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# Predictors of contrast-induced nephropathy in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention

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## Abstract

**Background:** Contrast-induced nephropathy (CIN) is a serious complication with primary percutaneous coronary intervention (PPCI). We aimed to study the different predictors of CIN and determine the cutoff point of contrast volume (CV)/creatinine clearance (CrCl) and the applicability of CHA2DS2-VASC score in the prediction of CIN after PPCI in ST-elevation myocardial infarction (STEMI) patients. Four hundred patients presented with STEMI and eligible for primary PCI were included in the study. Patients with GFR < 30 ml/min were excluded from the study.

**Results:** Fifty-four (13.5%) patients who developed CIN who were older ( $64.20 \pm 13.16$  vs.  $55.80 \pm 10.58$ ) had a higher prevalence of diabetes mellitus (DM), hypertension (HTN), and female gender than those without CIN. They also had a higher Killip class and lower hemoglobin (HB) level ( $P < 0.05$ ) compared to those with no CIN. The incidence of no CIN was (85.8%) in the low-risk Mehran score group and 14.2% in the moderate-risk group, and all patients of high and very high score group developed CIN ( $P < 0.001$ ). Multiple logistic regression showed that old age (OR= 1.06, 95% CI= 1.02–1.11,  $P < 0.001$ ), female sex (OR= 3.1, 95% CI= 2.65–6.99,  $P = 0.02$ ), high Mehran score (OR=2.48, 95% CI= 1.98–6.24,  $P = 0.01$ ), CV/CrCl > 2.8 (odds ratio=1.45, 95% CI= 1.22–2.01,  $P = 0.03$ ), and CHA2DS2-VASC score > 2 (odds ratio=1.90, 95% CI= 1.76–2.11,  $P = 0.04$ ) were predictors of CIN.

**Conclusions:** Old age, female sex, high Mehran score, CHADS2-VASC score > 2, CV/CrCl > 2.8 were predictors of CIN in STEMI patients who underwent PPCI.

**Keywords:** Contrast-induced nephropathy, Primary percutaneous coronary intervention, CHA2DS2-VASC score, Mehran score

## Background

Contrast-induced nephropathy (CIN) is considered the third most frequent cause of hospital-acquired acute kidney injury (AKI) because of decreasing renal blood flow and perfusion. CIN was defined as serum creatinine (Scr) elevation of  $\geq 25\%$  or  $\geq 0.5$  mg/dl from baseline within 48–72 h of the angiographic procedure [1].

CIN may occur after using intravascular iodinated contrast media (CM) during coronary procedure either

coronary angiography (CA) or percutaneous coronary intervention (PCI). It is responsible for 11–12% of in-hospital AKI cases [2].

CM is excreted in an unmetabolized state through the kidney, so creatinine clearance can be used to estimate its clearance. The role of CV/CrCl as a predictor of CIN was studied by several studies with conflicting results and different cutoff values [3].

The parameters of the CHA2DS2-VASC score, such as congestive heart failure, hypertension (HTN), old age, DM, and female sex, were associated with increased incidence of adverse clinical outcomes in cardiovascular

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diseases. CHADS2-VASC score is associated with more CIN risk in STEMI patients undergoing PPCI [4].

Therefore, we aimed to study the different predictors of CIN and determine the cutoff point of CV/CrCl and the applicability of CHA2DS2-VASC score in CIN prediction in STEMI patients who underwent PPCI.

## Methods

### Study design

This was a prospective observational study, performed between October 2018 and November 2019. The study included 400 patients who presented with STEMI and were eligible for primary PCI. We excluded patients with chronic peritoneal or hemodialytic treatment and who had pre-existing renal impairment (eGFR < 30 ml/min).

Based on the development of CIN, participants were subdivided into the following:

- Group I: (No-CIN group) included 346 (86.5%) patients who did not develop CIN
- Group II: (CIN group) included 54 (13.5%) patients who developed CIN

### Data collection

All patients were subjected to the following:

1. Personal history, e.g., age, gender, body mass index (BMI), and history of other medical disorders such as DM, HTN, and previous cardiac or vascular disease
2. Electrocardiogram: for diagnosis of STEMI as mentioned in the last ESC guidelines of acute myocardial infarction (AMI)
3. Vital signs on admission, e.g., systolic blood pressure (SBP), diastolic blood pressure (DBP), and basal heart rate (HR)
4. Chest and cardiac examination to detect signs of heart failure and define Killip class

The definition of Killip score is as follows: class I—no evidence of heart failure; class II—rales up to ½ of lung fields or S3 heart sound and SBP > 90 mmHg; class III—frank pulmonary edema and SBP > 90 mmHg; and class IV—cardiogenic shock with rales SBP < 90 mmHg and signs of tissue hypoperfusion [5].

