

## ORIGINAL ARTICLE

## Role of the CHA2DS2-Vasc Score in Predicting Contrast-Induced Nephropathy After Primary Percutaneous Coronary Intervention

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### Abstract

**Background:** Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for ST-elevation myocardial infarction (STEMI) with an onset time <12 h. However, it poses a risk of contrast-induced nephropathy (CIN), occurring in one out of five patients. In this context, the CHA2DS2-VASc score can be used as a predictor of CIN in patients with STEMI undergoing PPCI.

**Objectives:** To evaluate the role of the CHA2DS2-VASc score in predicting CIN in patients with STEMI who underwent PPCI.

**Methods:** In this retrospective cohort study, data were collected from the medical records of patients with STEMI who underwent PPCI at the department of cardiovascular medicine of our institution from January 1, 2019, to October 31, 2021. The association of CIN with the CHA2DS2-VASc and Mehran scores, the and neutrophil-lymphocyte ratio were evaluated using a logistic regression model with a p value < 0.05.

**Results:** This study included 66 patients with CIN from a total of 326 patients with STEMI who underwent PPCI. Patients with CIN showed a higher CHA2DS2-VASc score compared with those without CIN (median [interquartile range – IQR], 2 [1–3] vs. 1 [1–2], p < 0.001). The sensitivity, specificity, negative predictive value, and positive predictive value of the CHA2DS2-VASc score in predicting CIN after PPCI were 73.6%, 92.3%, 87.9%, and 82.1%, respectively.

**Conclusion:** A CHA2DS2-VASc score  $\geq 2.5$  is as accurate as a Mehran score  $\geq 6.5$  in predicting CIN following PPCI, suggesting that the CHA2DS2-VASc score is a practical and efficient tool for clinical use.

**Keywords:** Contrast Media; Percutaneous Coronary Intervention; Infarto do Miocárdio com Supradesnível do Segmento ST.

### Introduction

Primary percutaneous coronary intervention (PPCI) is the recommended reperfusion method for ST-elevation myocardial infarction (STEMI) with an onset time of <12 h. However, it poses the risk of reducing glomerular filtration rate due to contrast injection, commonly known as contrast-induced nephropathy (CIN).<sup>1</sup> CIN occurs in one out of every five patients undergoing PPCI<sup>2</sup> and is

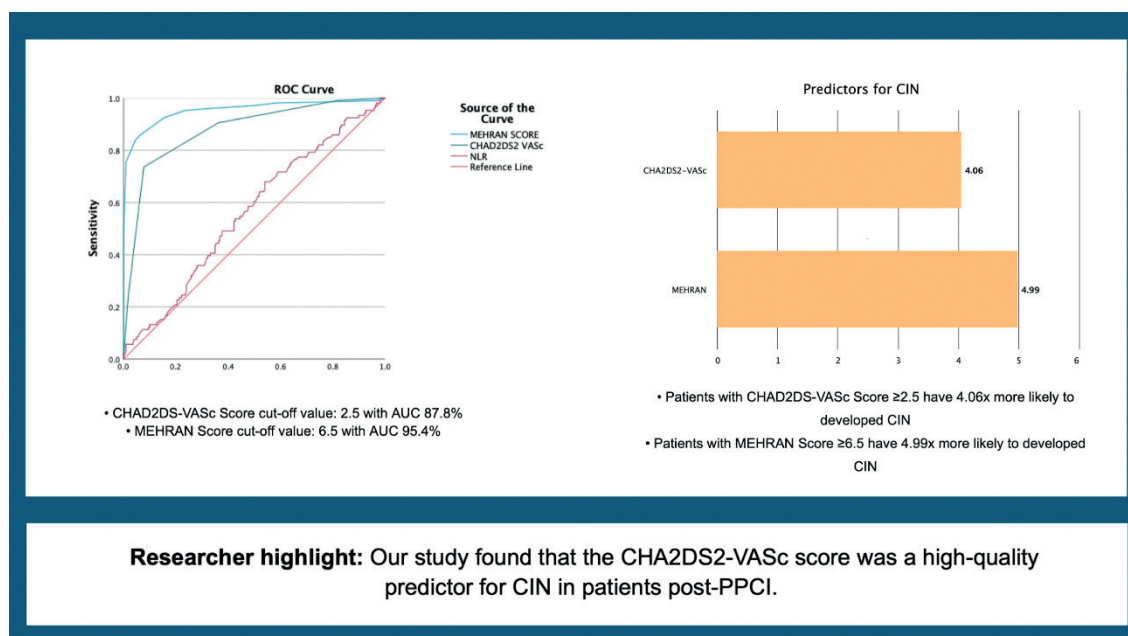
associated with increased mortality, morbidity, extended hospital stays, requirement for more medical devices, and higher costs.<sup>3</sup> A previous study showed a markedly elevated incidence of major adverse cardiac events among patients with CIN. Specifically, the rates of cardiogenic shock, cardiac arrest, and heart failure were 16.9%, 8.5%, and 18.6%, respectively.<sup>4</sup> In another study, patients with CIN experienced a 3.37-fold increase in 30-day mortality rates and a 1.84-fold increase in one-year mortality

