ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Predictive Value of CHA_2DS_2-VASc Score in Patients with Contrast-Induced Nephropathy After Primary Percutaneous Coronary Intervention for ST-Elevated Myocardial Infarction

ST Segment Yükselmeli Miyokard Enfarktüsü Tanısı İle Primer Perkütan Koroner Girişim Uygulanan Hastalarda CHA_2DS_2-VASc Skorunun Kontrast İlişkili Nefropati Gelişimi Öngördürücü Değeri

ABSTRACT

Objective: Contrast-induced nephropathy (CIN) is one of the well-known complications of cardiac catheterization and related with in-hospital and long-term morbidity and mortality. We aimed to evaluate if CHA_2DS_2-VASc score can also be used as a surrogate for CIN development and moreover the relationship between CIN development and in-hospital major adverse cardiac events (MACE) in patients presenting with STEMI and undergoing primary PCI.

Materials and Methods: All patients presented with STEMI and underwent primary PCI between 2015-2019 in our center were included retrospectively.

Results: A total of 572 patients were included. Age [$P=0.032$, β: 0.153, odds ratio (95% CI): 0.014-0.302], diabetes mellitus [($P=0.023$, β: 0.134, odds ratio (95% CI): 0.017-0.217], history of stroke [$P=0.034$, β: 0.118, OR (95% CI): 0.017-0.436], volume of contrast medium [$P=0.042$, β: 0.155, OR (95% CI): 0.109-0.462], left ventricular ejection fraction [$P=0.003$, β: 0.376, OR (95% CI): 0.214-0.517], and CHA_2DS_2-VASc score [$P=0.001$, β: 0.115, OR (95% CI): 0.054-0.177] were detected as independent risk factors associated with contrast-induced nephropathy development. The area under the curve for CHA_2DS_2-VASc score was 0.809 (95% CI: 0.760-0.857). A cut-off value of 2.5 for CHA_2DS_2-VASc score was associated with 80.1% sensitivity and 71.4% specificity in the prediction of contrast-induced nephropathy development.

Conclusion: Our current study showed that the CHA_2DS_2-VASc risk score has an effective discriminating power in determining the contrast-induced nephropathy development and a score ≥2 defines the group at risk in patients presenting with ST-elevation myocardial infarction and underwent primary percutaneous coronary intervention. Moreover, contrast-induced nephropathy development is associated with longer coronary care unit stay and major adverse cardiac events (in-hospital decompensated heart failure, cardiogenic shock, cardiac arrest, and mortality).

Keywords: Contrast-induced nephropathy, CHA_2DS_2-VASc, STEMI, CIN

ÖZET

Amaç: Kontrast kaynaklı nefropati (KKN) kardiyak kateterizasyonun iyi bilinen komplikasyonlarından biridir. Hastane içi ve uzun süreli morbidite ve mortalitede artışa neden olduğu bilinmektedir. Bu çalışmada, CHA_2DS_2-VASc skorunun ST segment yükselmeli miyokard enfarktüsü (STYME) tanısı ile birincil perkütan koroner girişim (PKG) yapılan hastalarda KKN gelişimi öngördürücüsü olup olmadığını araştırmayı ve STYME ile başvuran ve birincil PKG yapılan hastalarda KKN gelişimi ile hastane içi istenmeyen majör kardiyak olay gelişimi arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: 2015-2019 yılları arasında merkezimize STYME tanısı ile birincil PKG yapılan tüm hastalar geriye dönük olarak dahil edildi.

Bulgular: Bu çalışmaya, toplam 572 hasta dahil edildi. Yaş [$P=0.032$, β: 0.153, OR (%95 GA): 0.014-0.302], diabetes mellitus [$P=0.023$, β: 0.134, OR (%95 GA): 0.017-0.217], inme öyküsü [$P=0.034$, β: 0.118, OR (%95 GA): 0.017-0.436], kullanılan kontrast madde hacmi [$P=0.042$, β: 0.155, OR (%95 GA): 0.109-0.462], sol ventrikül ejeksiyon fraksiyonu [$P=0.003$, β: 0,376, OR (%95 GA): 0.214-0.517] ve CHA_2DS_2-VASc skoru [$P=0.001$, β: 0.115, OR

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

Esra Dönmez
Sevgi Özcan
Orhan İnce
İrfan Şahin
Ertuğrul Okuyan

Department of Cardiology, Bagcılar Training and Research Hospital, İstanbul, Türkiye

Corresponding author:
Ertuğrul Okuyan
✉ dreokuyan@hotmail.com

Received: September 26, 2022
Accepted: October 3, 2022

Cite this article as: Dönmez E, Özcan S, İnce O, Şahin İ, Okuyan E. Predictive value of CHA_2DS_2-VASc score in patients with contrast-induced nephropathy after primary percutaneous coronary intervention for ST-elevated myocardial infarction. *Turk Kardiyol Dern Ars.* 2023;51(2):97-103.

