ORIGINAL ARTICLE

CHA2DS2-VASc SCORE FOR PREDICTING THE RISK OF CONTRAST-INDUCED NEPHROPATHY AFTER TRANSCATHETER AORTIC VALVE REPLACEMENT

Transkateter Aort Kapak Replasmanı Sonrası Kontrasta Bağlı Nefropati Riskini Öngörmek için CHA2DS2-VASc Skoru

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ABSTRACT

Objective: Contrast induced nephropathy (CIN) is a condition that may develop due to percutaneous cardiac interventional procedures and may adversely affect the prognosis of patients. The CHA2DS2-VASc score has been shown to be an independent predictor of acute kidney injury (AKI) and indicates an unfavorable prognosis in patients with acute coronary syndrome (ACS). Awareness of the risk of AKI before transaortic valve replacement (TAVR) may help to reduce the rate of AKI. Therefore, i aimed to evaluate the utility of CHA2DS2 VASC score in patients undergoing TAVR.

Material and Methods: Retrospective date of 60 patients who underwent TAVR was collected between February 2022 and October 2023. The decision for the TAVR procedure was made according to international guidelines and the consensus of the local cardiac team for patients with advanced aortic stenosis and high surgical risk or contraindication to surgical valve replacement.

Results: There were no significant differences between the two groups in terms of age, gender, prevalence of diabetes mellitus, dyslipidemia, previous medications, baseline systolic and diastolic blood pressure, and body mass index. High CHA2DS2-VASc score (OR: 2.138, 95% confidence interval (CI): 1.356-4.125; p = 0.027) levels were independently associated with the presence of CIN. Furthermore, contrast volume (OR: 1.192, 95%CI: 1.022-1.390; p = 0.031) independently predicted the presence of CIN.

Conclusion: This study demonstrated that the CHA2DS2-VASc score can be used as a predictor of CIN in patients undergoing TAVR. Early prediction of CIN risk is critical to provide intensive preventive measures to patients at high risk. The CHA2DS2-VASc score is a simple and familiar scoring tool that can be applied in patients undergoing TAVR and can predict the development of CIN and can be easily applied in daily practice.

Keywords: *CHA2DS2-VASc Score; TAVR; Constrast Induced Nephropathy*

ÖZET

Amaç: Kontrast ilişkili nefropatisi (KİN), perkütan kardiyak girişimsel işlemlere bağlı olarak gelişebilen ve hastaların prognozunu olumsuz etkileyebilen bir durumdur. CHA2DS2-VASc skorunun akut böbrek hasarının (ABH) bağımsız bir belirleyicisi olduğu ve akut koroner sendromlu (AKS) hastalarda olumsuz bir prognoza işaret ettiği gösterilmiştir. Transkatater aort kapak implantasyonu (TAVİ) öncesinde ABH riskinin bilinmesi, ABH oranının azaltılmasına yardımcı olabilir. Bu nedenle, TAVİ uygulanan hastalarda CHA2DS2 VASC skorunun değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Şubat 2022 ve Ekim 2023 tarihleri arasında kurumumuzda TAVİ uygulanan 60 hastaya ait veriler retrospektif olarak toplandı. TAVİ prosedürü kararı, ileri aort darlığı ve yüksek cerrahi riski veya cerrahi kapak replasmanına kontrendikasyonu olan hastalar için uluslararası kılavuzlara ve yerel kardiyak ekibin fikir birliğine göre verildi.

Bulgular: İki grup arasında yaş, cinsiyet, diabetes mellitus sıklığı, dislipidemi, daha önce kullanılan ilaçlar, başlangıçtaki sistolik ve diyastolik kan basıncı ve vücut kitle indeksi açısından anlamlı bir fark yoktu. Yüksek CHA2DS2-VASc skoru (OR: 2,138, %95 güven aralığı (CI): 1,356-4,125; p = 0.027) düzeylerinin KİN varlığı ile bağımsız olarak ilişkili olduğu bulunmuştur. Ayrıca, kontrast hacmi (OR: 1,192, %95CI: 1,022-1,390; p=0,031) KİN varlığını bağımsız olarak tahmin etmiştir.

