



## Original Article

## CHA2DS2-VASc score as a novel predictor for contrast-induced nephropathy after percutaneous coronary intervention in acute coronary syndrome

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## ABSTRACT

**Background:** CHA2DS2-VASc score, used for atrial fibrillation to assess the risk of embolic complications, have shown to predict adverse clinical outcomes in acute coronary syndrome (ACS), irrespective of atrial fibrillation. This study envisaged to assess the predictive role of CHA2DS2-VASc score for contrast-induced nephropathy (CIN) in patients with ACS undergoing percutaneous coronary intervention (PCI). **Methods:** A total of 300 consecutive patients with ACS undergoing PCI were enrolled in this study. CHA2DS2-VASc score was calculated for each patient. These patients were divided into two groups as Group 1 (with CIN) and Group 2 (without CIN). CIN was defined as increase in serum creatinine level  $\geq 0.5$  mg/dL or  $\geq 25\%$  increase from baseline within 48 h after PCI. After receiver operating characteristic curve analysis, the study population was again classified into two groups: CHA2DS2-VASc score  $\leq 3$  group (Group A) and score  $\geq 4$  group (Group B).

**Results:** CIN was reported in 41 patients (13.6%). Patients with CIN had a higher frequency of hypertension, diabetes mellitus, and had a lower left ventricular ejection fraction and baseline estimated glomerular filtration rate. Receiver operating characteristic curve analysis showed good predictive value of CHA2DS2-VASc score for CIN (area under the curve 0.81, 95% CI 0.73–0.90). Patients with a CHA2DS2-VASc score of  $\geq 4$  had a higher frequency of CIN as compared with patients with score  $\leq 3$  (56.8% vs 4.8%;  $p = 0.0001$ ) with multivariate analysis demonstrating CHA2DS2-VASc score of  $\geq 4$  to be an independent predictor of CIN.

**Conclusion:** In patients with ACS undergoing PCI, CHA2DS2-VASc score can be used as a novel, simple, and a sensitive diagnostic tool for the prediction of CIN.

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## 1. Introduction

CHA2DS2-VASc is a composite scoring system comprising congestive heart failure (CHF)/left ventricular dysfunction, hypertension, age  $\geq 75$  years, diabetes 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.<sup>1</sup> The variables used in this score such as heart failure, hypertension, age, diabetes mellitus, and female sex 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.<sup>2–6</sup> 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.<sup>7</sup> The incidence of CIN ranges from 7% to 25%<sup>8,9</sup> in different population subgroups based on the risk

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status. Hence, risk stratification has an important bearing to provide the appropriate preventive therapies to these high-risk individuals even before contrast media exposure.

In the past, several risk prediction models have been proposed to envisage the CIN incidence. Mehran et al<sup>10</sup> proposed a scoring system comprising eight variables which correlated well with the CIN risk. In 2013, Gurm et al<sup>11</sup> suggested another model consisting of 15 parameters, which had a better predictive value for CIN. Despite having a fair degree of accuracy, complexity was one of the major limitations of these models. The components of the CHADS2 score viz. age, diabetes, and heart failure have been suggested as risk factors for CIN; hence, this simple scoring system can be used to predict risk of CIN. This scoring system was used in a recent study of patients with stable CAD undergoing elective PCI, wherein it correlated well with the occurrence of CIN.<sup>12</sup> Because patients with ACS have a far greater risk for CIN compared to patients with stable CAD, its utility as a predictive tool cannot be undermined.<sup>13</sup> This study sought to analyze the predictive value of CHA2DS2-VASc score as a simpler tool for predicting CIN in patients with ACS undergoing PCI.