DOI:10.5543/tkda.2022.46994

(%95 GA): 0.054-0.177], KKN gelişimi ile ilişkili bağımsız risk faktörleri olarak saptandı. CHA_2DS_2-VASc skoru için eğrinin altında kalan alan 0,809 [%95 CI: 0.760-0.857] idi. CHA_2DS_2-VASc skoru için 2.5'lik bir eşik değerinin KKN gelişimini %80,1 duyarlılık ve %71,4 özgüllük ile ön gördürebileceği saptandı.

Sonuç: Mevcut çalışmamız, STYME tanısı ile birincil PKG yapılan hastalarda CHA_2DS_2VASc skorunun KKN gelişimini belirlemede etkin bir ayırt edici güce sahiptir ve CHA_2DS_2VASc ≥2 değeri risk altındaki grubu göstermektedir. KKN gelişimi, daha uzun yoğun bakım kalış süresi ve hastane içi istenmeyen major kardiyak olay gelişimi ile ilişkili bulunmuştur.

Anahtar Kelimeler: Kontrast kaynaklı nefropati, CHA_2DS_2-VASc, ST segment yükselmeli miyokard enfarktüsü

Cardiac catheterization is widely used both for diagnostic and therapeutic purposes. Contrast-induced nephropathy (CIN) is one of the frequent complications of the procedure, mediated by contrast media, and causes acute kidney injury. The relation between CIN development and increased in-hospital and long-term morbidity and mortality has been shown.[1] The increase of serum creatinine (Cr) level of ≥0.5 mg/dL or ≥25% from baseline within 48-72 hours after contrast medium (CM) administration is the accepted definition of CIN.[2] In general population, the incidence of CIN is approximately >2% whereas it may be as frequent as 20%-30% in patients with comorbidities such as congestive heart failure (CHF), chronic kidney disease (CRF), diabetes mellitus (DM) and/or advanced age. Patients presenting with acute coronary syndrome (ACS) are at high-risk for CIN development.[3,4] Since the early diagnosis and preventive steps may alter progression and clinical outcomes, stratifying patients under risk is essential.[5] Different risk models were formed to estimate the risk of CIN development in different clinical conditions.[6-9] However, CIN risk estimation using the scoring system is not practical, especially in emergency situations, like ST-elevation myocardial infarction (STEMI), since the main goal is to provide adequate coronary reperfusion.

The $CHADS_2$ and CHA_2DS_2-VASc scores are mainly created to foresee embolic stroke risk and to manage the anticoagulant treatment in Atrial Fibrillation (AF) patients.[9,10] These variables are risk factors for coronary artery disease (CAD) and have been previously shown to be linked with mortality in chronic coronary syndromes and ACS.[11,12] The utility of CHA_2DS_2-VASc score in the prediction of long-term all-cause and cardiac mortality and stroke in patients undergoing percutaneous coronary intervention (PCI) was reported.[13] The ability of $CHADS_2$ and CHA_2DS_2-VASc scores in CIN development was established in other clinical scenarios than STEMI in previous studies.[14,15] We aimed to evaluate if CHA_2DS_2-VASc score can also be used as a surrogate for CIN development and the relationship between CIN development and in-hospital major adverse cardiac events (MACEs) in patients presenting with STEMI and undergoing primary PCI.

Materials and Methods

All patients presented with STEMI and underwent primary PCI between 2015 and 2019 in our center were included retrospectively. Demographic, clinical, and laboratory parameters and medical treatments were retrieved from the local hospital database and patients' files. ST-elevation myocardial infarction was diagnosed and treated according to recent guidelines.[16] Presence of stenosis ≥50% in 2 or more epicardial coronary arteries is defined as a multivessel disease. Patients requiring emergency surgery, patients with a history of organ transplantation, end-stage renal disease, severe hepatic disease, malignancy, chronic autoimmune disease, and/or patients under steroid or nonsteroidal anti-inflammatory therapy or CM exposure within the last 2 weeks were also excluded. Transthoracic echocardiography was performed (Vivid S70; GE Medical System, Horten, Norway), and left ventricular ejection fraction (LVEF) was measured using Simpson's method for all patients. Physiological (0.9%) saline was given intravenously at a rate of 1 and 0.5 mL/kg/h for those with reduced LVEF or CHF for 12 hours after contrast exposure, which was the routine follow-up regimen for ACS patients in our clinic. A non-ionic, low-osmolality contrast agent was the preferred CM in our catheterization laboratory routinely.

Congestive heart failure,[17] stroke and transient ischemic attack,[18,19] hypertension (HT),[20] diabetes mellitus (DM),[21] CAD,[22] and peripheral artery disease (PAD)[23] were described according to the established definitions. History of CAD, PAD, PCI, or coronary artery bypass graft surgery was indicated as vascular disease.

Two groups were generated regarding CHA_2DS_2-VASc scores; patients with a score ≤1 formed group 1 and those with a score ≥2 formed group 2. The baseline Cr value was accepted as the Cr level measured on admission and the maximal Cr value was accepted as the maximum serum Cr that was obtained at least 48 hours after CM exposure. In addition, 2 groups were created in terms of CIN development; CIN developed as CIN (+) and CIN non-developed as CIN (−). The development of CIN was defined as the primary endpoint of our study. In-hospital re-infarction, cardiac arrest, decompensated heart failure, cardiogenic shock, or mortality were defined as MACE and accepted as secondary endpoints of our study. The study was conducted in concordance with the Declaration of Helsinki and was approved by the Bağcılar Training and Research Hospital ethical committee (2022/09/10/017).