Sonuç: Bu çalışma, CHA2DS2-VASc skorunun TAVİ uygulanan hastalarda KİN öngördürücüsü olarak kullanılabileceğini göstermiştir. KİN riskinin erken öngörülmesi, yüksek risk altındaki hastalara yoğun önleyici tedbirler sağlamak için kritik önem taşımaktadır. CHA2DS2-VASc skoru, TAVİ uygulanan hastalarda uygulanabilen ve KİN gelişimini öngörebilen basit ve tanıdık bir skorlama aracıdır ve günlük pratikte kolayca uygulanabilir.

Anahtar Kelimeler: *CHA2DS2-VASc Skoru; TAVİ; Konstrast İlişkili Nefropati*

INTRODUCTION

Acute kidney injury (AKI) is defined as a sudden decrease in kidney function and encompasses both structural damage and dysfunction (1). Due to the toxic effects of contrast agents, it can cause serious damage to renal tubular cells. Contrast-induced nephropathy (CIN) is among the most common causes of acute renal failure. It is one of the most important adverse events especially after cardiac procedures (2). Currently, the most common definition of CIN is an increase in serum creatinine of 25% or more from baseline or an absolute increase of 0.5 mg/dl or more approximately 48-72 hours after contrast exposure (3). AKI has been associated with adverse outcomes after procedures using contrast, such as percutaneous coronary interventions (PCI) (4, 5).

Transcatheter aortic valve replacement (TAVR) is rapidly expanding as a less invasive alternative for the treatment of aortic stenosis (AS). Indications for TAVR are increasing to cover AS patients across the surgical risk spectrum, including low-risk patients (6). The incidence of CIN is higher in patients undergoing TAVR because these patients are usually elderly and often have various comorbidities such as heart failure (HF), hypertension (HTN), diabetes mellitus (DM) and anemia (7). These patients often have abnormal baseline renal function, and therefore hemodynamic changes during the procedure and the use of contrast media also put them at high risk for AKI after TAVR (8). Studies have also shown that AKI due to CIN is one of the most common complications in patients undergoing TAVR procedure. It has been shown to be associated with adverse outcomes such as increased morbidity and mortality (9, 10).

Various scoring systems are used to predict the risk of CIN after cardiac procedures (11, 12). The CHA2DS2-VASc (chronic heart failure, hypertension, age 75 years, diabetes mellitus, previous stroke, vascular disease, age 65 to 74 years, sex) score is used for embolic risk stratification in patients with atrial fibrillation (AF), It has also shown that it can predict adverse clinical outcomes in stable coronary artery disease (CAD) and acute coronary syndrome (ACS), independent of the presence of AF (13).

Awareness of the risk of AKI before TAVR may reduce the rate of CIN. In this study, it is aimed to investigate the predictive value of CHA2DS2-VASc score for CIN in patients undergoing TAVR.

MATERIAL AND METHOD

Retrospective data of 60 patients who underwent TAVR between February 2022 and October 2023 was collected. The decision for the TAVR procedure was made according to international guidelines and the consensus of the local cardiac team for patients w ith advanced a ortic stenosis and high surgical risk or contraindication to surgical valve replacement.

All data was collected retrospectively from hospital medical records. Laboratory data including DM, HTN, CAD, HT, cerebrovascular disease, left ventricular ejection fraction (LVEF), age at the time of procedure, serum blood urea nitrogen (BUN), serum creatinine (Cr), serum albumin (Alb), serum sodium (Na), serum potassium (K), hemoglobin (Hb) levels before and after the procedure were recorded. Estimated glomerular filtration rate (eGFR) was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (14).

All patients underwent detailed history taking, complete clinical examination, 12-lead electrocardiogram, echocardiography and TAVR. CHA2DS2-VASc score (age, gender, DM, HTN, HF at presentation, previous cerebral ischemic event, vascular event) was calculated in all patients enrolled in this study. Blood samples were obtained by traumatic puncture from the antecubital vein at admission before TAVR and sent to the laboratory for analysis: Serum cardiac biomarkers, renal function, eGFR were calculated for all patients before TAVR.

