CHA2DS2-VASC Score Predicts Risk of Contrast-Induced Nephropathy in Non-ST Elevation Myocardial Infarction Patients Undergoing Percutaneous Coronary Interventions

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Abstract

Background: The CHA2DS2-VASC score, used for embolic risk stratification in atrial fibrillation, has been reported recently to predict adverse clinical outcomes in patients with coronary artery disease. We investigated the correlation between the CHA2DS2-VASC score and contrast-induced nephropathy (CIN) in patients with non-ST elevation myocardial infarction (NSTEMI) who underwent percutaneous coronary intervention (PCI).

Methods: We retrospectively enrolled 363 (191; 52.6% men) NSTEMI patients undergoing PCI. The CHA2DS2-VASC score was calculated for each patient, and the study population was divided into 2 groups: CHA2DS2-VASC score < 2 group (low score; n = 259, 71.3%) and CHA2DS2-VASC score ≥2 group (high score; n = 104, 28.6%). Patients were then reallocated to 2 groups according to the presence or absence of CIN. CIN was defined as a rise in serum creatinine >0.5 mg/dL or >25% increase in baseline within 72 h after PCI.

Results: Overall, 56 cases (15.4%) of CIN were diagnosed. When patients with a CHA2DS2-VASC score of <2 were compared with those with a CHA2DS2-VASC score of ≥2, patients with a high score had a higher frequency of CIN (33.17% versus (23) 8.9%; p < 0.001. Also patients with CIN had higher CHADS2 VASC score (3.94 ± 1.13 vs. 1.68 ± 0.46, p < 0.001). Additionally, in-hospital mortality, length of hospital stay, major bleeding, requirement of mechanical ventilation, and dialysis were observed significantly higher in patients with CHA2DS2-VASC score of ≥2 (p = 0.001, p = 0.002, p = 0.006, p = 0.001, p = 0.001, respectively).

Conclusion: In NSTEMI patients undergoing PCI, CHADS2 VASC score is associated with an increased risk for CIN and in-hospital morbidity and mortality.

Introduction

Percutaneous coronary intervention (PCI) in patients with non-ST elevation myocardial infarction (NSTEMI) reduces ischemic complications and improves survival. Patients undergoing PCI are at high risk for contrast-in-
duced nephropathy (CIN) and this has been associated with renal dysfunction, longer hospital stay, increased cardiovascular events, and mortality [1, 2]. So many factors such as hypovolemia, contrast volume, and baseline estimated glomerular filtration rate (eGFR) may contribute to the development of CIN [3, 4]. Because of this, identifying patients at risk of CIN is important in patients undergoing PCI.

CHA2DS2-VASC score was initially developed for stroke risk stratification in patients with atrial fibrillation (AF). The components of the CHA2DS2-VASC score, such as older age, hypertension (HT), diabetes mellitus (DM), heart failure, and female gender, have also been reported as risk factors for adverse clinical outcomes in cardiovascular diseases. Furthermore, recent researches have extended the use of the CHA2DS2-VASC score to non-AF populations. Previously, studies have demonstrated that CHA2DS2-VASC score can predict in hospital and long-term adverse clinical outcomes, including mortality in stable coronary artery disease (CAD), acute coronary syndrome, and CHA2DS2-VASC score of >2 was an independent predictor for incidence of acute stent thrombosis, irrespective of the presence of AF [5–11]. Advanced age, female gender, DM, heart failure, and renal dysfunction are already well-known risk factors for CIN. The components of the CHA2DS2-VASC score include similar risk factors for CIN. Additionally, a recent study demonstrated that CHADS2 score is associated with risk of CIN in patients with stable CAD undergoing elective PCI [12], and the importance of this relation in patients with NSTEMI may be even more valuable. Thus, we aimed to investigate the predictive value of CHA2DS2-VASC score for CIN in patients with NSTEMI who underwent PCI, regardless of AF.