Statistical Analysis

The Statistical Package for the Social Sciences 22.0 (SPSS Inc., Chicago, Ill, USA) was used for statistical analysis. Categorical data are expressed as number (n) and percentages (%) and continuous variables are expressed as mean ± SD. Chi-square test was performed to assess differences in categorical variables between groups Student's *t*-test or Mann–Whitney *U* test was applied to compare unpaired samples. Variables having nonlinear correlation were analyzed by Spearman's correlation test and variables having linear correlation were analyzed by Pearson's correlation test. The association between CHA_2DS_2-VASc score and CIN development was investigated. Independent variables of CIN development were assessed by logistic regression analysis. Area

under the receiver operating curve was calculated to assess the ability CHA_2DS_2-VASc score to estimate CIN development. Two-sided *P* values <0.05 were accepted as statistically significant.

Results

Nine hundred thirty-three patients were screened, and after the exclusion of patients as defined in methodology and patients with lack of data, a total of 572 patients were involved in this retrospectively designed single-center study. The mean age was 65.1 ± 10.6 and 57.5% were male. The baseline Cr level was 0.99 ± 0.28 mg/dL. When patients were grouped according to CIN development as CIN (+) and (–), 103 (18%) patients formed the CIN (+) and 469 (82%) patients formed CIN (–) group. Both groups were similar in terms of gender, body mass index, smoking status, incidence of hyperlipidemia, and received medical treatment. However, age (70.5 ± 8.8 vs. 63.9 ± 10.6; *P*=0.001), DM (76.6% vs 25.7%; *P* < 0.0001), HT (92.2% vs. 49.8%; *P* < 0.0001), CAD (89.3% vs. 26.1%; *P* < 0.0001), PAD (19.4% vs. 0.4%; *P* < 0.0001), CHF (52.4% vs 10.7%; *P* < 0.0001), stroke (14.5% vs. 0.6%; *P* < 0.0001), the volume of CM (134 ± 63 vs. 93 ± 38; *P*=0.002), length of coronary care unit (CCU) stay (4.1 ± 1.3 vs. 2.0 ± 0.7; *P*=0.024), and CHA_2DS_2-VASc score (4.06 ± 1.67 vs. 2.1 ± 1.29; *P* < 0.0001) were significantly higher in CIN (+) group. In terms of laboratory markers, maximal urea (72.7 ± 18.8 vs. 44.4 ± 18.8; *P* < 0.0001), maximal Cr (1.57 ± 0.72 vs. 1.08 ± 0.28; *P* < 0.0001), uric acid (6.6 ± 1.9 vs. 5.8 ± 2.1; *P*=0.007), troponin T [29.0 (4.7-1383) vs. 17.5 (1-1383); *P*=0.001], fasting blood glucose (153.9 ± 79.7 vs. 136.9 ± 64.9; *P*=0.022), and aspartate aminotransferase (AST) [29.0 (8-1175) vs. 24.0 (6-1145); *P*=0.003] were significantly higher in CIN (+) group. In addition, LVEF (47.4 ± 11.5 vs. 51.2 ± 10.6; *P*=0.006) and albumin (4.1 ± 0.5 vs. 4.3 ± 0.5; *P*=0.001) levels were significantly lower in CIN (+) group. Furthermore, we evaluated secondary outcomes according to CIN development; mortality (9.7% vs. 4.1%; *P*=0.007), cardiac arrest (6.8% vs. 3.4%; *P*=0.021), heart failure (10.6% vs. 6.4%; *P*=0.014), and cardiogenic shock (8.7% vs. 5.3%; *P*=0.043) were significantly higher in CIN (+) group. All demographical, clinical, and laboratory data of the 2 groups are presented in detail in Table 1.

Two groups were formed based on CHA_2DS_2-VASc scores; group 1 (CHA_2DS_2-VASc score ≥2) and group 2 (CHA_2DS_2-VASc score ≤1). Three hundred ninety-five (69.1%) patients were in group 1 and 177 (30.9%) patients were in group 2. The volume of CM (141 ± 57 vs. 91 ± 47; *P*=0.001), length of CCU stay (3.7 ± 1.2 vs. 2.0 ± 1.4; *P*=0.041), and rate of CIN development (25.5% vs 1.2%; *P* < 0.0001) were significantly higher in group 1. Concerning laboratory markers, baseline urea (44.7 ± 19.7 vs. 36.9 ± 12.3; *P* < 0.0001) and maximal urea (53.7 ± 30.3 vs. 39.4 ± 15.7; *P* < 0.0001), baseline Cr (1.03 ± 0.30 vs. 0.94 ± 0.22; *P* < 0.0001) and maximal Cr (1.16 ± 0.51 vs. 0.95 ± 0.22; *P* < 0.0001), pro-brain natriuretic peptide (pro-BNP) [78.8 (50-12 679) vs. 54.8 (50-26 528); *P*=0.03], fasting blood glucose (145.1 ± 71.6 vs. 128.6 ± 58.1; *P*=0.009), and AST [26.0 (8-1175) vs. 24.0 (6-617); *P*=0.01] levels were significantly higher and LVEF (48.9 ± 11.1 vs. 54.4 ± 9.1; *P* < 0.0001), hemoglobin (12.8 ± 1.9 vs. 13.7 ± 1.7; *P*=0.04), and albumin (4.2 ± 0.5 vs. 4.4 ± 0.4; *P*=0.005) levels were significantly lower in Group 1. All demographical, clinical, and laboratory data of the 2 groups are presented in detail in Table 2.

