Heart Surgery Forum 2024; 27(2): E126–E133
doi: 10.59958/hsf.7065
https://journal.hsforum.com/

Article

CHA2DS2-VASc Score, Fibrinogen, and Neutrophil to Lymphocyte Ratio as Predictors of In-Stent Restenosis in Patients with Severe Kidney Disease

Yanmei Song[1,†], Bingxin Tang[1,†], Jingjin Che[1], Kangyin Chen[1], Yanmin Xu[1], Qingmiao Shao[1], Zhiqiang Zhao[1], Guangping Li[1], Tong Liu[1], Xiaowei Zhang[1,*]

[1]Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular Disease, Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, 300211 Tianjin, China
*Correspondence: doczxw@126.com (Xiaowei Zhang)
[†]These authors contributed equally.

Submitted: 30 November 2023 Revised: 10 January 2024 Accepted: 19 January 2024 Published: 19 February 2024

Abstract

Objective: This study examined the relationship between CHA2DS2-VASc score, fibrinogen (FIB), and neutrophil-to-lymphocyte ratio (NLR) with in-stent restenosis (ISR) in patients with severe kidney disease (SKD). **Methods**: Between January 2017 and January 2022, patients with SKD who underwent coronary stent implantation at the Second Hospital of Tianjin Medical University were retrospectively analyzed. According to whether ISR occurred within 2 years of postoperative follow-up, 164 patients were categorized into the ISR group (n = 62) and the non-ISR group (n = 102). According to the Modification of Diet in Renal Disease (MDRD) formula, SKD is defined as an estimated glomerular filtration rate (eGFR) less than 30 mL/(min·1.73 m^2). Angiographic ISR was defined as a stented coronary artery segment with more than 50% constriction during the follow-up angiography. Relevant clinical data and laboratory parameters were obtained from the hospital's medical records. **Results**: In total, 164 patients were included (mean age: 67.1 [10.2] years, 65.2% men), grouped into 62 patients with ISR and 102 patients without. A significant difference was found in the age, previous strokes, congestive heart failure (CHF), NLR, platelet-to-lymphocyte ratio (PLR), fibrinogen, CHA2DS2-VASc score, and risk classification of CHA2DS2-VASc score of patients in the ISR group as compared to those in the non-ISR group. In a multivariable logistic regression analysis, the CHA2DS2-VASc score, fibrinogen, and NLR were identified as independent predictors of ISR. The analysis of the receiver operating characteristic (ROC) curve revealed that the area under the curve (AUC) value was 0.714 (95% confidence interval (CI): 0.634–0.793) for the CHA2DS2-VASc score and 0.652 (95% CI: 0.565–0.739) for FIB, 0.707 (95% CI: 0.627–0.788) for NLR, and 0.797 (95% CI: 0.725–0.868) for the combination of CHA2DS2-VASc score, FIB and NLR. **Conclusions**: The combination of CHA2DS2-VASc score, FIB, and NLR can more accurately predict the occurrence of ISR in SKD patients.

Keywords

CHA2DS2-VASc score; fibrinogen; NLR; ISR; severe kidney disease

Introduction

Interventional cardiologists still encounter challenges associated with in-stent restenosis (ISR), despite advancements in materials, techniques, and medications. Clinical, procedural, and stent-related factors influence the incidence of ISR, which ranges from 20.0% to 50.3% [1]. An estimated glomerular filtration rate (eGFR) less than 30 mL/(min·1.73 m^2), with or without preexisting dialysis, is considered severe kidney disease (SKD) [2]. A systemic, chronic proinflammatory state is caused by chronic renal disease (CKD), contributing to calcification of cardiac valves, myocardial fibrosis, atherosclerotic lesions, as well as vascular calcification and vascular senescence. A study indicates that patients with chronic kidney disease (CKD), particularly those with end-stage kidney disease, are more susceptible to ISR [3]. However, previous research on coronary restenosis in stents has not included patients with SKD.

