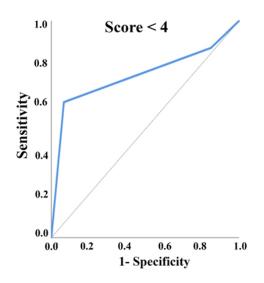


Fig. (1). ROC curve for CHA₂DS₂-VASc <4 score for prediction of CIN.

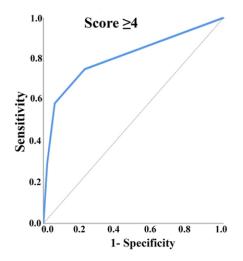


Fig. (2). ROC curve for CHA_2DS_2 -VASc \geq 4 score for prediction of CIN.

Discussion

Coronary artery disease (CAD), including acute coronary syndrome (ACS), remains common the most cause of death worldwide $^{(16)}$. Thus, reperfusion therapy with intravenous fibrinolysis or percutaneous intervention (PCI) has become the primary goal in the management of ACS which makes patients undergoing PCI at high risk of contrast-induced nephropathy (CIN), which may lead to persistent worsening of renal function $^{(17)}$.

In the past, several risk predictions models have been proposed to anticipate the CIN incidence. Despite having a fair degree of accuracy, complexity was one of their major limitations. Since the CHA2DS2-VASc is widely used, questioning whether it can be useful to predict CIN, is unclear and because patients with ACS have a far greater risk for CIN compared to patients with stable CAD, its use as a predictive tool cannot be undermined⁽¹⁸⁾.

This was a single center, prospective cohort, non-randomized, observational study. It included 200 patients with acute coronary who planned syndrome were for percutaneous intervention referred to the Department of Cardiology, Universal medical insurance tertiary hospital, Port Said, in the period between September, 2021 to January 2022. These patients were divided into two groups as: Group 1 (with CIN) and Group 2 (without CIN).

In the current study, contrast-induced nephropathy (CIN) incidence was about 16% among the studied population. Contrast-induced nephropathy in the study conducted in 2019 ⁽²⁾ to assess the predictive role of CHA₂DS₂-VASc score for CIN in patients with ACS undergoing percutaneous coronary intervention (PCI), was reported in 41 patients (13.6%).

According to the study conducted in 2017 ⁽⁴⁾ which investigated the correlation between the CHA₂DS₂-VASc score and contrastinduced nephropathy in patients with ACS who underwent urgent percutaneous coronary intervention (PCI), it reported that a total of 159 patients were diagnosed with CIN within 48-72 hours after PCI, bringing the incidence rate to 11.3% in the study population.

In the current study, CIN was significantly associated with higher frequency of DM (46.9% versus 29.2%), hypertension (68.8% versus 45.2%), CAD (31.3% versus 11.3%), and renal diseases (12.5% versus 0%) (p=0.049,0.015, 0.003,<0.001 respectively).Otherwise, no significant association was found regarding baseline demographic, history and clinical data of studied cases according to presence or absence of CIN(p>0.05 for each).

This was in agreement with study conducted in 2019 ⁽²⁾ which demonstrated significant

correlation between CIN and diabetes [29(70.7%) versus 33(12.7%)], hypertension [28(68.3%) versus 92(35.5%)], higher systolic blood pressure 148.39 ± 34.75 versus 134.32 ± 24.29 , CHF as evident from (i)a higher Killip class [29 (70.7%) vs 25 (9.6%)] and (ii)a lower left ventricular systolic function.

This was also in accordance with the study conducted in 2014 (11) which investigated the relationship of patients' variables, including gender, CIN and mortality after primary PCI. They found that female gender (23(46.9) versus 69(25.2)), older age (18(36.7))versus 61(22.3)),diabetes (10(20.4) versus 45(16.4)), hypertension 24(49.0) versus 145(52.9), CHF, and renal dysfunction $(1.2 \pm 1.0 \text{ versus } 1.0 \pm 0.4)$ are well known risk factors for development of CIN (P value = 0.003, 0.05, 0.022, 0.001, 0.0001, 0.01 receptively). A reduced glomerular volume in women compared to their male counterpart has been proposed as a possible mechanism to explain a greater susceptibility to acute renal failure.

Our results showed that CIN cases were significantly associated with higher RBS (185.6 versus 157.6 p=0.032), HbA1C (8.2 versus 7, p=0.031), LDL(106.3 versus 82.7,p<0.001), TG(140.5 versus 124.2,

p<0.001), lower eGFR pre-PCI (62.8 versus 93.2, p<0.001), serum creatinine 48 hrs. (1.5 versus 0.9, p<0.001) and serum creatinine 7 days after contrast (1.3 versus 1.1,p<0.01) when compared to those with no CIN. Otherwise, no significant differences were found regarding laboratory parameters of studied cases according to presence or absence of CIN.

This was in concordance with the study conducted in 2014 ⁽¹²⁾ which reported that the use of an iso-osmolar contrast media in patients with a lower baseline eGFR was significantly associated with reduced CIN in their study. Hence, limiting the amount of contrast media used along with use of iso-osmolar contrast agents and adequate hydration may serve as a crucial strategy to limit the incidence of CIN in patients with known baseline reduced renal function.