Regression analysis revealed that the CHA_2DS_2-VASc score [*P*=0.001, β: 0.115, OR (95% CI): 0.054-0.177], the volume of CM [*P*=0.042, β: 0.155, OR (95% CI): 0.109-0.462] and LVEF [*P*=0.003, β: 0.376, OR (95% CI): 0.214-0.517] were independent risk factors associated with CIN development. Then, we decided to find out which components of the CHA_2DS_2-VASc score accounted for this result. Accordingly, the subsequent analysis indicated that age [*P*=0.032, β: 0.153, OR (95% CI): 0.014-0.302], DM [*P*=0.023, β: 0.134, OR (95% CI): 0.017-0.217] and history of stroke [*P*=0.034, β: 0.118, OR (95% CI): 0.017-0.436] were independent risk factors associated with CIN development, while HT, CHF, PAD, and CAD did not reach statistical significance. Receiver operating characteristic (ROC) curve analysis was performed to identify the optimal cut-off value and area under the curve (AUC) for CHA_2DS_2-VASc score. Receiver operating characteristic curve for the accuracy of CHA_2DS_2-VASc score for predicting CIN development in STEMI patients is shown in Figure 1. The AUC for CHA_2DS_2-VASc score was 0.809 [95% CI: 0.760-0.857]. A cut-off value of 2.5 for CHA_2DS_2-VASc score was associated with 80.1% sensitivity and 71.4% specificity in the prediction of CIN development.

Discussion

The results of this study suggest that preprocedural assessment of the CHA_2DS_2-VASc score gives additional information to predict the incidence of CIN development in patients with STEMI who underwent primary PCI. Although the baseline Cr level was 0.99 ± 0.28 in our study, this finding supports that increased risk may be seen at all stages of kidney function. Other independent predictors of CIN development were advanced age, DM, stroke, volume of CM, and reduced LVEF. Given its easiness in clinical practice, close follow-up of patients with CHA_2DS_2-VASc score >2 and prophylaxis against CIN may be suggested.

Contrast medium use, rises in concordance with diagnosis and treatment techniques, and medical developments especially in cardiology and CIN is one of the vital complications that can occur due to CM use. Contrast-induced nephropathy was found to be related to in-hospital and 1-year mortality; moreover, prolonged hospital stays, increased need for intensive care, and hemodialysis due to CIN development creates an additional burden on healthcare costs.[24] We revealed that length of CCU stay, incidence of mortality, in-hospital cardiac arrest, decompensated heart failure, and cardiogenic shock were significantly higher in CIN (+) group, as well. Contrast-induced nephropathy development is multifactorial: advanced age, DM, CHF, HT, renal dysfunction, amount and type of CM used, exposure to nephrotoxic agents, being in dehydrated status, and urgent interventions. Most of the comorbidities related to CIN development are variables included in CHA_2DS_2-VASc score. We found CHA_2DS_2-VASc score as an independent risk factor for CIN development. When the variables were evaluated individually, DM, advanced age, history of stroke, and reduced LVEF were established as independent risk factors for CIN development. Moreover, higher CM volume was found as an independent risk factor for CIN development in our study. Although history of HT, CHF, CAD, and PAD was

Table 1. Clinical and Demographic Data of Study Population and 2 Groups According to Contrast-Induced Nephropathy Development