Methods

We retrospectively observed 363 consecutive patients with NSTEMI undergoing PCI at the Avicenna Hospital Cardiology Department between January 2014 and January 2018. NSTEMI was defined according to the current guidelines [13]. All patients were treated with aspirin (300 mg) and a P2Y12 antagonist (clopidogrel 600 mg, ticagrelor 180 mg, or prasugrel 60 mg) and dual-antiplatelet therapy (aspirin 100 mg/day and clopidogrel 75 mg/day or ticagrelor 180 mg/day or prasugrel 10 mg/day) continued for at least 12 months. All PCI procedures were performed using unfractioned heparin (70–100 U/kg). The use of glycoprotein IIb/IIIa inhibitors during PCI was at the physician’s discretion and the type of stents (bare metal or drug eluting) was also left to the operator’s discretion. Transthoracic echocardiography was performed for all patients (Vivid 3; GE Medical System, Horten, Norway), and left ventricular ejection fraction was measured using the Simpson method. We excluded patients with a severe valvular heart disease, severe or uncompensated heart failure, intra-aortic balloon pressure support requirement, severe renal failure, and patients undergoing urgent cardiac surgery for revascularization. The study was approved by the Local Ethics Committee. The CHA2DS2-VASC score was calculated for each patient. Based on the CHA2DS2-VASC score, patients were given 1 point for congestive heart failure (CHF), HT, age 65–74 years, DM, vascular disease, and female gender and 2 points for age ≥75 years and previous stroke or transient ischemic attack [14]. All patients had at least a score of 1 because all of them underwent PCI; thus, they suffered from vascular atherosclerosis. HT was defined as blood pressure >140/90 mm Hg or being on treatment with antihypertensive medications. Also, DM was defined as fasting glucose levels >126 mg/dL or being on treatment with oral antidiabetic drugs or insulin. Finally, hyperlipidemia was defined by reference to current guidelines [15]. Serum creatinine concentration level was observed at hospital admission, every day for the following days and at hospital discharge. eGFR was calculated using the modified formula of Levey et al. [16]. CIN was defined as an increase in creatinine 25% or 0.5 mg/dL from the baseline value within the 48–72-h period following PCI [17].

Statistical Analysis

All analyses were performed using SPSS version 22 for Windows (SPSS Inc., Chicago, IL, USA). Numerical variables are presented as mean ± SD and as percentages. All variables were subjected to Kolmogorov-Smirnov testing to determine whether they were normally distributed. The independent samples t test was used to compare the values of continuous variables between the 2 groups. Nonparametric values were compared using the Mann-Whitney U test. The chi-square test was used to compare categorical data. To evaluate the effects of various factors on CIN development, we performed multivariate regression analyses using the backward Logistic Regression method. Variables for which the unadjusted p < 0.05 was considered significant. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cutoff values of the presence of CHA2DS2-VASC score and the number of CHA2DS2-VASC score to predict the development of CIN.

Results

We retrospectively enrolled 363 (191; 52.6% men) NSTEMI patients undergoing PCI. The CHA2DS2-VASC score was calculated for each patient, and the study population was divided into 2 groups: CHA2DS2-VASC score <2 (low score) group (n = 259, 71.3%) and CHA2DS2-VASC score ≥2 group (high score; n = 104, 28.6%). There was no significant difference between the 2 groups in terms of weight and hyperlipidemia. But high score group is significantly older. Also, DM, previous cerebrovascular accident, and HT were detected significantly higher in high score group. Grace scores, peak troponin levels, time to reperfusion, and contrast volume
were not differed between 2 groups. But left ventricular ejection fraction and eGFR were significantly lower in high score group. The baseline clinical and procedural characteristics of patients were shown in Tables 1 and 2. Patients were then reallocated to 2 groups according to the presence or absence of CIN. Overall, 56 cases (15.4%) of CIN were diagnosed. When patients with a CHA2DS2-VASC score of < 2 were compared with those with a CHA2DS2-VASC score of ≥2, patients with high score had a higher frequency of CIN (33) 31.7% versus (23) 8.9%; p < 0.001. Patients with CIN had higher CHADS2 VASC score (3.94 ± 1.13 vs. 1.68 ± 0.46, p < 0.001), and CHADS2 VASC score was significantly correlated with creatinine levels after PCI and contrast volume/eGFR ratio (r = 0.289, p < 0.001, r = 0.495, p < 0.001, respectively). Additionally, in-hospital mortality, length of hospital stay, major bleeding, requirement of mechanical ventilation, and dialysis were observed significantly higher in patients with CHA2DS2-VASC score of ≥2 (p = 0.001, p = 0.002, p = 0.006, p = 0.001, p = 0.001, respectively; Table 3). CHA2DS2-VASC score and eGFR were also detected as independent risk factors of CIN in logistic regression analysis (Table 4). In ROC curve analysis, the area under the curve for predicting CIN was 0.702 (p < 0.001, 95% CI