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Editor responsible for the review: Sandro Cadaval Gonçalves

**Central Illustration: Role of the CHA2DS2-Vasc Score in Predicting Contrast-Induced Nephropathy After Primary Percutaneous Coronary Intervention**

Int J Cardiovasc Sci. 2024; 37:e20240111

CHA2DS2-VASc score in predicting CIN after PPCI. PPCI: primary percutaneous coronary intervention; CIN: contrast-induced nephropathy; NLR: neutrophil-to-lymphocyte ratio; AUC: Area under the curve; Sens: Sensitivity; ROC: receiver operating characteristic.

rates compared with patients without CIN.<sup>5</sup> Therefore, assessing the risk of renal complications is important for treatment decisions, particularly in patients with chronic kidney disease, and reducing the risk of CIN.<sup>6,7</sup>

Although multiple risks for CIN have been established, the overall risk of their combination is poorly known. Mehran et al. established the Mehran score as a predictive tool for assessing the risk of CIN in patients following PCI; this has since become the gold standard.<sup>7</sup> The Mehran score is typically applied post-PPCI, thereby postponing the evaluation of CIN risk. Another study indicated that the neutrophil-to-lymphocyte ratio (NLR), a straightforward measure, can predict CIN post-PCI.<sup>8</sup>

Recently, the use of CHA2DS2-VASc has been studied as a predictor of CIN, offering an alternative to previously established scoring methods such as the Mehran score.<sup>9</sup> Abo Egela et al. reported in an Egyptian cohort that a CHA2DS2-VASc score  $>3$  upon admission was associated with CIN in patients who underwent PPCI, and a higher CHA2DS2-VASc score was associated with a higher risk of CIN.<sup>10</sup> Therefore, in this study, we aimed to determine the association between preprocedural CHA2DS2-VASc scores and the risk of CIN in patients with STEMI who

underwent PPCI. To our knowledge, this has not been studied in Indonesia before.

## Methods

This retrospective cohort study followed the Strengthening The Reporting of OBServational studies in Epidemiology (STROBE) guideline to ensure quality in reporting. In this hospital-based study, data were collected from the medical records of patients with STEMI who underwent PPCI in the department of cardiovascular medicine of our institution between January 1, 2019, and October 31, 2021. Most patients were transferred to our facility from other cities because our institution is the only primary teaching hospital in our province.