## 2. Methods

### 2.1. Study population

This was a single-center observational, cross-sectional study carried out in the Department of Cardiology, S.M.S. Medical College and attached Hospitals, Jaipur, Rajasthan, India. A total of 316 consecutive patients presenting with ACS and undergoing PCI were initially enrolled between March 2017 and October 2018. These patients with ACS comprised both ST elevation myocardial infarction (STEMI) and non-ST-elevation ACS subgroups who were planned for PCI. Patients with STEMI and undergoing primary PCI were not included. All these patients were diagnosed based on history, physical examination findings, electrocardiographic criteria, and cardiac biomarkers evaluation as per the task force definition.<sup>14</sup> The exclusion criteria included: 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 radiographic contrast media (within 10 days of enrollment), or having contraindications for PCI. Patients who died during or early after procedure ( $n = 4$ ) or lack of data on serum creatinine during the 48 h after the procedure ( $n = 12$ ) were excluded from the study.

### 2.2. Study protocol

The study conforms to widely accepted ethical principles guiding human research (the Declaration of Helsinki) and the study protocol was approved by the Institutional Ethical Committee. A written informed consent was obtained from all the patients before enrollment. Assuming an incidence of CIN among patients undergoing PCI to be 10%, the sample size was estimated to be a minimum of 225 subjects at 95% confidence interval and 4% absolute allowable error. After exclusion of the 16 patients, a total of 300 patients' data were analyzed, which consisted of detailed history including information regarding the symptomatology, presence of traditional cardiovascular risk factors (smoking/tobacco use, diabetes, hypertension), family history of CAD, previous history of CAD/coronary artery bypass graft, previous atherosclerotic cerebrovascular events, and current medical therapy. Serum creatinine and serum urea levels were determined at the time of admission, daily up to 48 h after PCI, and then at seventh day after PCI. The eGFR was calculated using the Cockcroft–Gault method:  $[140 - \text{age (years)}] \times \text{weight (kg)} / 72 \times \text{serum creatinine (mg/dL)}$

$dl]$   $\{ \times 0.85 \text{ for female subjects} \}$  taking the serum creatinine measured at admission.<sup>15</sup> Baseline investigations included complete blood counts, fasting and postprandial plasma sugar levels, glycated hemoglobin, and fasting lipid profiles. Left ventricular ejection fraction (LVEF) was estimated by 2D echocardiography at admission using Simpson's method.

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  $EF \leq 40\%$ , (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. A minimum score of 1 was assigned to every patient as they had an episode of CAD due to vascular atherosclerosis, hence, mandating a PCI. All these PCI procedures were performed by experienced interventional cardiologists either through the transfemoral or transradial approach depending on the expertise and technical feasibility. Nonionic, low-osmolar contrast medium (Iohexol, Omnipaque 350 mg/mL) or nonionic, IOCM (iso-osmolar dimeric contrast medium) (Iodixanol, Visipaque 320 mg/mL) were used during the PCI. Iodixanol was used in patients with a baseline eGFR < 60 mL/min who were also hydrated with intravenous 0.9%, isotonic saline before the procedure, except for patients with frank congestive cardiac failure. Rate of intravenous hydration consisted of 1 mL/kg of body weight/hour or 0.5 mL/kg/hr for 12 h in patients with LVEF < 40%. It was started 3–12 h before contrast agent injection and continued for 12 h after PCI. Nephrotoxic drugs such as metformin and nonsteroidal anti-inflammatory drugs were withdrawn before PCI. All patients were pretreated with aspirin (300 mg) and a P2Y12 antagonist (clopidogrel 600 mg or ticagrelor 180 mg or prasugrel 60 mg) before PCI. In addition, unfractionated heparin in a dose of 70–100 U/kg was administered during the procedure. The use of glycoprotein IIb/IIIa inhibitors during PCI was at the operator's discretion.