CIN was defined as an increase in creatinine concentration of 0.5 mg/dL or 25% above baseline within 48 hours after contrast administration. Patients were divided into two groups according to the development of CIN (15).

The study protocol was approved by Bursa City Hospital and was conducted according to the principles of the Declaration of Helsinki. Written informed consent could not be obtained from the patients due to the retrospective design of the study (Institutional Ethics Committee (decision no: 2023-17/3, date: 11.10.2023).

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Statistical Analysis

Statistical analyses were conducted via SPSS software version 20.0 for Windows (SPSS Inc., Chicago, IL, USA), in addition to analyzing the distribution patterns of the variables via the Kolmogorov–Smirnov test. While categorical determinants were given in percentage and number, permanent agents were demonstrated as mean ± standard deviation or as median with interquartile range, depending on the distribution pattern. The Mann–Whitney U-test was preferred to calculate the differencesamong nonparametric permanent variables, besidescomparing the categorical variables via Pearson'schi-square test, displaying them in percentages. Thevariables determined through a univariable analysiswere evaluated in detail using the logistic regressionanalysis to perform the multivariable regressionanalysis and to detect the independent markers of the CIN. Receiver operating characteristic (ROC) curve analysis was used to detect the optimal cut-off value of the CHA2DS2-VASc score in defining CIN and investigated specificity and sensitivity by using the Youden index.

A two-tailed p-value of < 0.05 was accepted to be statistically significant.

RESULTS

This study included 60 TAVR patients (female: 33; mean age: 81.4 ± 5.7 years) in total, as the target population was separated into two different groups according to developing CIN. Contrastinduced nephropathy was observed in 22 (36.6%) patients. A comparison of the demographic and clinical outcomes related to patients with and without CIN is presented in Table 1. There was no significant difference in terms of age, sex, frequencies of diabetes mellitus, dyslipidemia, previous medications, baseline systolic and diastolic blood pressure, and body mass index between the two groups. Patients in the CIN (+) group had significantly higher numbers of hypertension, history of CAD and creatinine as well as a lower LVEF and eGFR as compared with the CIN (-) group. In addition, patients in the CIN (+) group were exposed to a significantly higher contrast volume. Also, the CHA2DS2-VASc score [3.89 ± 0.72 vs. 5.31 ± 0.71; p < 0.001] was considerably high for the CIN (+) group in comparison to the CIN (-) group.

Any possible factors that were detected to be determinants in univariable analyses were evaluated by analyzing multivariable logistic regression to detect independent markers of the CIN. Higher levels of CHA2DS2-VASc score (OR: 2.138, 95% confidence interval (CI): 1.356-4.125; p = 0.027) were found to be independently associated with the presence of the CIN. Moreover, contrast volume (OR: 1.192, 95%CI: 1.022-1.390; p = 0.031) independently estimated the presence of the CIN (Table 2).

In receiver-operating characteristic (ROC) curve analysis, CHA2DS2-VASc score over a cut-off level of 4.5 predicted CIN with a sensitivity o f 7 1.4% a nd a specificity of 72.6% (AUC: 0.813; 95%CI: 0.694-0.932; p < 0.001) (Figure).

DISCUSSION

This study demonstrated that the CHA2DS2-VASc score can be used as a predictor of CIN in patients undergoing TAVR. It is also, to our knowledge, the first study to examine the efficacy of the pre-procedural CHA2DS2-VASc score for CIN after TAVR.