The inclusion criteria were patients with STEMI (confirmed by history and electrocardiography) who underwent PPCI,  $>17$  years of age, and with complete supporting examination data. The exclusion criteria were presence of hematologic abnormalities, hepatobiliary disease, immune disorders, secondary infection, neoplastic disease, or recent major surgery or trauma. The sample size was calculated as 279 participants according to Hsieh and Lavory's formula for Cox proportional

hazard regression.<sup>11</sup> The CHA2DS2-VASc score was assessed based on specific patient conditions: congestive heart failure or left ventricular ejection fraction <40%, hypertension, diabetes mellitus, age 64–75 years, female sex, and vascular disease (1 point each), and age >75 years and history of stroke/transient ischemic attack/venous thromboembolism (2 points each).<sup>12</sup> The Mehran score was determined by assigning 5 points to each of the following variables: hypotension (systolic blood pressure <80mmHg), congestive heart failure, and use of an intra-aortic balloon. Four points was assigned to each of these conditions: age >75 years and serum creatinine levels >1.5 mg/dL. Three points were given to anemia and diabetes, and one point was added for every 100cc<sup>3</sup> of contrast media used. The cumulative score of those variables was calculated, and patients were stratified into distinct risk categories: low risk (0-5 points), moderate risk (6-10 points), high risk (11-15 points), and very high risk (≥16 points).<sup>7</sup> The NLR was calculated by dividing the neutrophil count by the lymphocyte count. The normal range of NLR is between 1 and 2, while values exceeding 3 or falling below 0.7 are considered abnormal.<sup>13</sup>

### Statistical analysis

Categorical variables are presented as frequencies and percentages, while continuous variables are expressed as mean ± standard deviation. The normality of the data was assessed using the Kolmogorov–Smirnov test. Continuous variables with normal distribution are presented as mean and standard deviation, whereas non-normally distributed data are presented as median and interquartile range (IQR). Dependent variables were patients with CIN, and independent variables were CHA2DS2-VASc score, the NLR ratio, and the Mehran score. Patient information included demographic data, medical history, clinical characteristics, and angiographic and echocardiographic results. Recordings of the PPCI procedure included the number of stenotic blood vessels and the type and volume of contrast.<sup>11</sup>

A multivariate logistic regression model was used to evaluate the association between CIN and CIN predictors of the two scores with odds ratio and 95% confidence interval (CI). Comparative analysis was conducted using the unpaired t-test, Mann–Whitney U, Chi-square, and Fisher exact tests. The cut-off value and accuracy of the scores in predicting CIN post-PPCI were determined by constructing receiver operating characteristic (ROC) curves. A p-value of <0.05 was considered significant.

Statistical analysis was conducted using SPSS version 27 for Mac.

This study was conducted in accordance with the 2008 Declaration of Helsinki and approved by the research ethics committee of our hospital (ID: 003/EC/KEPK-KANDOU/I/2022).

### Results

Overall, this study included 326 patients with STEMI who underwent PPCI. We identified 66 patients with CIN and 260 patients without CIN. The mean age of the patients was 58.1 ± 10 years. Age appeared to be a critical factor in patients with CIN, with the CIN+ group with an average age of 62 years, compared with 57 years in the CIN– group. Sex differences were also pronounced, with a higher proportion of females in the CIN+ group than in the CIN– group (35% vs. 11%). Regarding clinical severity at presentation, according to Killip classification, the CIN+ group showed higher severity, with a larger proportion of patients in Killip class 2. Pre-PPCI laboratory results revealed lower hemoglobin and hematocrit levels in the CIN+ group. Glycemic control parameters, including HbA1c and both random and fasting blood glucose levels, were elevated in the CIN+ group, corroborating the higher metabolic risk profile of the group. Furthermore, sodium and chloride levels were lower in the CIN+ group.

Regarding cardiac function and risk assessment, left ventricular ejection fraction (LVEF) was lower in the CIN+ group (0.4 vs 0.5), and the CHA2DS2-VASc score was higher in the CIN+ group than in the CIN– group (3 vs 1). Similarly, Mehran’s scores were higher in the CIN+ group than in the CIN– group (10 vs 3), reinforcing its predictive value in this setting. However, not all parameters showed significant differences. The NLR was not significantly different between the CIN+ and CIN– groups (Table 1).