**Table 1**

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

|                                           |                |
|-------------------------------------------|----------------|
| Mean age (years)                          | 55.04 ± 9.55   |
| Male                                      | 215 (71.7%)    |
| Female                                    | 85 (28.3%)     |
| STEMI                                     | 118 (39.3%)    |
| NSTE-ACS                                  | 182 (60.7%)    |
| Mean LVEF%                                | 46.63 ± 9.19   |
| Smoking/tobacco use                       | 198 (66.0%)    |
| Hypertension                              | 120 (40.0%)    |
| Diabetes mellitus                         | 62 (20.7%)     |
| Previous CAD                              | 39 (13.0%)     |
| Previous CABG                             | 5 (1.7%)       |
| Previous CVA                              | 9 (3.0%)       |
| Peripheral vascular disease               | 19 (6.3%)      |
| Pre-existing renal disease                | 10 (3.3%)      |
| Killip class $\geq 2$                     | 54 (18%)       |
| Mean hemoglobin (g/dL)                    | 12.80 ± 1.44   |
| Mean baseline serum creatinine (mg/dL)    | 1.00 ± 0.29    |
| Mean baseline eGFR (mL/min)               | 89.68 ± 20.65  |
| Mean contrast volume (mL)                 | 145.37 ± 50.78 |
| Multivessel CAD (no of vessels $\geq 2$ ) | 144 (48%)      |
| Multivessel PCI (no of Stents $\geq 2$ )  | 162 (54%)      |
| Use of ACE Inhibitor/ARB                  | 168 (56%)      |
| Previous use of Metformin                 | 37 (12.3%)     |
| CHA2DS2-VASc score                        | 2.51 ± 1.18    |
| Contrast-induced nephropathy (CIN)        | 41 (13.7%)     |

ACE; angiotensin converting enzyme; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CVA, cerebrovascular accidents; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; NSTE-ACS, non-ST-elevation ACS; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; STEMI, ST elevation myocardial infarction.

### 2.3. Definitions

The primary outcome for this study was the occurrence of CIN. Based on the occurrence of CIN, the study population was divided into two groups: Group 1 (patients with ACS and CIN) and Group 2 (patients with ACS without CIN). CIN was defined as the elevation of serum creatinine  $\geq 0.5$  mg/dL or  $\geq 25\%$  increase in the baseline serum creatinine levels within 48 hrs after PCI.<sup>16</sup> Pre-existing renal disease was defined as past history of renal artery stenosis, renal failure, glomerulonephritis, renal obstruction, nephrotic syndrome, or nephrectomy. Previous history of CAD was defined as a definitive history of myocardial infarction or coronary obstruction  $\geq 50\%$  on angiography.

### 2.4. Statistical analysis

The results were calculated as mean  $\pm$  standard deviation for quantitative variables and counts/percentages for categorical variables. The groups were compared using the chi-square test for the categorical variables, whereas unpaired Student *t*-test was used for analysis of quantitative variables. A multivariate logistic regression analysis was performed for confounding variables affecting CIN development. For this, the variables significantly associated with CIN in univariate analyses were taken for multivariate logistic regression analysis to investigate their significance as independent predictors. Odds ratios and 95% confidence interval were determined. A *p*-value  $\leq 0.05$  was considered to be statistically significant. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cutoff values of the CHA2DS2-VASc score and the number of CHA2DS2-VASc score to predict the development of CIN. The enrolled patients were further divided

into two groups according to CHA2DS2-VASc score after ROC analysis. All statistical analyses were performed using SPSS version 24.0 (SPSS Inc., Chicago, Ill., USA).

## 3. Results

### 3.1. Clinical characteristics

A total of 300 patients with ACS (215 males, 71.7%) having a mean age of  $55.04 \pm 9.55$  years were enrolled in this study. Non-ST-elevation ACS was the most frequent clinical diagnosis in 182/300 (60.7%) patients, followed by STEMI in 118/300 (39.3%). The mean CHA2DS2-VASc score in the study population was  $2.51 \pm 1.18$  (range: 1 to 8). Baseline characteristics have been reported in Table 1.