CIN is one of the most important complications of percutaneous cardiovascular procedures and has a significant i mpact o n long-term prognosis (16). The incidence of CIN as a complication o f diagnostic and interventional procedures using contrast media varies depending on variables such as the type of procedure performed, the amount and type of contrast media and different patient populations in terms of the number and type of risk factors (17). The pathogenesis of AKI after TAVR is multifactorial. It is thought to develop due to hemodynamic instability and the use of nephrotoxic contrast media. Studies show that AKI after TAVR is a frequent complication in patients. These patients have been found to have a worse prognosis (18). There are many factors that may facilitate the development of CIN. The incidence of CIN is thought to be as high as 30% in high-risk patients; diabetic patients, patients with a history of congestive h eart failure, patients with chronic renal failure and elderly patients (19). In different studies, the rate of CIN after TAVR may vary between 8.3-58% (20). In different studies, these rates were found to be 25-30% (21). In our study, we found that this rate was as high as 36%. This high rate was due to the fact that the patients had

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Table 1. Baseline demographic and clinical characteristics of patients with and without CIN

Variables	Total study population (n=60)		p value
	CIN (-) group (n= 38)	**CIN (+) group (n=22)**	
Baseline characteristics			
Age, years	80.7 ± 6.0	82.6 ± 5.1	0.275
Female gender, n (%)	20 (52.6)	13 (59.1)	0.628
Diabetes Mellitus, n (%)	10 (26.3)	11 (50)	0.064
Hypertension, n (%)	27 (71.1)	21 (95.5)	**0.041**
Dyslipidemia, n (%)	10 (26.3)	8 (36.4)	0.413
Previous CAD, n (%)	18 (47.4)	17 (77.3)	**0.024**
Left ventricle EF, %	55 (43-60)	42 (30-55)	**0.016**
SBP at admission, mmHg	129.2 ± 14.7	127.8 ± 12.3	0.812
DBP at admission, mmHg	81.3 ± 10.0	78.2 ± 11.0	0.519
Body mass index (kg/m2)	26.2 ± 3.5	26.2 ± 3.3	0.707
Contrast volume (ml)	90 (80-110)	110 (100-120)	**0.001**
Previous medications			
ACEI/ARBs, n (%)	21 (55.3)	13 (59.1)	0.773
MRA, n (%)	6 (15.8)	2 (9.1)	0.698
Furosemide, n (%)	13 (34.2)	8 (36.4)	0.866
Thiazide, n (%)	3 (7.9)	2 (9.1)	0.611
Laboratory parameters			
Glucose, mg/dL	103.5 (95-115)	110.5 (94.5-155.7)	0.290
BUN, mg/dL	26 (18.7-30.2)	28 (22.5-39.5)	0.107
Creatinine, mg/dL	1.05 (0.87-1.30)	1.33 (1.23-1.70)	**0.001**
eGFR, mL/min/1.73m^2	56.1 ± 14.6	40.3 ± 13.9	**<0.001**
Sodium, mmol/L	135.7 ± 3.5	133.9 ± 3.3	0.052
Potassium, mmol/L	4.33 ± 0.51	4.25 ± 0.57	0.549
High-sensitivity CRP, mg/L	0.5 (0.2-1.57)	0.8 (0.5-2.15)	0.053
Albumin, g/dL	3.67 ± 0.42	3.63 ± 0.46	0.719
WBC count, x10^3/µL	7.57 ± 2.01	8.32 ± 2.52	0.238
Neutrophil count, x10^3/µL	4.8 ± 1.8	5.5 ± 2.3	0.213
Lymphocyte count, x10^3/µL	1.57 (1.2-2.0)	1.62 (1.1-2.0)	0.951
Hemoglobin, g/dL	10.3 ± 1.9	10.5 ± 1.6	0.634
Platelet count, x10^3/µL	226 (185-305)	236 (199-304)	0.982
CHA2DS2-VASc score	3.89 ± 0.72	5.31 ± 0.71	**<0.001**
In-hospital complications			
Vascular, n (%)	3 (7.9)	5 (22.7)	0.129
Permanent pacemaker implantation, n (%)	6 (15.8)	5 (22.7)	0.511

All values are expressed as mean ± standard deviation, median (25th and 75th interquartile range), and number (%). Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BUN, blood urea nitrogen; CAD, coronary artery disease; CIN, contrast-induced nephropathy; CRP, C-reactive protein; DBP, diastolic blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure; WBC, white blood cell. p values in bold signify statistically significant differences.