The ROC curve (Figure 1) showed the capability of the CHA2DS2-VASc score to predict CIN after PPCI. The optimal cut-off value for the CHA2DS2-VASc score was 2.5, with the area under the curve (AUC) representing an accuracy of 87.8%. The CHA2DS2-VASc had a sensitivity and specificity of 73.6% and 92.3%, respectively, for predicting CIN post-PPCI. Similarly, the Mehran score accurately predicted CIN post-PPCI at a cut-off value of 6.5 (AUC: 95.4%), with a sensitivity of 85.8% and specificity of 93.6%. The NLR had a lower predictive value than other predictors at a cut-off of 3.9 (AUC: 56%), with a sensitivity of 54.7% and specificity of 54.5% for

**Table 1 – Characteristics of patients with STEMI included in the study**

Characteristics	Total (n = 326)	CIN+ (n = 66)	CIN- (n = 260)	P <sup>a</sup>
Age	58.1 ± 10	62 ± 9	57.1 ± 10	<0.001
Sex				<0.001
Female	51 (16%)	23 (35)	28 (11)	
Male	275 (84%)	43 (65)	232 (89)	
Killip class				<0.001
Killip 1	231 (71%)	30 (45%)	201 (78%)	
Killip 2	87 (27%)	34 (52%)	53 (20%)	
Killip 3	-	-	-	
Killip 4	8(2%)	2 (3%)	6 (2%)	
<b>Pre-PPCI laboratory results</b>				
Hemoglobin (g/dL)	13.9 (12.8–15.1)	13.5 (12.6–14.2)	14 (12.9–15.3)	<b>0.006</b>
Leukocyte (x10 <sup>3</sup> /μL)	12.4 (10–14.7)	12.8 (11–14.9)	12.2 (9.9–14.7)	0.162
Hematocrit (%)	40.1 (36.5–43.6)	38.9 (35.4–40.7)	40.2 (36.7–44)	<b>0.006</b>
Platelets (x10 <sup>3</sup> /μL)	239 (200.2–284)	252 (208.2–285.5)	235.5 (199–283.2)	0.125
Neutrophil (%)	73(65.2–97.8)	74,5 (66–79.8)	72 (65–79.2)	0.330
Lymphocyte (%)	19 (14–24)	17.5 (13–21.8)	19 (14–24)	0.177
AST (mg/dL)	72 (37–137)	105 (48–158.5)	66 (34.2–131)	0.053
ALT (mg/dL)	35 (23–50)	38 (24.5–51)	33 (22.2–50)	0.599
Albumin (g/dL)	3.7(3.5–4)	3,7 (3.4–3.9)	3.8 (3.5–4)	0.363
Urea (mg/dL)	29.5 (23–39)	31 (25.2–40)	28 (22–38)	0.071
Creatinine (mg/dL)	1 (0.9–1.3)	1 (0.8–1.4)	1 (0.9–1.3)	0.622
eGFR	76.6 (57–95)	69.6 (51.2–89)	78.6 (57.7–95.8)	0.095
Cholesterol (mg/dL)	185 (161–217)	187 (168–217)	185 (156–216.2)	0.273
HDL (mg/dL)	36 (32–43)	37 (32–43)	36 (32–43)	0.710
LDL (mg/dL)	122 (94–148)	123 (104–153)	121.5 (92.5–145.2)	0.296
Triglyceride (mg/dL)	133 (103–175)	142 (114–179)	131 (100–168)	0.256
A1c (%)	6.1 (5.7–7.6)	6.7 (6–9)	6.1 (5.7–6.9)	<b>0.001</b>
RBG (mg/dL)	134 (115–174)	159 (123.8–236)	130 (114–164)	<b>0.001</b>
FBG (mg/dL)	99 (85–127)	110 (94–148)	95 (83–119)	<b>0.001</b>
Uric acid (mg/dL)	7.3 (5.9–8.7)	7.7 (6.6–9.4)	7.3 (5.8–8.4)	0.065
Sodium (mg/dL)	136 (133–139)	135 (130–138)	136 (133–139)	0.029
Potassium (mg/dL)	3.9 (3.6–4.3)	3.9 (3.6–4.1)	3.9 (3.6–4.4)	0.796
Chloride (mg/dL)	98 (95–101)	96.1 (92.8–98.8)	98.8 (96–101.1)	< <b>0.001</b>
Magnesium (mg/dL)	2 (1.8–2.2)	1.9 (1.8–2.2)	2 (1.8–2.2)	0.646
Calcium (mg/dL)	3.9 (3.6–4.3)	8.5 (8.1–8.8)	8.4 (8.1–8.8)	0.710