### 3.2. Study outcomes

#### 3.2.1. Univariate analysis

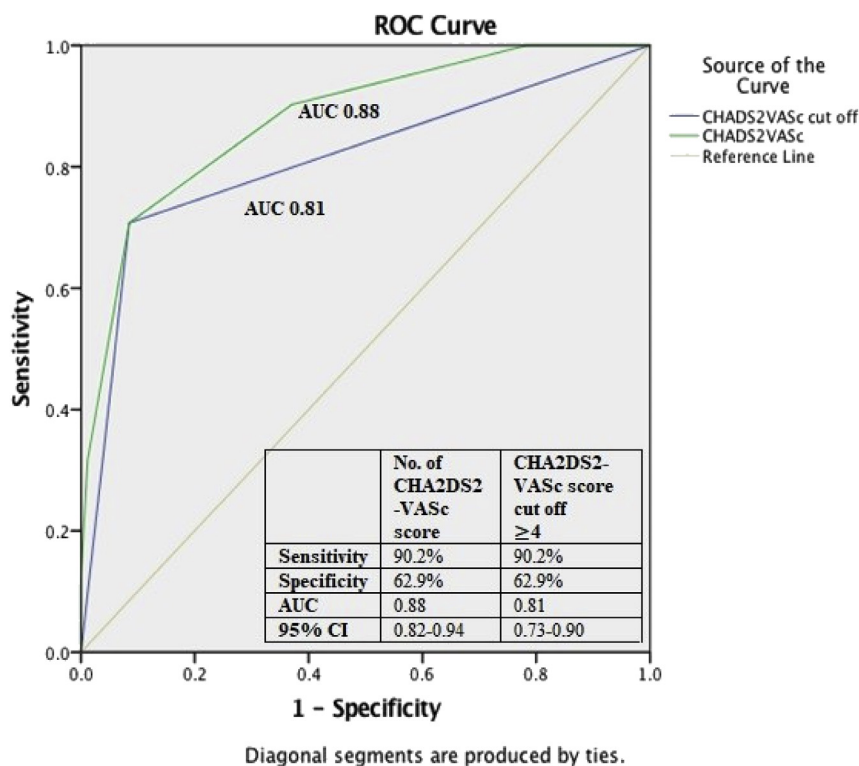
CIN occurred in 41/300 (13.7%) patients after PCI mandating dialysis in 3 (0.01%) of them. Based on the presence or absence of CIN, the enrolled participants were divided into Group 1 (CIN) and Group 2 (no CIN). The clinical, laboratory, and angiographic data of each of the groups have been depicted in Table 2. Patients in Group 1 (CIN subgroup) had significantly higher number of hypertensives and diabetics as well as a lower LVEF and baseline eGFR as compared with Group 2. In addition, a higher number of patients in Group 1 had multivessel CAD mandating multivessel PCI and hence were exposed to a significantly higher contrast volume. Pre-existing renal disease, previous history of CAD, cerebrovascular accidents, systolic blood pressure, Killip class  $\geq 2$  on admission

**Table 2**

Clinical, laboratory, and angiographic data of the patients with and without contrast-induced nephropathy.