Variables	All (n=572)	Group 1 CIN (+) (n=103)	Group 2 CIN (–) (n=469)	*P*
Clinical characteristics and comorbidities				
Age (years)	65.1 ± 10.6	70.5 ± 8.8	63.9 ± 10.6	0.001
Male, n (%)	329 (57.5)	62 (60.1)	267 (56.9)	0.544
BMI (kg/m^2)	28.4 ± 4.3	28.6 ± 4.7	28.4 ± 4.2	0.668
Smoker, n (%)	136 (23.8)	26 (25.2)	110 (23.6)	0.724
HT, n (%)	329 (57.5)	95 (92.2)	234 (49.8)	<0.0001
HPL, n (%)	59 (10.3)	45 (9.6)	14 (13.6)	0.227
DM, n (%)	200 (35.0)	79 (76.6)	121 (25.7)	<0.0001
Previous CAD, n (%)	214 (37.4)	92 (89.3)	122 (26.1)	<0.0001
Previous PAD, n (%)	22 (3.8)	20 (19.4)	2 (0.4)	<0.0001
Previous stroke, n (%)	18 (3.1)	15 (14.5)	3 (0.6)	<0.0001
Previous CHF, n (%)	104 (18.2)	54 (52.4)	50 (10.7)	<0.0001
LVEF (%)	52.1 ± 10.1	47.4 ± 11.5	51.2 ± 10.6	0.006
Volume of CM (mL)	123 ± 61	134 ± 63	93 ± 38	0.002
CHA_2DS_2-VASc score	2.7 ± 1.8	4.06 ± 1.67	2.1 ± 1.29	<0.0001
Duration of CCU stay (days)	3.2 ± 1.6	4.1 ± 1.3	2.0 ± 0.7	0.024
Drugs, n (%)				
Aspirin	368 (64.3)	70 (67.9)	298 (63.5)	0.641
ACE inhibitor/ARB use	308 (53.8)	54 (52.4)	254 (54.2)	0.846
Calcium channel blocker	151 (26.3)	24 (23.3)	127 (27.1)	0.132
β-blocker	167 (29.2)	35 (33.9)	132 (28.1)	0.171
Laboratory parameters				
Urea (mg/dL)				
Baseline	42.3 ± 18.1	46.1 ± 18.8	41.6 ± 17.8	0.056
After 48 hours	49.7 ± 27.9	72.7 ± 18.8	44.4 ± 18.8	<0.0001
Creatinine (mg/dL)				
Baseline	0.99 ± 0.28	1.08 ± 0.27	0.98 ± 0.28	0.051
After 48 hours	1.09 ± 0.46	1.57 ± 0.72	1.08 ± 0.28	<0.0001
Hemoglobin (g/dL)	13.1 ± 1.9	12.8 ± 2.2	13.2 ± 1.8	0.072
Albumin (g/dL)	4.2 ± 0.5	4.1 ± 0.5	4.3 ± 0.5	0.001
Uric acid (mg/dL)	5.9 ± 2.1	6.6 ± 1.9	5.8 ± 2.1	0.007
Pro-BNP (pg/mL)	72.9 (50-28 679)	73.6 (66-28 679)	72.1 (50-26 528)	0.413
Troponin T (pg/mL)	21.0 (1-1383)	29.0 (4.7-1383)	17.5 (1-1383)	0.001
Fasting blood glucose (mg/dL)	140.1 ± 68.1	153.9 ± 79.7	136.9 ± 64.9	0.022
AST (U/L)	24.8 (6-1175)	29.0 (8-1175)	24.0 (6-1145)	0.003
ALT (U/L)	32.6 (3-673)	22.0 (9-622)	22.0 (3-673)	0.895
Total cholesterol (mg/dL)	188.9 ± 49.8	186.1 ± 43.6	189.5 ± 51.2	0.526
Triglycerides (mg/dL)	171.3 ± 107.9	156.2 ± 67.9	174.5 ± 114.6	0.123
LDL cholesterol (mg/dL)	113.9 ± 38.3	113.6 ± 35.5	113.9 ± 38.9	0.936
HDL cholesterol (mg/dL)	43.1 ± 12.4	41.9 ± 9.1	43.4 ± 12.9	0.272
Major adverse cardiac events: In-hospital				
Re-infarction, n (%)	9 (1.6)	2 (1.9)	7 (1.5)	0.538
Mortality, n (%)	29 (5.1)	10 (9.7)	19 (4.1)	0.007
Cardiac arrest, n (%)	23 (4.1)	7 (6.8)	16 (3.4)	0.021
Heart failure, n (%)	41 (7.2)	11 (10.6)	30 (6.4)	0.014
Cardiogenic shock, n (%)	34 (5.9)	9 (8.7)	25 (5.3)	0.043

ACE/ARB, angiotensin converting enzyme/angiotensin receptor blocker; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAD, coronary artery disease; CCU, coronary care unit; CHF, congestive heart failure; CIN, contrast-induced nephropathy; CM, contrast medium; DM, diabetes mellitus; HPL, hyperlipidemia; HDL, high-density lipoprotein; HT, hypertension; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; PAD, peripheral artery disease; Pro-BNP, pro-brain natriuretic peptide.

Table 2. Clinical and Demographic Data of 2 Groups According to CHA_2DS_2-VASc Scores