The CHA2DS2-VASc score is utilized to assess the risk of embolism in patients with atrial fibrillation (AF) based on congestive heart failure (CHF), hypertension, diabetes mellitus, stroke history, vascular disease, and female gender [4]. Recently, several studies have proved that the CHA2DS2-VASc score is predictive of ISR in various patient populations [2,5–7]. Underexpansion or fracture are the primary mechanical factors leading to stent failure, while local inflammation, aggressive neointimal proliferation, late acquired malposition, or neoatherosclerosis are the main biological factors [8]. It is well established that inflammation and neointima formation are the primary mechanisms of ISR [9]. In recent years, fibrinogen (FIB) and neutrophil-to-lymphocyte ratio (NLR) have been identified as new inflammatory markers. This study aims to analyze

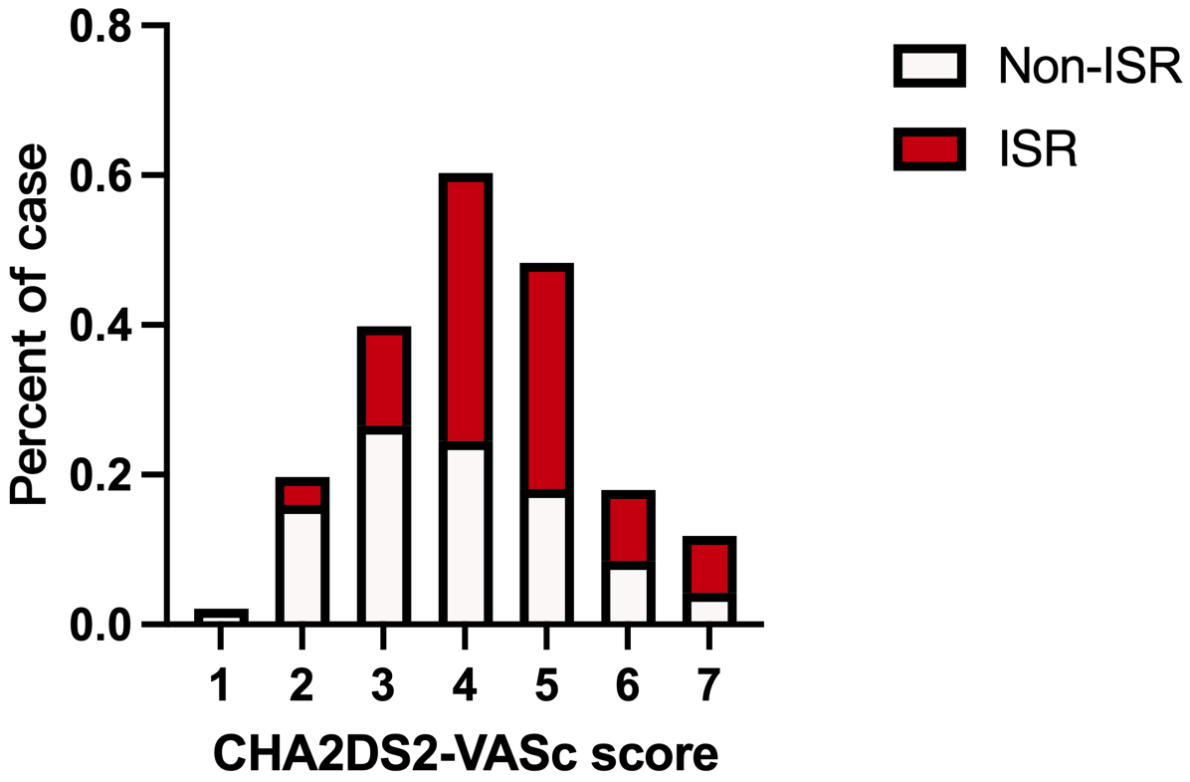

Fig. 1. Comparison of the incidence of in-stent restenosis based on the CHA2DS2-VASc scores. ISR, in-stent restenosis.

the prognostic significance of the combined CHA2DS2-VASc score with FIB and NLR for the occurrence of ISR in individuals with SKD prior to undergoing percutaneous coronary intervention (PCI).

Materials and Methods

Study Population

In this retrospective analysis, individuals diagnosed with SKD who received effective stent placement from January 2017 to January 2022 were examined. One hundred and sixty-four patients were divided into two groups: the ISR group (n = 62) and the non-ISR group (n = 102), based on whether ISR occurred within 2 years of postoperative follow-up. Coronary angiograms were independently interpreted by two cardiologists who were blinded to the study. Angiographic ISR was defined as >50% stenosis in the coronary artery segment where the stent was placed during follow-up angiography. According to the Modification of Diet in Renal Disease (MDRD) formula, SKD is defined as an eGFR less than 30 mL/(min·1.73 m^2), with or without dialysis. The following information, including gender, age, smoking habits, hypercholesterolemia, hypertension, diabetes mellitus, history of stroke, and laboratory results, was extracted from medical records.