In our study, CIN cases were significantly associated with lower LVEF when compared to those with no CIN (57.2 ± 7.4 versus. 50.3 ± 7.2) (P value <0.001). No significant differences were found between both groups regarding STEMI and NSTEMI (P value = 0.386).

This was consistent with the study conducted in 2014 ⁽¹³⁾ which found that

patients with CHF are further at an increased risk for CIN as poor renal perfusion leads to a greater degree of renal vasoconstriction in adjunct with a low preload status in these subjects.

This was also supported by the study conducted in 2004 ⁽³⁾ which sought to develop a simple risk score of contrastinduced nephropathy (CIN) after percutaneous coronary intervention (PCI), that other predictors such as higher contrast volume were also found significantly correlated with risk of CIN (P value = 0.003), which are parts of Mehran risk model.

In the present study, CIN cases were significantly associated with higher contrast volume (mean=170 versus 134.6, p<0.001) and number of stents (median =2.5 versus 2, p<0.001). (Table 6)

When compared to those with no CIN these data were concurrent with the study done in 2017 ⁽⁴⁾ which found that multivessel CAD and multivessel PCI were the new predictors of CIN as established in their study probably due to the fact that a complete revascularization in these patients precluded a greater usage of radio contrast media. This

was carried out on 1408 patients with ACS undergoing urgent PCI (P<0.001).

Our results agreed with the study conducted in 2019 ⁽²⁾ which reported that higher contrast volume was significantly correlated with risk of CIN (P=0.001), which are parts of Mehran risk model ⁽³⁾.

The study done in 2019., ⁽²⁾ also reported that, multivessel CAD and multivessel PCI were the new predictors of CIN as established in their study probably due to the fact that a complete revascularization in these patients precluded a greater usage of radio contrast media (P=0.004).

The current study showed that, CIN cases were significantly associated with higher CHA₂DS₂-VASc score when compared to those with no CIN (median= 5 versus 3 respectively, p<0.001).

This was in agreement with the study conducted in 2016 ⁽¹⁴⁾ which investigated the association of the CHA₂DS₂-VASc-HSF score with the severity of CAD as assessed by SYNTAX score (SxS) in patients with ST segment elevation myocardial infarction (STEMI) and deducted that, CHADS₂ and CHA₂DS₂-VASc scores were found to be associated with both short- and long-term adverse clinical outcomes and mortality in

patients with stable CAD and ACS. (Role of the CHADS₂ score in acute coronary syndromes: risk of subsequent death or stroke in patients with and without atrial fibrillation) (Predictive value of newly defined CHA₂DS₂-VASc-HSF score for severity of coronary artery disease in STEMI).

However, in our study, we used the CHA_2DS_2 -VASc score instead of $CHADS_2$ as it's a more comprehensive tool and had been applied on patients with ACS rather than stable CAD.

Moreover, the study conducted in 2019 ⁽²⁾ reported that CHA₂DS₂-VASc score \geq 4 is independently associated with the occurrence of CIN in patients with ACS treated by PCI (P=0.02).

Receiver operating characteristic(ROC) curve of CHA₂DS₂-VASc score was conducted for prediction of CIN in our study.

Among all studied cases in our research, CHA₂DS₂-VASc score showed moderate accuracy AUC (AUC=0.784). The optimal cut off value was 4, sensitivity was 75%, specificity was 71.4%, PPV was 33.3%, NPV was 93.7%, and accuracy was 72%. For the presence of CHA₂DS₂-VASc score <4, AUC for predicting CIN was 0.749 (sensitivity 62.5%, specificity 93.3%). For the presence of CHA₂DS₂-VASc score \geq 4, AUC for predicting CIN was 0.807 (sensitivity 77.1%, specificity 86.8) (**Figure 1 & 2**).

Our results were concordant with the study conducted in 2017 ⁽⁴⁾ which demonstrated that the adequate cut off score of CHA₂DS₂-VASc to predict CIN in ACS setting, was as follows, a score of 4 was highly predictive of developing CIN.

The study conducted in 2019 ⁽²⁾ also determined the adequate cutoff score of CHA₂DS₂-VASc to predict CIN in ACS setting. A score of \geq 4 was highly predictive of developing CIN (P= 0.0001).

Moreover, we reached the same result as the study conducted in 2015 ⁽¹⁵⁾ which found that CHA₂DS₂-VASc score due to its ease of usage permits us to predict the occurrence of CIN in patients with ACS and implement prophylactic measures (intravenous hydration) before contrast exposure to prevent CIN.

Conclusion:

CHA₂DS₂-VASc score has a positive predictive value being sensitive and specific

for prediction of risk of contrast-induced nephropathy in a population which underwent PCI. Thus, CHA₂DS₂-VASc could be used easily in day-to-day clinical practice before PCI to give protective measures for patients at high risk.