1. Coronary angiography and primary PCI were done by an experienced cardiologist.
2. Echocardiography was done immediately after PPCI to assess the ejection fraction (EF) of the heart using the modified Simpson's method.
3. Assessment of HB level and Scr was done before and after the procedure then 24, 48, and 72 h after

the procedure. Also, kidney function assessment using CrCl used the Cockcroft-Gault formula.

4. CV/CrCl, CHA2DS2-VASC, and Mehran scores were calculated for each patient.

Mehran risk score includes 8 prognostic variables: hypotension (5 points, if systolic blood pressure < 80 mmHg for at least 1 h requiring inotropic support), use of intra-aortic balloon pump (5 points), congestive heart failure (CHF) (5 points, if class III/IV by New York Heart Association classification or history of pulmonary edema), age (4 points, if > 75 years), anemia (3 points, if hematocrit < 39% for men and < 36% for women), diabetes mellitus (3 points), contrast media volume (1 point per 100 mL), and eGFR (2 points, if GFR 60 to 40 GFR mL/min per 1.73 m<sup>2</sup>; 4 points, if GFR 40 to 20; 6 points, if GFR < 20) [6].

The CHA2DS2-VASC score includes the following variables: CHF, hypertension (HTN), age ≥ 75 years, DM, previous stroke, vascular disease, age 65 to 74 years, and sex (Kurtul, et al. 2016).

### Statistical analysis

Collection and analysis of the data were done using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, NY). The expression of continuous data was in the form of mean ± standard deviation (SD) or median (range) while the expression of nominal data was in the form of frequency (percentage).

The comparison of the different groups' nominal data in the study was done using the  $\chi^2$  test while for the comparison of the mean of different two groups, the Student *t* test was used. Multivariate regression analysis was used to determine the independent risk factors for the prediction of CIN among the studied cases. The receiver operating characteristic (ROC) curve was used for the assessment of the diagnostic accuracy of different scores for the prediction of CIN. The level of confidence was kept at 95%, and the *P* value was significant if < 0.05.

## Results

Four hundred patients who underwent PPCI were included in the study. Based on the development of CIN, participants were subdivided into the following:

- Group I: (No-CIN group) included 346 (86.5%) patients who did not develop CIN
- Group II: (CIN group) included 54 (13.5%) patients who developed CIN

### Clinical characteristics of all studied patients

The mean of age was significantly higher in group II (*P* < 0.001). Prevalence of female sex, DM, HTN, and baseline

heart rate were significantly higher in group II ( $P < 0.05$ ) while BMI, previous ischemic heart disease (IHD), cerebrovascular stroke (CVS), and EF were not different between the two groups. Male sex was significantly higher among group I ( $P < 0.001$ ). KILLIP class I was frequently higher in group I while KILLIP class IV was more frequent in group II ( $P < 0.001$ ) (Table 1).

In the current study, group II had a significantly lower baseline HB level than those in group I. None of the patients who developed CIN needs renal replacement therapy. It was noticed that both groups had an insignificant difference as regards CrCl, and hematocrit value, CV, and type of contrast as shown in Table 2.

CV/CrCl, CHA2DS2VASC score, and Mehran score had a higher significance in group II in comparison with group I ( $P < 0.05$ ) (Table 3).

At a cutoff point of  $> 2.8$ , CV/CrCl had 26% sensitivity and 95% specificity for the prediction of CIN among the studied patients with an overall accuracy of 76.5% while at a cutoff point of  $> 2$ , CHA2DS2VASC score had 50% sensitivity and 82% specificity for the prediction of CIN among the studied patients with an overall accuracy of 73.5%. We found that the Mehran score had 46% sensitivity and 85% specificity for the prediction of CIN among the studied patients with an overall accuracy of 74.5% (Table 4).

We used a multivariate regression analysis to determine the independent predictors of CIN among the studied patients. These factors were age (odds ratio = 1.06, 95% confidence interval = 1.02–1.11,  $P < 0.001$ ), female sex (odds ratio = 3.1, 95% confidence interval = 2.65–6.99,  $P = 0.02$ ), Mehran score (odds ratio = 2.48, 95%