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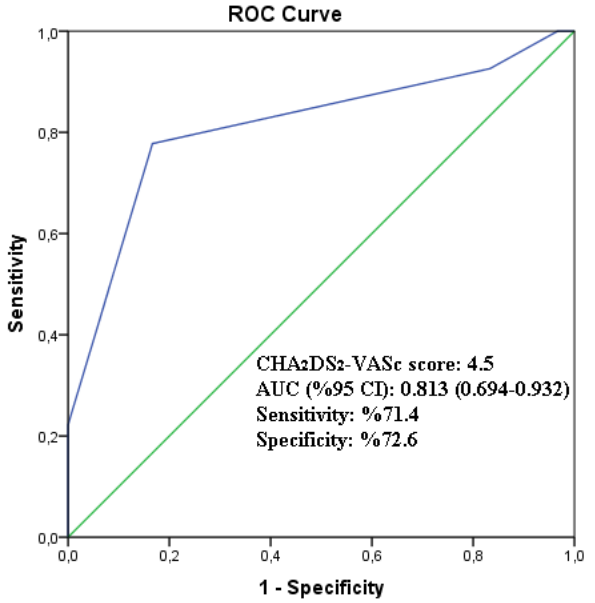
Table 2. Univariable and multivariable logistic regression analysis for assessment of predictors of contrast-induced nephropathy

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	**p value**	**OR (95% CI)**	**p value**
Contrast volume	1.060 (1.021-1.101)	0.002	1.192 (1.022-1.390)	0.031
CHA2DS2-VASc	4.213 (2.568-7.152)	<0.001	2.138 (1.356-4.125)	0.027
eGFR	0.923 (0.879-0.968)	0.001	0.823 (0.669-1.011)	0.064
Hypertension	2.078 (1.096-4.032)	0.048	1.476 (0.685-3.182)	0.359
LVEF	0.949 (0.906-0.994)	0.026	0.906 (0.768-1.068)	0.237
Previous CAD	3.778 (1.157-12.333)	0.028	0.627 (0.026-15.107)	0.774

Abbreviations: CAD, coronary artery disease; CI, confidence interval; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; OR, odds ratio.

Figure 1. ROC curve analysis, CHA2DS2-VASc score



high surgical risk, had multiple comorbidities, were frail and elderly. However, some variables such as age and DM were not different between patients with and without CIN in our study. Patients with CIN had significantly higher rates of HTN and a history of CAD. HTN has been found to be an independent risk factor for the development of contrast nephropathy in some studies (22, 23).

In this study, it was also found that individuals who developed CIN had higher creatinine values and lower LVEF and eGFR values. In a study by SK Gualano et al. significantly higher creatinine values, lower eGFR and LVEF were found in patients who developed AKI compared to the group who did not develop AKI (24). Similarly, in another study, high creatinine and low eGFR values were found to be risk factors for the development of CIN (25, 26).

The volume of contrast medium used also affects CIN formation. Administration of a hi gher vo lume of contrast medium is associated with increased CIN and mortality (26, 27). Contrast media volume has been associated with an increased risk of AKI in previous studies. In this study, the volume of contrast medium used independently predicted the presence of CIN (24).

The aim of this study was to evaluate the CHA2DS2-VASc score as a predictor for CIN in patients undergoing TAVR. This study showed that CHA2DS2-VASc score had a statistically significant correlation with the risk of developing AKI. Ahmed F. et al. showed that the incidence of CIN after PCI increased with increasing CHA2DS2-VASc score in patients with acute MI treated with PCI . Similarly, Kurtul A. et al. showed that the CHA2DS2-VASc score is an independent predictor of CIN, indicating an unfavorable prognosis in patients with ACS (28). Chou et al. showed that CHADS2 score predicted the risk of CIN in stable CAD patients undergoing elective PCI (29).

CONCLUSION

Early prediction of CIN risk is critical to provide intensive preventive measures for patients at high risk. The CHA2DS2-VASc score is a simple and familiar scoring tool that is applicable in patients undergoing TAVR and can predict the development of CIN and can be easily applied in daily practice.

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