Patients who underwent successful stent implantation between 2017 and 2022 and had an eGFR of <30 mL/(min·1.73 m^2) were enrolled. If they refused or abandoned treatment, did not report for the control visit, or suffered from autoimmune disease, blood system disease, serious lung, liver, tumor, or other underlying diseases, or cachexia, they were not eligible for enrollment.

Clinical Characteristics

Based on the CHA2DS2-VASc scoring system, individuals with CHF, women, age 65–74 years, hypertension, diabetes mellitus, and vascular disease were assigned 1 while those aged ≥75 years and with a history of stroke or transient ischemic attack were assigned 2 points [3]. Patients with left ventricular ejection fraction (LVEF) below 40% and presenting clinical symptoms or chest X-ray findings indicative of congestion were categorized as having CHF. Patients with a systolic blood pressure greater than 140 mm Hg and/or a diastolic blood pressure greater than 90 mm Hg in two separate measurements or while on continuous antihypertensive treatment were defined as hypertensive. Patients were determined to have diabetes mellitus if they adhered to a diabetic diet, were using antidiabetic medication, or had a fasting venous glucose level exceeding 126 mg/dL on two separate occasions. The diagnosis of hypercholesterolemia relied on the identification of a total cholesterol level of ≥200 mg/dL in the fasting state. Based

Table 1. Baseline characteristics.

Variables	Non-ISR group (n = 102)	ISR group (n = 62)	*p*
Men, n (%)	72 (70.6)	35 (56.5)	0.090
Age/years	65.56 ± 10.46	69.56 ± 9.2	0.014
Hypertension, n (%)	87 (85.3)	59 (95.2)	0.070
Diabetes mellitus, n (%)	56 (54.9)	42 (67.4)	0.139
Hypercholesterolemia, n (%)	89 (87.3)	54 (87.1)	0.291
Prior stroke, n (%)	16 (15.7)	18 (29.0)	0.046
Prior AF, n (%)	7 (6.9)	4 (6.5)	1.000
Dialysis, n (%)	29 (28.4)	24 (38.7)	0.228
Smoking, n (%)	34 (33.3)	14 (22.6)	0.160
Drinking, n (%)	15 (14.7)	5 (8.1)	0.324
CHF, n (%)	12 (11.8)	17 (27.4)	0.019
LVEF (%)	53.05 ± 10.45	48.25 ± 12.54	0.010
Medications, (%)			
Aspirin	88 (86.3)	53 (85.5)	1.000
Indobufen	11 (10.8)	9 (14.5)	0.473
Clopidogrel	89 (87.3)	52 (83.9)	0.644
Ticagrelor	12 (11.8)	10 (16.1)	0.482
β-blockers	96 (94.1)	57 (91.9)	0.749
Statins	92 (90.2)	53 (85.5)	0.451
Calcium channel blocks	83 (81.4)	54 (87.1)	0.391
Site of lesion			
Left anterior descending, n (%)	41 (40.2)	26 (41.9)	0.871
Right coronary artery, n (%)	40 (39.2)	24 (38.7)	0.869
Left circumflex artery, n (%)	24 (23.5)	19 (30.6)	0.363

Abbreviations: LVEF, left ventricular ejection fraction; CHF, congestive heart failure; ISR, in-stent restenosis; AF, atrial fibrillation.

on the echocardiographic and demographic profiles of individual patients, CHA2DS2-VASc scores were calculated before PCI. All patients had a minimum score of 1 following PCI. The eGFR was calculated using the MDRD [10].

Statistical Analysis

SPSS (version 26.0 for Mac, SPSS, Inc., Chicago, IL, USA) was used to analyze the data. Continuous variables were represented as mean (standard deviation) or median (interquartile range), and categorical variables were displayed as percentages and counts. The Student's *t*-test or the Mann-Whitney U test was used to compare continuous variables, while the χ^2 test or Fisher's exact test was used to compare categorical variables. Simple logistic regression analysis was conducted to examine the relationship between the variables and ISR, while multivariate logistic regression analysis was performed to evaluate variables with a significance level of $p < 0.10$. The study employed the adjusted odds ratio (OR) and a 95% confidence interval (CI) to present the findings of the regression analysis. The predictive capacity of the CHA2DS2-VASc score, FIB, and NLR for ISR was assessed through ROC curve analyses. Statistical significance was defined as a two-sided *p* value of less than 0.05.