| Variables                            | Group 1 CIN (n = 41) | Group 2 No CIN (n = 259) | P-Value |
|--------------------------------------|----------------------|--------------------------|---------|
| Age (years)                          | 55.68 $\pm$ 8.31     | 54.93 $\pm$ 9.74         | 0.64    |
| Female                               | 10 (24.3%)           | 75 (28.9%)               | 0.54    |
| Smoking/tobacco use                  | 29 (70.7%)           | 169 (65.3%)              | 0.49    |
| Hypertension                         | 28 (68.3%)           | 92 (35.5%)               | 0.0001  |
| Diabetes mellitus                    | 29 (70.7%)           | 33 (12.7%)               | 0.0001  |
| Previous CAD                         | 10 (24.4%)           | 29 (11.2%)               | 0.02    |
| Previous CABG                        | 2 (4.9%)             | 3 (1.2%)                 | 0.08    |
| Previous CVA                         | 5 (12.2%)            | 4 (1.5%)                 | 0.0001  |
| Pre-existing renal disease           | 4 (9.8%)             | 6 (2.3%)                 | 0.01    |
| Peripheral vascular disease          | 3 (7.3%)             | 16 (6.2%)                | 0.78    |
| LVEF (%)                             | 40.29 $\pm$ 9.15     | 47.63 $\pm$ 8.81         | 0.0001  |
| Killip class $\geq 2$                | 29 (70.7%)           | 25 (9.6%)                | 0.0001  |
| Weight (kg)                          | 76.59 $\pm$ 10.63    | 76.47 $\pm$ 9.56         | 0.94    |
| Body mass index (kg/m <sup>2</sup> ) | 23.24 $\pm$ 2.20     | 23.10 $\pm$ 1.97         | 0.68    |
| Total cholesterol (mg/dL)            | 213.39 $\pm$ 32.64   | 202.51 $\pm$ 29.98       | 0.034   |
| HDL (mg/dL)                          | 41.22 $\pm$ 4.13     | 42.56 $\pm$ 14.16        | 0.55    |
| LDL (mg/dL)                          | 141.90 $\pm$ 27.33   | 132.04 $\pm$ 29.07       | 0.04    |
| Triglyceride (mg/dL)                 | 151.93 $\pm$ 46.36   | 138.27 $\pm$ 30.15       | 0.01    |
| Systolic blood pressure (mm of Hg)   | 148.39 $\pm$ 34.75   | 134.32 $\pm$ 24.29       | 0.001   |
| Diastolic blood pressure (mm of Hg)  | 89.37 $\pm$ 15.12    | 85.08 $\pm$ 50.12        | 0.59    |
| Hemoglobin (g/dL)                    | 11.74 $\pm$ 1.35     | 12.97 $\pm$ 1.38         | 0.0001  |
| Serum creatinine (mg/dL)             | 1.07 $\pm$ 0.35      | 0.99 $\pm$ 0.28          | 0.12    |
| eGFR (mL/min)                        | 83.76 $\pm$ 19.22    | 90.61 $\pm$ 20.75        | 0.04    |
| 48 h peak serum creatinine (mg/dL)   | 1.96 $\pm$ 0.33      | 1.07 $\pm$ 0.30          | 0.0001  |
| 7th day serum creatinine (mg/dL)     | 1.34 $\pm$ 0.46      | 1.01 $\pm$ 0.28          | 0.0001  |
| Contrast volume (mL)                 | 204.39 $\pm$ 52.49   | 136.03 $\pm$ 43.81       | 0.0001  |
| Iodixanol use                        | 5 (31.2%)            | 11 (68.8%)               | 0.04    |
| No. of vessels                       | 1.98 $\pm$ 0.79      | 1.55 $\pm$ 0.67          | 0.0001  |
| No. of stents                        | 2.24 $\pm$ 0.83      | 1.62 $\pm$ 0.70          | 0.0001  |
| CHA2DS2-VASc score                   | 4.15 $\pm$ 1.35      | 2.25 $\pm$ 0.92          | 0.0001  |
| ACE inhibitor/ARB use                | 29 (70.7%)           | 139 (53.7%)              | 0.04    |
| Previous metformin use               | 19 (46.3%)           | 18 (6.9%)                | 0.0001  |

ACE; angiotensin converting enzyme; ARB; angiotensin receptor blocker; CAD, coronary artery disease; CVA, cerebrovascular accidents; CABG, coronary artery bypass graft; CIN, contrast-induced nephropathy; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; LVEF, left ventricular ejection fraction.



**Fig. 1.** ROC curve for CHA2DS2-VASc score for prediction of CIN. Area under the curve of ROC curve for no. of CHA2DS2-VASc score for prediction of CIN is 0.88 (CI 0.82–0.94). Optimal cutoff point of CHA2DS2-VASc score for prediction of CIN is 04 with sensitivity of 90.2% and specificity 62.9% for prediction of CIN with AUC 0.81 (CI 0.73–0.90). AUC, area under the curve; ROC, receiver operating characteristic; CIN, contrast-induced nephropathy.

were significantly higher in patients developing CIN (Group 1). There was no significant difference in terms of age, sex, smoking status, and body mass index between the two groups. Previous use of metformin in diabetics and angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers were significantly associated with an increased risk of CIN. Use of IOCM had a protective role with a lower incidence of CIN ( $p = 0.035$ ) in patients with a lower baseline eGFR. The mean CHA2DS2-VASc score was significantly higher in patients with CIN (Group 1) than those without CIN ( $4.15 \pm 1.35$  vs  $2.25 \pm 0.92$ ,  $p = 0.0001$ ).