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**Table 1. Main characteristics of patients**

|                     | CHA2DS2-VASC score <2 group | CHA2DS2-VASC score ≥2 group | p value |
|---------------------|-----------------------------|-----------------------------|---------|
| Age, years          | 52.1±7.8                    | 69.1±8.0                    | <0.001  |
| Men, n (%)          | 148 (57.1)                  | 43 (41.3)                   | 0.006   |
| Weight, kg          | 76.0±5.5                    | 75.4±6.1                    | ns      |
| HT, n (%)           | 123 (47.5)                  | 96 (92.3)                   | <0.001  |
| HL, n (%)           | 92 (35.5)                   | 37 (35.6)                   | ns      |
| DM, n (%)           | 53 (20.5)                   | 50 (48.1)                   | <0.001  |
| Smoker, n (%)       | 81 (31.3)                   | 21 (20.2)                   | 0.034   |
| Previous CVA, n (%) | 0 (0)                       | 25 (24.0)                   | <0.001  |
| Previous myocardial infarction, n (%) | 72 (27.8) | 41 (39.4) | 0.031 |
| Previous CABG, n (%)| 62 (23.9)                   | 30 (28.8)                   | ns      |
| Creatinine before PCI, mg/dL | 1.0±0.8 | 1.0±0.1 | ns |
| EF, n (%)           | 54.5±7.7                    | 52.1±7.6                    | 0.008   |
| eGFR, mL/min/1.73 m²| 95.0±14.0                   | 74.8±13.3                   | <0.001  |

ns, nonsignificant; HT, hypertension; DM, diabetes mellitus; HL, hyperlipidemia; CVA, cerebrovascular accident; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; CABG, coronary artery bypass grafting; EF, ejection fraction.

**Table 2. Medication characteristics of in patients with decompensated heart failure and other group**

| Medication, n (%) | CHA2DS2-VASC score <2 group | CHA2DS2-VASC score ≥2 group | p value |
|-------------------|-----------------------------|-----------------------------|---------|
| Acetylsalicylic acid | 241 (93.1)                  | 88 (91.7)                   | ns      |
| ACE I, ARB         | 111 (42.9)                  | 82 (78.8)                   | <0.001  |
| Beta blocker       | 183 (70.7)                  | 47 (45.2)                   | <0.001  |
| Spironolactone     | 6 (2.4)                     | 11 (10.7)                   | 0.001   |
| Statin             | 81 (31.3)                   | 41 (39.4)                   | ns      |
| Klopidogrel        | 241 (93.1)                  | 93 (89.4)                   | ns      |
| Furosemide         | 18 (6.9)                    | 11 (10.6)                   | ns      |
| Calcium channel blockers | 18 (6.9) | 20 (19.2) | 0.001 |
| Ticagrelor         | 54 (20.8)                   | 26 (32.5)                   | ns      |
| Nitrates           | 34 (13.1)                   | 26 (25)                     | 0.006   |

ns, nonsignificant; ACE I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.
0.617–0.787), and cutoff value was 2.5 (sensitivity 58.9%, specificity 76.9%) for the number of CHA2DS2-VASC score (Fig. 1).

**Discussion**

CIN is a frequent complication after invasive treatment of NSTEMI, even in patients with normal baseline renal function [18]. It is associated with increased in-hospital mortality and a prolonged hospitalization. However, identification of patients at risk for CIN is challenging. Although pathophysiological mechanisms of CIN are not fully understood, researchers concluded that CIN is caused by renal vasoconstriction, endothelial dysfunction, endothelium cell damage, followed by renal tubular injury and medullary hypoxia [19–22]. Advanced age, female gender, DM, CHF, and renal dysfunction [23–26] are already well-known risk factors for CIN. The components of the CHA2DS2-VASC score include similar risk factors for CIN [27].

The CHA2DS2-VASC scores were initially developed for stroke risk stratification in patients with AF [14]. Furthermore, recent studies have extended the use of the CHA2DS2-VASC score to non-AF patients [5–11]. As for patients with CAD, the CHA2DS2-VASC score has been associated with in-hospital and long-term adverse clinical outcomes, including mortality, in patients with both stable CAD and acute coronary syndrome [5–12]. In accordance with previous studies, we found that high CHA2DS2-VASC score (≥2) was significantly correlated with in-hospital all-cause mortality. Chou et al. [12] showed that the CHADS2 score predicts risk of CIN in patients with stable CAD undergoing elective PCI, but they did not enroll patients with NSTEMI. We evaluated CHA2DS2-VASC score, which is more comprehensive risk scoring tool, and included patients with NSTEMI in our study. In our study, we found that CHA2DS2-VASC score for CIN in patients with NSTEMI who underwent PCI, and CIN rate was significantly increased in patients with high CHA2DS2-VASC score (≥2). The number of CHA2DS2-VASC score (≥2) was significantly correlated with in-hospital all-cause mortality.