Variables	Group 1 CHA_2DS_2-VASc Score ≥2 (n=395)	Group 2 CHA_2DS_2-VASc Score ≤1 (n=177)	*P*
BMI (kg/m²)	28.3 ± 4.3	28.6 ± 4.3	0.435
Smoker, n (%)	89 (22.6)	47 (26.7)	0.294
HPL, n (%)	46 (11.6)	13 (7.3)	0.118
LVEF, %	48.9 ± 11.1	54.4 ± 9.1	<0.0001
Volume of CM (mL)	141 ± 57	91 ± 47	0.001
Duration of CCU stay (days)	3.7 ± 1.2	2.0 ± 1.4	0.041
Drugs, n (%)			
Aspirin	240 (60.8)	128 (72.3)	0.102
ACE inhibitor/ ARB use	208 (52.6)	100 (56.5)	0.217
Calcium channel blocker	103 (26.1)	48 (27.1)	0.846
β-blocker	117 (29.6)	50 (28.2)	0.623
Laboratory parameters			
Urea (mg/dL)			
Baseline	44.7 ± 19.7	36.9 ± 12.3	<0.0001
After 48 hours	53.7 ± 30.3	39.4 ± 15.7	<0.0001
Creatinine (mg/dL)			
Baseline	1.03 ± 0.30	0.94 ± 0.22	<0.0001
After 48 hours	1.16 ± 0.51	0.95 ± 0.22	<0.0001
Hemoglobin (g/dL)	12.8 ± 1.9	13.7 ± 1.7	0.04
Albumin (g/dL)	4.2 ± 0.5	4.4 ± 0.4	0.005
Uric acid (mg/dL)	6.1 ± 2.1	5.7 ± 1.9	0.220
Pro-BNP (pg/mL)	78.8 (50-12 679)	54.8 (50-26 528)	0.03
Troponin T (pg/mL)	23 (1-1383)	14.0 (1-500)	0.144
Fasting blood glucose (mg/dL)	145.1 ± 71.6	128.6 ± 58.1	0.009
AST (U/L)	26.0 (8-1175)	24.0 (6-617)	0.01
ALT (U/L)	22.0 (5-673)	24.0 (3-379)	0.230
Total cholesterol (mg/dL)	187.7 ± 49.6	191.7 ± 50.6	0.405
Triglycerides (mg/dL)	167.1 ± 108.6	180.5 ± 105.9	0.176
LDL cholesterol (mg/dL)	113.5 ± 39.1	114.7 ± 36.7	0.738
HDL cholesterol (mg/dL)	43.2 ± 11.9	43.0 ± 13.3	0.916
CIN, n (%)	101 (25.5)	2 (1.2)	<0.0001

ACE/ARB, angiotensin-converting enzyme/angiotensin receptor blocker; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CCU, coronary care unit; CIN, contrast-induced nephropathy; CM, contrast medium; HDL, high-density lipoprotein; HPL, hyperlipidemia; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; Pro-BNP, pro-brain natriuretic peptide.

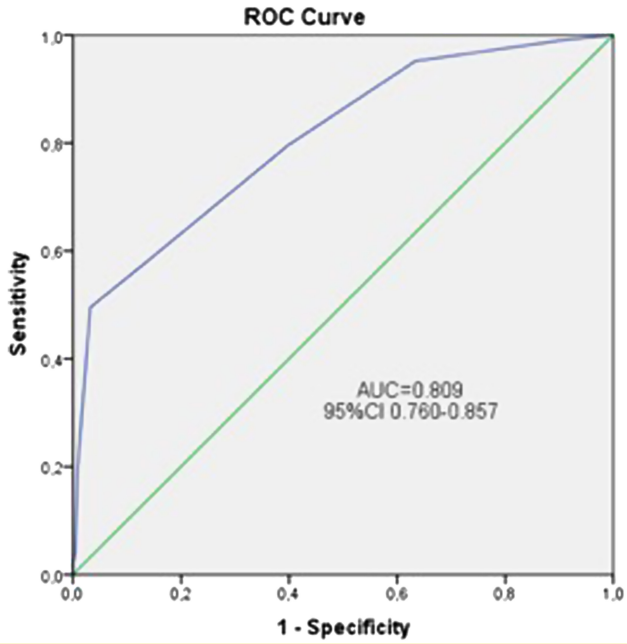

Figure 1. ROC curve for accuracy of CHA_2DS_2-VASc score for predicting CIN development in STEMI patients. CIN, contrast-induced nephropathy; ROC, receiver operating characteristics; STEMI, ST-elevation myocardial infarction.

observed significantly higher in CIN (+) group, they were not found as independent predictors. Complex pathophysiological mechanisms such as inflammation, thrombosis, vasoconstriction, and vascular remodeling play role in CIN. Renin-angiotensin-aldosterone system activation, elevated endothelin-1, and reactive oxygen species levels were thought to be parts of CIN pathogenesis via inducing intrarenal vasoconstriction.[25] The impact of renin-angiotensin-aldosterone system blocking agents on CIN development is still controversial.[26-28] In our study, we did not observe any effect of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker treatment on the incidence of CIN development in STEMI patients who underwent primary PCI. However, the dosages and length of treatment were not achieved; these factors might be associated with the protective effects.