References:

- 1. Bozbay M., Uyarel H., Cicek G, Oz A, Keskin M, Murat A, et al. CHA₂DS₂-VASc score predicts in-hospital and long-term clinical outcomes in patients with ST-segment elevation myocardial infarction who were undergoing primary percutaneous coronary intervention. *Clin Appl Thromb Hemost. 2017;23:132–138.*
- 2. Chaudhary AK, Pathak V, Kunal S, Shukla S and Pathak P. CHA₂DS₂-VASc score as a novel predictor for contrast-induced nephropathy after percutaneous coronary intervention in acute coronary syndrome. *Indian Heart J. 2019 Jul-Aug;71(4):303-308.*
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;44:1393–9.
- Kurtul A, Yarlioglues M and Duran M. Predictive value of CHA₂DS₂-VASc score for contrast-induced nephropathy after percutaneous coronary intervention for acute coronary syndrome. *Am J Cardiol. 2017;119:819e825.*
- Wang Y, Zhang H, Yang Z, Miao D and Zhang D. Rho kinase inhibitor, Fasudil, attenuates contrast-induced acute kidney injury. *Basic Clin Pharmacol Toxicol.* 2018;122(2):278–87.
- Mohammed NM, Mahfouz A, Achkar K, Rafie IM and Hajar R. Contrastinduced nephropathy. *Heart Views.* 2013;14(3):106–16.
- 7. **Redlarski G, Palkowski A and Krawczuk M**. Body surface area formulae: an alarming ambiguity. *Sci Rep.* 2016 Jun 21;6:27966.
- 8. **Hubbard BL, Newton CR, Carter PM, Fowler JJ, Schaldenbrand J, Singal B, et al.** The inability of B-type natriuretic protein to predict short-term

risk of death or myocardial infarction in non-heartfailure patients with marginally increased troponin levels. *Ann Emerg Med.* 2010 Nov. 56(5):472-80.

- Cockcroft DW and Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976;16:31e41.
- Siddiqi TJ, Usman MS, Shahid I, Ahmed J, Khan SU, Ya'qoub L, Rihal CS and Alkhouli M. Utility of the CHA2DS2-VASc score for predicting ischaemic stroke in patients with or without atrial fibrillation: a systematic review and meta-analysis. *European Journal of Preventive Cardiology*. 2022 Mar;29(4):625-31.
- 11. Lucreziotti S, Centola M, Salerno-Uriarte D, Ponticelli G, Battezzati PM, Castini D, et al. Female gender and contrastinduced nephropathy in primary percutaneous intervention for ST-segment elevation myocardial infarction. *Int J Cardiol.* 2014;174:37e42.
- 12. Ando G, de Gregorio C, Morabito G, Trio O, Saporito F and Oreto G. Renal function adjusted contrast volume redefines the baseline estimation of contrast-induced acute kidney injury risk in patients undergoing primary percutaneous coronary intervention. *Circ Cardiovasc Interv.* 2014;7:465e472.
- 13. Andreucci M, Faga T, Pisani A, Sabbatini M and Michael A. Acute kidney injury by radiographic contrast media: pathogenesis and prevention. *Biomed Res Int.* 2014;2014(1):362725.

- 14. Uysal OK, Turkoglu C, Duran M, Kaya MG, Sahin DY, Gur M et al. Predictive value of newly defined CHA₂DS₂-VASc-HSF score for severity of coronary artery disease in STEMI. *Kardiol Pol.* 2016;74:954e960.
- 15. Chong E, Poh KK, Lu Q, Zhang JJ, Tan N, Hou XM, et al. Comparison of combination therapy of high-dose oral N-acetylcysteine and intravenous sodium bicarbonate hydration with individual therapies in the reduction of Contrast-induced Nephropathy during Cardiac Catheterization and Percutaneous Coronary Intervention (CONTRAST): a multi-centre, randomised, controlled trial. Int J Cardiol. 2015;201:237e242.
- 16. Ralapanawa, Udaya and Ramiah Sivakanesan. "Epidemiology and the magnitude of coronary artery disease and acute coronary syndrome: A narrative review." Journal of Epidemiology and Global Health 11.2 2021: 169.
- 17. Muraca I, Pennesi M, Mattesini A, Migliorini A, Carrabba N, Virgili G, et al. Comparison of myocardial reperfusion between intracoronary versus intravenous cangrelor administration in patients undergoing primary percutaneous coronary intervention. *Cardiology journal* 2021, 10.5603/CJ.a2021.0108
- 18. Chou RH, Huang PH, Hsu CY, Leu HB, Huang SS, Huang CC, et al. CHADS2 score predicts risk of contrastinduced nephropathy in stable coronary artery disease patients undergoing percutaneous coronary interventions. J Formos Med Assoc. 2016;115:501e509.

To cite this article: Saad M. Ammar, Mohamed A. Hamouda, Mohamed W. Abdelhamid, Shereen M. Ahmed.CHA2DS2-Vasc Score as a Novel Predictor for Contrast-Induced Nephropathy, Irrespective to Atrial Fibrillation, after Percutaneous Coronary Intervention in Acute Coronary Syndrome. BMFJ 2022;39(3):954-970.