### 3.2.2. ROC curve analysis

In the ROC curve analysis (Fig. 1), area under the curve for predicting CIN was 0.88 (sensitivity 90.2%, specificity 62.9%; 95% confidence interval [CI]: 0.82–0.94) for the number of CHA2DS2-VASc score and was 0.81 (sensitivity 90.2%, specificity 62.9%; 95% CI 0.73–0.90) for the presence of CHA2DS2-VASc score  $\geq 4$ .

### 3.2.3. Multivariate analysis

Multivariate analysis reported that CHA2DS2-VASc score  $\geq 4$  ( $p = 0.02$ ), diabetes mellitus ( $p = 0.02$ ), Killip class  $\geq 2$  ( $p = 0.001$ ), and contrast volume ( $p = 0.001$ ) were independent predictors for CIN (Table 3).

Based on the optimum cutoff defined by the ROC curve analysis, the patients were also divided into two groups: subjects with CHA2DS2-VASc score  $\leq 3$  (Group A) and score  $\geq 4$  (Group B). The demographic, clinical, and angiographic characteristics of these two groups have been depicted in Table 4. The frequency of CIN was significantly higher in Group B with hypertension, diabetes mellitus, Killip class  $\geq 2$ , left ventricular systolic dysfunction, higher SBP at admission, history of previous stroke/transient ischemic attack, pre-existing renal disease being higher in patients with CHA2DS2-

VASc score  $\geq 4$ . In addition, these patients had lower hemoglobin, eGFR, higher serum total cholesterol, serum LDL and triglyceride levels, and greater incidence of multivessel CAD.

## 4. Discussion

This study demonstrates the incidence of CIN in patients with ACS undergoing PCI. In addition, this is the first study in Indian population to report that CHA2DS2-VASc score  $\geq 4$  is independently associated with the occurrence of CIN in patients with ACS treated by PCI. CIN is an important and a notorious complication of PCI performed in an acute setting leading to a higher morbidity and mortality as well as greater health care utilization escalating the costs and duration of hospital stay.<sup>17,18</sup> The exact mechanisms of CIN is not clear and is thought to be multifactorial. Previous studies have shown that renal vasoconstriction, endothelial dysfunction, endothelial cell damage followed by renal tubular damage and medullary hypoxia are the various mechanisms responsible for contrast-induced renal injury.<sup>19,20</sup> Female gender, older age, diabetes, hypertension, high

**Table 3**  
Independent predictors of CIN in multivariate regression analysis.

| Variables              | p-Value | Odds ratio | 95% CI     |
|------------------------|---------|------------|------------|
| Diabetes mellitus      | 0.02    | 0.11       | 0.02–0.70  |
| Killip class           | 0.001   | 12.84      | 4.21–39.21 |
| Contrast volume        | 0.001   | 1.04       | 1.02–1.05  |
| CHA2DS2-VASc score     | 0.02    | 2.61       | 1.15–5.94  |
| Previous metformin use | 0.54    | 1.81       | 0.28–11.91 |
| eGFR                   | 0.22    | 0.98       | 0.95–1.01  |
| ACE inhibitor/ARB use  | 0.06    | 0.19       | 0.03–1.05  |
| Hypertension           | 0.76    | 1.28       | 0.27–6.09  |

ACE; angiotensin converting enzyme; ARB; angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; CIN, contrast-induced nephropathy.

**Table 4**

Study population according to CHA2DS2-VASc score.