The discriminative ability of CHA_2DS_2-VASc in predicting CIN development in patients presenting with ACS previously[29,30] and CHA_2DS_2-VASc ≥4 was detected as an independent predictor of CIN. Patients presenting either with STEMI or non-ST segment elevation myocardial infarction (NSTEMI) were included in these studies. Patients presenting with NSTEMI were known to have more co-morbidities and this may result in a higher CHA_2DS_2-VASc score since our study solely consisted of STEMI patients. The number of participants and gender difference may also affect the results. On the other hand, a CHA_2DS_2-VASc score ≥ 2 was found as an independent predictor of CIN development in STEMI similar to our results.[31]

The CHA_2DS_2-VASc score was found more sensitive than the $CHADS_2$ score in terms of predicting stroke risk.[32] Although these risk scores were created mainly to predict thromboembolism in atrial fibrillation, the CHA_2DS_2-VASc score was shown to estimate

adverse events in those with chronic coronary syndromes, ACS, sick sinus syndrome, CHF and patients with Takotsubo syndrome.[13,33,34] Our results revealed the CHA_2DS_2-VASc score as an indicator of CIN development in STEMI patients who underwent primary PCI. This may be explained by the similarity between risk factors of CIN and CHA_2DS_2-VASc score. Serum Cr level was observed higher in patients with higher $CHADS_2$ scores.[14] Similarly, higher Cr, fasting blood glucose, and pro-BNP levels were found higher in patients with higher CHA_2DS_2-VASc scores in our study.

Limitations

Our study was designed retrospectively and performed in a single center. The study design was primarily based on risk factor assessment. However, a combined biomarker study such as neutrophil gelatinase-associated lipocalin and cystatin C level measurement would give further information and opportunity to correlate with the CHA_2DS_2-VASc score. The post-procedural Cr level was obtained at least 48 hours after contrast exposure; therefore, patients who had a later increase in Cr levels may have been missed. The female gender gets 1 point as a component of the CHA_2DS_2-VASc score in the original form of the score. Similarly, female gender was found as an independent risk factor for CIN development in previous studies.[24] The female patients older than 65 years without additional co-morbidities have a CHA_2DS_2-VASc ≥ 2 and would be evaluated as high risk according to our results. Further studies generated to overcome gender and age bias would be beneficial.

Conclusions

Our current study showed that the CHA_2DS_2-VASc risk score has an effective discriminating power in determining the CIN development in patients presenting with STEMI and who underwent primary PCI. Moreover, CIN development is also associated with longer CCU stay and MACE (in-hospital decompensated heart failure, cardiogenic shock, cardiac arrest, and mortality). Prospectively designed studies involving larger patient numbers are needed to demonstrate the relationship between CHA_2DS_2-VASc score and prevalence of CIN.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards and were approved by Bağcılar Training and Research Hospital ethical committee (2022/09/10/017).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.D., S.Ö.; Design – E.D., S.Ö.; Supervision – İ.Ş., E.O.; Materials – E.D., S.Ö.; Data Collection and/or Processing – E.D., S.Ö., O.İ.; Analysis and/or Interpretation – E.D., S.Ö., O.İ.; Literature Review – E.D., S.Ö., O.İ., İ.Ş., E.O.; Writing – E.D., S.Ö.; Critical Review – İ.Ş., E.O.

Declaration of Interests: The authors declare that they have no competing interests.

Funding: This study received no funding.

References

1. Zuo T, Jiang L, Mao S, Liu X, Yin X, Guo L. Hyperuricemia and contrast-induced acute kidney injury: a systematic review and meta-analysis. *Int J Cardiol*. 2016;224:286-294. [CrossRef]
2. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. *Kidney Int Suppl*. 2006;100(100):S11-S15. [CrossRef]
3. Yang Y, George KC, Luo R, et al. Contrast-induced acute kidney injury and adverse clinical outcomes risk in acute coronary syndrome patients undergoing percutaneous coronary intervention: a meta-analysis. *BMC Nephrol*. 2018;19(1):374. [CrossRef]
4. Wu MY, Lo WC, Wu YC, et al. The incidence of contrast-induced nephropathy and the need of dialysis in patients receiving angiography: A systematic review and meta-analysis. *Front Med (Lausanne)*. 2022;9:862534. [CrossRef]
5. Ludwig U, Keller F. Prophylaxis of contrast-induced nephrotoxicity. *BioMed Res Int*. 2014;2014:308316. [CrossRef]
6. Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *J Am Coll Cardiol*. 2004;44(7):1393-1399. [CrossRef]
7. Gurm HS, Seth M, Kooiman J, Share D. A novel tool for reliable and accurate prediction of renal complications in patients undergoing percutaneous coronary intervention. *J Am Coll Cardiol*. 2013;61(22):2242-2248. [CrossRef]
8. Silver SA, Shah PM, Chertow GM, Harel S, Wald R, Harel Z. Risk prediction models for contrast induced nephropathy: systematic review. *BMJ*. 2015;351:h4395. [CrossRef]
9. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137(2):263-272. [CrossRef]
10. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of atrial fibrillation. *JAMA*. 2001;285(22):2864-2870. [CrossRef]
11. Hioki H, Miura T, Miyashita Y, et al. Risk stratification using the CHA2DS2-VASc score in patients with coronary heart disease undergoing percutaneous coronary intervention; sub-analysis of SHINANO registry. *Int J Cardiol Heart Vasc*. 2015;7:76-81. [CrossRef]
12. Ma X, Shao Q, Dong L, et al. Prognostic value of CHADS2 and CHA2DS2-VASc scores for post-discharge outcomes in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Med (Baltim)*. 2020;99(30):e21321. [CrossRef]
13. Chua SK, Lo HM, Chiu CZ, Shyu KG. Use of $CHADS_2$ and CHA_2DS_2-VASc scores to predict subsequent myocardial infarction, stroke, and death in patients with acute coronary syndrome: data from Taiwan acute coronary syndrome full spectrum registry. *PLoS One*. 2014;9(10):e111167. [CrossRef]
14. Chou RH, Huang PH, Hsu CY, et al. CHADS2 score predicts risk of contrast-induced nephropathy in stable coronary artery disease patients undergoing percutaneous coronary interventions. *J Formos Med Assoc*. 2016;115(7):501-509. [CrossRef]
15. Baydar O, Kilic A. CHA2DS2-VASC score predicts risk of contrast-induced nephropathy in non-ST elevation myocardial infarction patients undergoing percutaneous coronary interventions. *Kidney Dis (Basel)*. 2019;5(4):266-271. [CrossRef]
16. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39(2):119-177. [CrossRef]
17. McDonagh TA, Metra M, Adamo M, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599-3726. [CrossRef]