PPCI characteristics				
<b>Occlusion</b>				0.623
One vessel	106 (32.5%)	20 (30%)	86 (33.1%)	
One vessel + LM	1 (0.3%)	0 (0%)	1 (0.4%)	
Two vessels	107 (32.8%)	18 (27%)	89 (34.2%)	
Two vessels + LM	5 (1.5%)	1 (2%)	4 (1.5%)	
Three vessels	86 (26.4%)	21 (32%)	65 (25.0%)	
Three vessels + LM	21 (6.5%)	6 (9%)	15 (5.8%)	
<b>Volume of contrast (ml)</b>	145 (100–180)	150 (100–200)	140 (100–180)	0.368
<b>Type of contrast agent</b>				0.699
Iodixamol	52 (16%)	9 (14%)	43 (17%)	
Iopronide	274 (84%)	57 (86%)	217 (83%)	
<b>PPCI access</b>				0.565
Brachial	7 (2%)	0	7 (3%)	
Femoral	10 (3%)	2 (3%)	8 (3%)	
Radial	309 (95%)	64 (97%)	245 (94%)	
<b>Ejection fraction and CHA2DS2-VASc</b>				
LVEF	0.5 (0.4–0.5)	0.4 (0.4–0.5)	0.5 (0.4–0.5)	<0.001
CHA2DS2-VASc score	2 (1–3)	3 (2–3)	1 (1–2)	<0.001
NLR	3.8 (2.8–5.8)	4.3 (3.1–5.9)	3.7 (2.7–5.7)	0.211
Mehran	4 (1–9)	10 (9–14)	3 (1–4)	<0.001

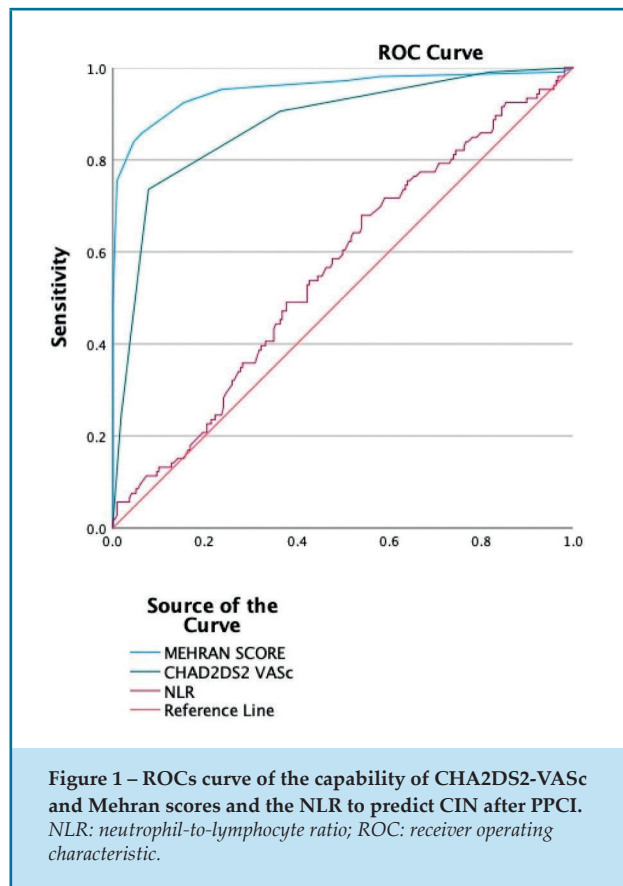
*ALT: alanine aminotransferase; AST: aspartate aminotransferase; eGFR: estimated glomerular filtration rate; RBG: random blood glucose; FBG: fasting blood glucose; LDL: low-density lipoprotein; HDL: high-density lipoprotein; PPCI: primary percutaneous coronary intervention; LVEF: left ventricular ejection fraction; NLR: neutrophil-to-lymphocyte ratio; CIN: contrast-induced nephropathy; LM: left main. aT-test, Mann–Whitney U test,  $\chi^2$  test, or Fisher-exact test*