| Variables                            | CHA2DS2-VASc score                  |                                    | P-Value |
|--------------------------------------|-------------------------------------|------------------------------------|---------|
|                                      | Group A (score $\leq 3$ ) (n = 249) | Group B (score $\geq 4$ ) (n = 51) |         |
| Age (year)                           | 55.06 $\pm$ 9.7                     | 54.92 $\pm$ 8.9                    | 0.93    |
| Females                              | 74 (29.7%)                          | 11 (21.5%)                         | 0.24    |
| Smoking/tobacco use                  | 169 (67.8%)                         | 29 (56.8%)                         | 0.13    |
| Hypertension                         | 77 (30.9%)                          | 43 (84.3%)                         | 0.0001  |
| Diabetes mellitus                    | 32 (12.8%)                          | 30 (58.8%)                         | 0.0001  |
| Previous CAD                         | 29 (11.6%)                          | 10 (19.6%)                         | 0.12    |
| Previous CABG                        | 4 (1.6%)                            | 1 (1.9%)                           | 0.86    |
| Previous CVA                         | 1 (0.4%)                            | 8 (15.6%)                          | 0.0001  |
| Pre-existing renal disease           | 4 (1.6%)                            | 6 (11.7%)                          | 0.0001  |
| Peripheral vascular disease          | 15 (6.0%)                           | 4 (7.8%)                           | 0.63    |
| ACE inhibitor/ARB use                | 130 (52.2%)                         | 38 (74.5%)                         | 0.003   |
| Previous use of metformin            | 16 (6.4%)                           | 21 (41.1%)                         | 0.0001  |
| LVEF (%)                             | 48.11 $\pm$ 8.65                    | 39.39 $\pm$ 8.37                   | 0.0001  |
| Weight (kg)                          | 76.39 $\pm$ 9.64                    | 77.00 $\pm$ 10.03                  | 0.68    |
| Body mass index (kg/m <sup>2</sup> ) | 23.06 $\pm$ 1.99                    | 23.41 $\pm$ 2.061                  | 0.26    |
| SBP (mm of Hg)                       | 132.01 $\pm$ 23.73                  | 156.94 $\pm$ 28.82                 | 0.0001  |
| DBP (mm of Hg)                       | 84.41 $\pm$ 51.03                   | 91.84 $\pm$ 13.94                  | 0.30    |
| Killip class                         | 1.14 $\pm$ 0.45                     | 1.78 $\pm$ 0.92                    | 0.0001  |
| Total cholesterol (mg/dL)            | 201.92 $\pm$ 28.97                  | 214.18 $\pm$ 35.81                 | 0.009   |
| LDL (mg/dL)                          | 131.76 $\pm$ 28.61                  | 141.31 $\pm$ 29.83                 | 0.03    |
| HDL (mg/dL)                          | 42.58 $\pm$ 14.40                   | 41.35 $\pm$ 4.44                   | 0.55    |
| Triglyceride (mg/dL)                 | 136.94 $\pm$ 29.38                  | 155.78 $\pm$ 44.29                 | 0.0001  |
| Hemoglobin (g/dL)                    | 12.92 $\pm$ 1.41                    | 12.2 $\pm$ 1.47                    | 0.001   |
| Serum creatinine (mg/dL)             | 0.99 $\pm$ 0.28                     | 1.04 $\pm$ 0.35                    | 0.28    |
| eGFR (mL/min)                        | 91.16 $\pm$ 20.38                   | 82.45 $\pm$ 20.66                  | 0.006   |
| 48 h peak serum creatinine (mg/dL)   | 1.10 $\pm$ 0.33                     | 1.60 $\pm$ 0.58                    | 0.0001  |
| 7th day serum creatinine (mg/dL)     | 1.00 $\pm$ 0.28                     | 1.26 $\pm$ 0.47                    | 0.0001  |
| CIN                                  | 12 (4.8%)                           | 29 (56.8%)                         | 0.0001  |
| No. of vessels                       | 1.55 $\pm$ 0.67                     | 1.86 $\pm$ 0.83                    | 0.004   |
| No. of stents                        | 1.64 $\pm$ 0.71                     | 2.04 $\pm$ 0.87                    | 0.0001  |
| Contrast volume (mL)                 | 138.54 $\pm$ 46.63                  | 178.73 $\pm$ 57.16                 | 0.0001  |

ACE; angiotensin converting enzyme; ARB; angiotensin receptor blocker; CAD, coronary artery disease; CVA, cerebrovascular accidents; CABG, coronary artery bypass graft; CIN, contrast-induced nephropathy; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure.