18. Caplan LR. Intracranial branch atheromatous disease: a neglected, understudied, and underused concept. *Neurology*. 1989;39(9):1246-1250. [CrossRef]
19. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke*. 2009;40(6):2276-2293. [CrossRef]
20. Brook RD, Rajagopalan S. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Soc Hypertens*. 2018. 2018;12(3):238. [CrossRef]
21. Petersmann A, Müller-Wieland D, Müller UA, et al. Definition, classification and diagnosis of diabetes mellitus. *Exp Clin Endocrinol Diabetes*. 2019;127(S 01):S1-S7. [CrossRef]
22. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37(3):267-315. [CrossRef]
23. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of peripheral arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Rev Esp Cardiol (Engl Ed)*. 2018;71(2):111. [CrossRef]
24. Iakovou I, Dangas G, Mehran R, et al. Impact of gender on the incidence and outcome of contrast-induced nephropathy after percutaneous coronary intervention. *J Invasive Cardiol*. 2003;15(1):18-22. [CrossRef]
25. Persson PB, Hansell P, Liss P. Pathophysiology of contrast medium-induced nephropathy. *Kidney Int*. 2005;68(1):14-22. [CrossRef]
26. Gupta RK, Kapoor A, Tewari S, Sinha N, Sharma RK. Captopril for prevention of contrast-induced nephropathy in diabetic patients: a randomised study. *Indian Heart J*. 1999;51(5):521-526.
27. Umruddin Z, Moe K, Superdock K. ACE inhibitor or angiotensin II receptor blocker use is a risk factor for contrast-induced nephropathy. *J Nephrol*. 2012;25(5):776-781. [CrossRef]
28. Kiski D, Stepper W, Brand E, Breithardt G, Reinecke H. Impact of renin-angiotensin-aldosterone blockade by angiotensin-converting enzyme inhibitors or AT-1 blockers on frequency of contrast medium-induced nephropathy: a post-hoc analysis from the Dialysis-versus-Diuresis (DVD) trial. *Nephrol Dial Transplant*. 2010;25(3):759-764. [CrossRef]
29. Chaudhary AK, Pathak V, Kunal S, Shukla S, Pathak P. CHA2DS2-VASc score as a novel predictor for contrast-induced nephropathy after percutaneous coronary intervention in acute coronary syndrome. *Indian Heart J*. 2019;71(4):303-308. [CrossRef]
30. Kurtul A, Yarlioglues M, Duran M. Predictive value of CHA2DS2-VASC score for contrast-induced nephropathy after percutaneous coronary intervention for acute coronary syndrome. *Am J Cardiol*. 2017;119(6):819-825. [CrossRef]
31. Kumar R, Batra MK, Khowaja S, et al. CHA2DS2-VASc, a simple clinical score expanding its boundaries to predict contrast-induced acute kidney injury after primary percutaneous coronary interventions. *Int J Nephrol Renovasc Dis*. 2021;14:495-504. [CrossRef]
32. Elmore JB, Mehanna E, Parikh SA, Zidar DA. Restenosis of the coronary arteries: past, present, future directions. *Interv Cardiol Clin*. 2016;5(3):281-293. [CrossRef]
33. Mirbolouk F, Gholipour M, Salari A, et al. CHA2DS2-VASc score predict no-reflow phenomenon in primary percutaneous coronary intervention in primary percutaneous coronary intervention. *J Cardiovasc Thorac Res*. 2018;10(1):46-52. [CrossRef]
34. Taşolar H, Çetin M, Ballı M, et al. CHA2DS2-VASc-HS score in non-ST elevation acute coronary syndrome patients: assessment of coronary artery disease severity and complexity and comparison to other scoring systems in the prediction of in-hospital major adverse cardiovascular events. *Anatol J Cardiol*. 2016;16(10):742-748. [CrossRef]