**Table 3. In-hospital clinical course of patients**

|                         | CHA2DS2-VASC score <2 | CHA2DS2-VASC score ≥2 group | p value |
|-------------------------|------------------------|----------------------------|---------|
| Contrast volume, mL, mean ± SD | 229.15±17.4            | 227.12±16.3                | ns      |
| Contrast nephropathy, n (%) | 23 (8.9)               | 33 (31.7)                  | <0.001  |
| Time to reperfusion, h, mean ± SD | 4.70±2.3              | 4.99±2.24                  | ns      |
| Troponin peak, ng/dL, mean ± SD | 2.3±1.09              | 2.17±0.8                   | ns      |
| Length of hospital stay, days, mean ± SD | 4.62±1.6              | 5.14±2.3                   | 0.002   |
| GRACE score, mean ± SD | 123.3±10.6             | 124.81±10.8                | ns      |
| Major bleeding, n (%) | 6 (2.3)                | 9 (8.7)                    | 0.006   |
| Dialysis, n (%) | 4 (1.5)                | 9 (8.7)                    | 0.001   |
| Mechanical ventilation, n (%) | 4 (1.7)                | 9 (13.2)                   | 0.001   |
| In-hospital mortality, n (%) | 6 (2.3)                | 11 (10.6)                  | 0.001   |
| PCI, n (%) | 197 (76.1)             | 78 (75.0)                  | ns      |
| CABG, n (%) | 24 (9.3)               | 16 (15.4)                  | ns      |
| Medical treatment, n (%) | 36 (13.9)              | 10 (9.6)                   | ns      |

ns, nonsignificant; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

**Table 4. Independent risk factors of CIN in logistic regression analysis**

| Variables      | OR (95% CI) | p value |
|----------------|-------------|---------|
| Weight         | 0.9 (0.9–1.0) | ns      |
| HT             | 1.5 (0.6–4.1) | ns      |
| Age, years     | 0.9 (0.9–1.0) | ns      |
| CHA2DS2-VASC score | 3.1 (1.5–6.3) | 0.002   |
| DM             | 1.0 (0.4–2.8) | ns      |
| CVA            | 3.8 (0.5–27.1) | ns      |
| Gender         | 0.75 (0.39–1.4) | ns      |
| eGFR           | 1.07 (1.02–1.11) | 0.001   |
| ACE I, ARB     | 0.387 (0.14–1.02) | ns      |

ns, nonsignificant; HT, hypertension; DM, diabetes mellitus; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; CIN, contrast-induced nephropathy; ACE I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.
VASC score (≥2) and also demonstrated that the CHA2DS2-VASC score was independently associated with CIN. Additionally, ROC curve analysis showed that CHA2DS2-VASC score has good sensitivity and specificity for detection of CIN in these patients.

Grace score is one of the most important indicators of mortality and morbidity in patients with NSTEMI [28]. Also it is a very useful in identification of high-risk patients and determination of treatment strategy. In our study, there was no difference between the general risk factors and GRACE score in both groups, and in-hospital mortality and morbidity were found to be significantly higher in patients with high score patients. But long-term follow-up is needed to clarify the mortality difference between the 2 groups.

Contrast volume is an important risk factor for CIN and dose minimization, on the background of a known baseline reduced renal function, may serve as an important strategy to limit the incidence of CIN [29]. However, we used a relatively small amount of contrast, and we did not find significant difference in terms of dose of contrast used in patients with and without CIN. We suggested that other factors, such as impaired renal function and DM, age and weight might contribute more to the development of CIN than contrast volume.

CHA2DS2-VASC score is also a simple risk score containing only preprocedural variables and developed in the setting of NSTEMI. Thus, risk scores that are based on variables which are available before the procedure permit to implement prophylactic measures such as intravenous hydration, sodium bicarbonate, and N-acetylcysteine administration, which are capable of preventing CIN [30]. In comparison to other available CIN risk stratification tools, the CHA2DS2-VASC score is a simple scoring tool and therefore may be easily applied in daily practice.

Our study had some limitations. First, our study was a single-center study. Second, the study cohort was relatively small. Finally, some risk factors of CIN, such as proteinuria and nephrotoxic agents, could not be fully assessed.

**Conclusion**

In NSTEMI patients undergoing PCI, CHADS2 VASC score is associated with an increased risk for CIN and in-hospital mortality and morbidity. CHA2DS2-VASC score can be used as a new, simple, and reliable tool to predict CIN in patients with NSTEMI who underwent urgent PCI.

**Statement of Ethics**

The authors have no ethical conflicts to disclose.

**Disclosure Statement**

The authors have no conflicts of interest to declare.

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