**Table 1** Clinical characteristics of studied patients based on CIN development

	No-CIN (n=346)	CIN (n= 54)	P value
Age (years)	55.80 ± 10.58	64.20 ± 13.16	< 0.001
BMI (kg/m <sup>2</sup> )	26.45 ± 3.19	28.27 ± 4.09	0.31
Sex			
Male	302 (87.3%)	35 (64.8%)	< 0.001
Female	44 (12.7%)	19 (35.2%)	
Diabetes mellitus	86 (24.9%)	22 (40.7%)	0.01
Hypertension	63 (18.2%)	19 (35.2%)	< 0.001
IHD	31 (9%)	6 (11.1%)	0.83
CVS	39 (2.6%)	0	0.26
Heart rate (beat/min)	79.73 ± 13.74	86.20 ± 15.07	< 0.001
DBP (mmHg)	79.12 ± 12.77	76.85 ± 12.41	0.80
SBP (mmHg)	120.56 ± 12.45	124.07 ± 26.31	0.20
Ejection fraction (%)	48.95 ± 12.57	49.78 ± 11.47	0.65

Data were expressed as frequency (percentage) and mean (SD).  $P$  value was significant if  $< 0.05$

CIN contrast-induced nephropathy, IHD ischemic heart disease, CVS cerebrovascular stroke, BMI body mass index

**Table 2** Baseline laboratory data and amount of contrast among studied patients

	No-CIN (n=346)	CIN (n= 54)	P value
CrCl (ml/min)	113.05 ± 50.11	108.72 ± 64.81	0.57
Hemoglobin (mg/dl)	13.22 ± 1.98	12.56 ± 1.76	0.01
Hematocrit value (%)	39.71 ± 3.92	39.03 ± 3.18	0.23
Contrast volume (ml)	140.27 ± 88.95	145.18 ± 59.95	0.69
Type of contrast			
Low osmolar non-ionic CM (Ultravist)	340 (98.3%)	52 (96.3%)	0.92
Ionic iodinated CM (Telebrix)	6 (1.7%)	2 (3.7%)	

Data were expressed as frequency (percentage) and mean (SD).  $P$  value was significant if  $< 0.05$

CIN contrast-induced nephropathy, CrCl creatinine clearance

confidence interval = 1.98–6.24,  $P = 0.01$ ), CV/CrCl (odds ratio = 1.45, 95% confidence interval = 1.22–2.01,  $P = 0.03$ ), and CHA2DS2VASC score (odds ratio = 1.90, 95% confidence interval = 1.76–2.11,  $P = 0.04$ ) with overall adjusted  $R^2 = 0.54$  (Table 5).

## Discussion

CIN incidence in our study resembled 13.5%, which is similar to the published study by Mehran et al. [7] in which the overall incidence of CIN development was 13.1%. But it was different from the study of Maioli et al. [8] in which the percentage of CIN development was 27.3%.

In the present study, the risk factors of significance in CIN development were determined using logistic regression analysis. In group II, age was significantly higher than in group I. It was considered as an independent predictor of CIN development and similar to that reported by Li et al. [9] who noticed that CIN development was associated with old age. The higher incidence of CIN in old age was explained by the age-related

**Table 3** CV/CrCl, CHA2DS2VASC score, and Mehran score among the studied patients

	No-CIN (n=346)	CIN (n= 54)	P value
CV/CrCl	1.33 ± 0.78	2.01 ± 1.78	< 0.001
CHA2DS2VASC score	1.71 ± 0.58	2.37 ± 1.20	< 0.001
Mehran score			
Low	297 (85.8%)	29 (53.7%)	< 0.001
Moderate	49 (14.2%)	18 (33.3%)	
High	0	5 (9.3%)	
Very high	0	2 (3.7%)	

Data were expressed as frequency (percentage) and mean (SD).  $P$  value was significant if  $< 0.05$

CIN contrast-induced nephropathy, CV/CrCl contrast volume-creatinine clearance ratio

**Table 4** Accuracy of different scores for the prediction of CIN among the studied patients

Indices	CV/CrCl	CHA2DS2VASC score	Mehran score
Sensitivity	26%	50%	46%
Specificity	95%	82%	85%
PPV	67%	50%	53%
NPV	78%	82%	81%
Accuracy	76.5%	73.5%	74.5%
Cutoff point	> 2.8	> 2	–
Area under the curve	0.57	0.67	0.66

PPV positive predictive value, NPV negative predictive value, CV/CrCl contrast volume creatinine clearance

changes in kidney function such as decreased GFR, tubular secretion, and impaired concentrating ability. Co-morbid diseases such as HTN that affect kidney function may be an additional factor for CIN in the elderly [10].

Female sex was also significantly more frequent than male sex in group II and was a strong independent predictor for CIN development similar to that reported by Ioannidis and Katritsis [11]. This may be due to female gender ovarian hormones that affect the blood flow of the kidney and renin-angiotensin system [12].

Diabetes is considered an important precipitating factor for CIN, especially in patients with renal dysfunction. The kidneys of diabetic patients are more vulnerable to severe hypoxic and oxidative stress following the exposure to CM which in turn had a major role in CIN pathogenesis [13]. Therefore, the frequency of DM was significantly higher among group II in comparison with group I patients. This is consistent with Akkoyun et al.'s [14] study in which DM was significantly higher in patients who developed CIN than those who did not and was considered one of the independent predictors of CIN development.