the prediction of CIN post-PPCI (Table 2). Multivariate regression analysis showed CHA2DS2-VASc (OR 4.06,  $p < 0.001$ ) and Mehran scores (OR 4.99,  $p < 0.001$ ) as significant predictors of CIN post-PPCI (Table 3).

## Discussion

In this study, we aimed to evaluate the role of the CHA2DS2-VASc score in predicting CIN in patients with STEMI who underwent PPCI. Our cohort study showed that the CHA2DS2-VASc score calculated for patients prior to the PPCI accurately predicted CIN. Furthermore, overall accuracy of the CHA2DS2-VASc score was similar to that of Mehran score, which, in turn, is calculated after the completion of the procedure and laboratory workup.

Participants' age was significantly higher in the CIN+ group than in the CIN- group, which is in line with the observation of Khalfallah et al., who reported a significant association between CIN development and old age.<sup>4</sup> The increased incidence of CIN in older individuals can be attributed to age-related renal function decline, such as reduced glomerular filtration rate, which impairs the clearance of the nephrotoxic contrast agent used in PPCI. Additionally, prevalent comorbidities in older patients, including diabetes and hypertension, further compromise renal function.<sup>14,15</sup> Another contributing factor is dehydration, which is more prevalent among older people due to a diminished sense of thirst and lower fluid intake, exacerbating the harmful effects of contrast media on the kidneys.<sup>16,17</sup> These combined factors increase the susceptibility of older patients to renal complications post-PCI.<sup>18,19</sup>



Our findings indicate that higher fasting blood glucose, random blood glucose, and A1c contributed to an increased susceptibility to CIN. This aligns with the results of a previous study that found a higher incidence of CIN in individuals with A1c levels above 8.5% compared to those with levels below 6.5%.<sup>20</sup> Diabetes results in elevated reactive oxygen species (ROS) production due to hyperglycemia, and the administration of contrast media further increases ROS levels, exacerbating oxidative stress. This stress damages cellular structures, leading to inflammatory

responses and renal dysfunction.<sup>21</sup> These mechanisms underscore the importance of strict glucose control in patients with diabetes undergoing PPCI to mitigate the risk of CIN.

In the present study, lower hemoglobin levels were significantly associated with an increased incidence of CIN. Multiple studies have demonstrated that anemia elevates the risk of developing CIN by reducing oxygen delivery to the kidneys, leading to increased oxidative stress and damage to renal cells. It also causes a reduction in blood volume and circulation, decreasing renal perfusion. Anemia also triggers inflammatory responses and forms small thrombi, causing renal ischemia and reperfusion injury.<sup>22,23</sup> Therefore, clinicians need to carefully monitor and manage hemoglobin levels in patients at risk of developing CIN.<sup>8</sup>