central pulse pressure, CHF, and renal dysfunction are well known risk factors for development of CIN.<sup>21–24</sup>

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.<sup>24</sup> Our study too demonstrated significant correlation between CIN and diabetes, hypertension, higher systolic blood pressure, CHF as evident from (i) a higher Killip class and (ii) a lower left ventricular systolic function, and pre-existing renal disease. Other predictors such as low hemoglobin and higher contrast volume were also found significantly correlated with risk of CIN, which are parts of Mehran risk model.<sup>10</sup> These findings were concurrent with those of a previous study carried out in 1408 patients with ACS undergoing urgent PCI.<sup>13</sup> No correlation could be established with age and gender in this study. Multivessel CAD and multivessel PCI were the new predictors of CIN established in our study probably due to the fact that a complete revascularization in these patients precluded a greater usage of radio contrast media. In the present study, baseline eGFR and not baseline serum creatinine was a better predictor for occurrence of CIN concurrent with the fact that eGFR is a more reliable indicator of renal function than serum creatinine.<sup>15</sup> Use of an iso-osmolar contrast media in patients with a lower baseline eGFR was significantly associated with reduced CIN in our 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.<sup>25</sup>

Previously, 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.<sup>2–7,13,26,27</sup> The study by Chou et al.<sup>12</sup> demonstrated that CHADS2 score predicts

the risk of CIN in patients with stable CAD undergoing elective PCI. However, in our study, we used the CHA2DS2-VASc score instead of CHADS2 as it's a more comprehensive tool and had applied it on patients with ACS rather than stable CAD. CHA2DS2-VASc score is a simpler risk score containing only preprocedural variables which makes it easy to compute and, hence, more practical. The current risk model Mehran risk score is more complex and contains both preprocedural variables and procedural parameters.<sup>10</sup> In our study, we 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 similar to the previous study carried out in the Turkish cohort by Kurtul et al.<sup>13</sup> Thus, 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.<sup>28</sup>

## 5. Study limitations

There are certain limitations to this study: 1) this was a single-center study and had an adequate but smaller study population; 2) definition of CIN was based on absolute or relative increase in serum creatinine levels compared with baseline value. Other factors such as proteinuria and kidney morphology were not assessed; 3) Our study did not report long-term mortality and morbidity due to CIN. These findings should be confirmed in a large-scale multicentric trial and long-term effects of CIN should be evaluated.

## 6. Conclusions

The development of CIN after PCI in patients with ACS is a frequent complication even in patients with normal renal function

and is usually multifactorial. In resource-limited setups, CIN may remain underreported because of the day care procedures and early discharges. The course of CIN is mostly benign in patients with normal renal function and is usually followed by complete recovery in most of the cases. However, at times, there may be progressive decline in renal functions mandating dialysis further adding to morbidity and cost of hospitalization. Hence, risk stratification and early identification of patients predisposed for CIN should be carried out to provide preventive strategies of renal protection before, during, and after PCI. CHA2DS2-VASc score serves as a simple yet effective tool for predicting CIN preprocedure, which can be easily implemented in day-to-day clinical practice.

### Key messages:

#### What is already known about this subject?

Contrast-induced nephropathy is an important and preventable complication of percutaneous coronary intervention (PCI) with a higher risk seen in patients with acute coronary syndrome, and CHA2DS2-VASc score has been previously reported as a good predicting tool for adverse clinical outcomes in patients with coronary artery disease such as stable angina pectoris and acute coronary syndrome, irrespective of atrial fibrillation.

#### What does this study add?

Preprocedural CHA2DS2-VASc score  $\geq 4$  can identify patients with acute coronary syndrome at high risk for contrast-induced nephropathy after PCI in whom renal protective preventive strategies may be used before, during, and after PCI.

### Contributors

AKC and VP conceived and designed the study and obtained ethical approval. SK analyzed the data and provided the results. AKC and VP prepared the manuscript; SS and other authors contributed to critical revision of the manuscript.

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### Conflict of interests

Authors have none to disclose.

### Patient consent for publication

Not required.

### Ethical approval

Approval was obtained from local institutional ethical committee.

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