Similar to Andò et al. [15], HTN and baseline heart rate in the present study were significantly higher among group II. This may be due to the associated renal arteriosclerosis and tubulointerstitial changes which may lead to chronic renal dysfunction predisposing to CIN [16].

**Table 5** Predictors of CIN among the studied patients

Predictors	Odds ratio	95% confidence interval	P value
Age	1.06	1.02–1.11	< 0.001
Female sex	3.1	2.65–6.99	0.02
Mehran score	2.48	1.98–6.24	0.01
CV/CrCl	1.45	1.22–2.01	0.03
CHA2DS2VASC score	1.90	1.76–2.11	0.04

CV/CrCl contrast volume to creatinine clearance ratio

Also, both groups showed significant differences regarding KILLIP class. Killip class I was more frequent in group I while Killip class IV was frequently higher in group II. Andò et al. [15] investigated the AGEF risk score dependent on age, eGFR, and left ventricular EF, and their predictive value for CIN development in 481 patients with AMI undergoing primary PCI. They observed that patients with CIN had a more severe impairment of global hemodynamic status, expressed by the Killip score than patients without CIN. Hemodynamic instability in the form of hypotension or congestive heart failure reduces renal blood flow and renal perfusion with the subsequent renal injury which predisposes to CIN [10].

In our study, CIN patients had significantly higher CV/CrCl in comparison with those with no CIN. The ROC curve analysis of our study showed that a CV/CrCl > 2.8 was the best discriminator and independent predictor for the development of CIN after PPCI. This is similar to the study by Barbieri et al. [3], who investigated the correlation of CV/CrCl ratio and CIN incidence after PCI and found that CV/CrCl was considered as a strong independent predictor for the development of CIN in patients who underwent PCI.

In the present study, CHA2DS2VASC and Mehran scores were significantly higher in group II in comparison with group I and were approved to be strong independent predictors for CIN. This is similar to the studies of Kurtul et al. [4] and Liu et al. [17].

## Conclusion

Old age, female sex, high Mehran score, CHADS2VASC score >2, and CV/CrCl > 2.8 were predictors of CIN in patients with STEMI who underwent PPCI.

## Abbreviations

CIN: Contrast-induced nephropathy; STEMI: ST-segment elevation myocardial infarction; PPCI: Primary percutaneous coronary intervention; CV: Contrast volume; CrCl: Creatinine clearance; CV/CrCl: CM volume to creatinine clearance ratio; SCr: Serum creatinine; DM: Diabetes mellitus; HTN: Hypertension; HB: Hemoglobin; AKI: Acute kidney injury; CM: Contrast media; CA: Coronary angiography; PCI: Percutaneous coronary intervention; BMI: Body mass index; AMI: Acute myocardial infarction; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; EF: Ejection fraction; SD: Standard deviation; ROC: Receiver operating characteristic; OR: Odds ratio; IHD: Ischemic heart disease; CVS: Cerebrovascular stroke

## Acknowledgements

This work was supported by the Cardiology Department in Assiut University Hospitals and by my beloved family.

## Cover letter for the *Egyptian Journal of Internal Medicine*

- My manuscript is asked to be published in the *Egyptian Journal of Internal Medicine* because the topic is relevant to the policy of the journal and discussing predictors of contrast-induced nephropathy in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention which is an important repeated complication in these patients.
- There are no issues relating to journal policies.



- There are no potential competing interests.
- I confirmed that all authors have approved the manuscript for submission.
- All the content of the manuscript has not been published or submitted for publication elsewhere.
- The manuscript is relevant to coronary artery disease and primary percutaneous coronary intervention.

#### Authors' contributions

MAHA has contributed to the format and study design and revised the collected data. MEFA participated in patients' recruitment, clinical examination, and data collection and drafted the manuscript. SRD contributed to the conception and design of the work, established the results and interpretation of the data, and substantially revised the work. MAFA contributed to the design of the work, carried out the statistical analysis and interpretation of the results, and did the final formatting of the work. All authors have read, revised, and approved the final manuscript.

#### Funding

Not applicable; no funding was received for this study.

#### Availability of data and materials

All data generated and/or analyzed during this study are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

This study was approved by the Committee of Medical Ethics of the Faculty of Medicine, Assiut University in 2016 (IRB code no: 17101214). Informed written consent was obtained from all participants.

##### Consent for publication

Consent for publication was obtained from the patients.

##### Competing interests

The authors declare that they have no competing interests.

Received: 12 December 2020 Accepted: 26 April 2021

Published online: 01 June 2021

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