Our study found a significant association between CIN and congestive heart failure (as evidenced by a higher Killip class and lower ventricular ejection fraction). Patients with congestive heart failure are at an increased risk of developing CIN because poor renal perfusion leads to heightened renal vasoconstriction and a low preload.<sup>18</sup> Patients with CIN experienced impaired hemodynamic status, as indicated by the higher Killip scores than those who did not develop CIN. This suggests that hemodynamic instability, manifested as hypotension or congestive heart failure, can decrease renal blood flow and perfusion, leading to renal injury and increased risk of CIN. Some studies have shown that proper hydration minimizes the risk of CIN after angiography in patients with chronic kidney disease and congestive heart failure. The HYDRA study demonstrated that assessing patients' hydration status before a procedure and thereby providing individualized hydration, effectively reduce the risk of CIN.<sup>19,24</sup>

Our study found that a CHA2DS2-VASc cut-off score  $\geq 2.5$  is highly predictive of CIN occurrence in patients

**Table 2 – Diagnostic accuracy of the CHA2DS2-VASc score, Mehran score, and the NLR for the prediction of CIN post-PPCI**

	Cut-off	AUC	Sens	Spec	NPV	PPV	p value
CHA2DS2_VASc_total	2.5	0.878	73.6	92.3	87.9	82.1	<0.001
Mehran	6.5	0.954	85.8	93.6	93.2	86.7	<0.001
NLR	3.9	0.560	54.7	54.5	72.9	36.6	0.77

AUC: Area under the curve; Sens: Sensitivity; Spec: Specificity; NPV: Negative Predictive value; PPV: Positive predictive value; NLR: neutrophil-to-lymphocyte ratio.

**Table 3 – Predictors for CIN**

Variables	Logistic regression	
	OR (95% CI)	p
CHA2DS2-VASc	4.06 (2.56–6.43)	<0.001
Mehran	4.99 (4.14–6.02)	<0.001

OR: odds ratio; CI: confidence interval

with STEMI. Patients with a CHA2DS2-VASc score  $\geq 2.5$  were found to be four times more likely to develop CIN. This is consistent with the findings of Samir et al.<sup>9</sup> and Abdel-Ghany et al.<sup>25</sup> The comparable accuracy of the CHA2DS2-VASc score to the Mehran score in predicting CIN can be attributed to its comprehensive coverage of relevant risk factors, overlap of key predictive components, robust statistical validation, and ease of clinical application. Therefore, our study provides evidence that the CHA2DS2-VASc score, calculated at the time of presentation, can be an effective and feasible tool for predicting CIN in patients with STEMI. Unlike the Mehran risk score, which incorporates both preprocedural and procedural parameters, the CHA2DS2-VASc score solely relies on the preprocedural factors, making it simpler and more accessible.<sup>7</sup>

### Limitations of the study

This study was limited by being a single-center study with a comparatively small retrospective cohort, which reduced the robustness of our findings. The long-term outcomes related to CIN, including mortality and morbidity, were not assessed and need further exploration.

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### Conclusions

Our study found that the CHA2DS2-VASc score was a high-quality predictor of CIN in patients post-PPCI. A CHA2DS2-VASc score  $\geq 2.5$  demonstrated comparable predictive accuracy to the gold-standard Mehran score of 6.5. This makes the CHA2DS2-VASc score a valuable tool for clinical decision-making and patient management, offering a simpler alternative to the Mehran score without compromising predictive accuracy.

### Author Contributions

Conception and design of the research, acquisition of data and critical revision of the manuscript for intellectual content: Rantung NOH; analysis and interpretation of the data: Jim EL; statistical analysis: Langi FLFG; writing of the manuscript: Ananda DGP.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Sources of Funding

There were no external funding sources for this study.

### Study Association

This study is not associated with any thesis or dissertation work.

### Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of the RSUP Prof DR R.D Kandou under the protocol number 003/EC/KEPK-KANDOU/I/2022.

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