Results

Based on the presence of ISR, a total of 164 individuals (mean age: 67.1 [10.2] years, 65.2% men) were categorized into two groups, with 62 patients exhibiting ISR. The baseline characteristics of the study population are presented in Table 1. In comparison to the non-ISR group, patients in the ISR group were of advanced age, had a higher incidence of previous stroke and CHF, and a lower LVEF. There were no significant differences in the prevalence of hypertension, diabetes, and hyperlipidemia between the two groups. However, the prevalence of hyperlipidemia was observed to be higher in the ISR group as opposed to the non-ISR group.

The laboratory parameters are listed in Table 2. In comparison to the non-ISR group, the NLR, platelet-to-lymphocyte ratio (PLR), and FIB exhibited significantly elevated levels in the ISR group. The evaluation results of the CHA2DS2-VASc score are presented in Table 3. The mean score (5.45 [1.28] *vs.* 4.35 [1.37], $p < 0.001$) and risk classification were notably higher in the ISR group. The incidence of ISR increased as the CHA2DS2-VASc score values increased (Fig. 1).

Table 2. Laboratory findings.

Laboratory findings	Non-ISR group (n = 102)	ISR group (n = 62)	*p*
NLR	4.06 ± 3.16	6.58 ± 5.10	<0.001
PLR	178.65 ± 111.59	214.62 ± 99.22	0.039
MLR	0.38 ± 0.25	0.46 ± 0.27	0.065
Hemoglobin, g/L	117.32 ± 23.07	114.71 ± 21.16	0.469
FIB	3.53 ± 1.26	4.11 ± 1.34	0.007
Fasting glucose, mmol/L	7.97 ± 3.39	9.10 ± 3.92	0.055
Hemoglobin A1c (%)	6.93 ± 1.30	7.03 ± 1.28	0.742
Total cholesterol, mmol/L	4.76 ± 1.61	4.65 ± 1.64	0.662
Triglyceride, mmol/L	1.71 ± 0.92	1.96 ± 1.01	0.102
HDL, mmol/L	1.09 ± 0.60	0.93 ± 0.26	0.050
LDL, mmol/L	2.73 ± 1.02	2.97 ± 1.11	0.167
Albumin, g/L	52.50 ± 15.15	51.23 ± 14.67	0.601
Globulin, g/L	30.92 ± 8.92	30.81 ± 6.05	0.938

Abbreviations: NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; FIB, fibrinogen; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 3. CHA2DS2-VASc score and evaluation results.

Variables	Non-ISR group (n = 102)	ISR group (n = 62)	*p*
CHA2DS2-VASc score	3.85 ± 1.28	4.87 ± 1.40	<0.001
Low risk (0–1 score)	1 (1%)	0 (0%)	0.014
Medium risk (2–3 score)	37 (36.3%)	10 (16.1%)	
High risk (≥4 score)	64 (62.7%)	52 (83.9%)	

Abbreviations: CHA2DS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke, vascular disease, age 65 to 74 years, female gender.

The significant predictors of ISR were identified using logistic regression (Table 4). Univariate analysis showed that age, prior stroke, CHF, LVEF, FIB, NLR, CHA2DS2-VASc score, and CHA2DS2-VASc score risk were significant predictors. Multivariable regression analysis revealed that FIB, NLR, and CHA2DS2-VASc score were independent predictors. ROC curve analysis showed that the AUC value was 0.714 (95% CI: 0.634–0.793) for CHA2DS2-VASc score, 0.652 (95% CI: 0.565–0.739) for FIB, 0.707 (95% CI: 0.627–0.788) for NLR and 0.797 (95% CI: 0.725–0.868) for CHA2DS2-VASc score combined with FIB and NLR (Table 5 and Fig. 2).

Discussion

Our study highlights that the CHA2DS2-VASc score, FIB and NLR are independent predictors of increased risk for ISR in SKD patients. Compared to other available risk stratification tools for ISR, the combination of these factors provides a reliable and easily applicable predictor in clinical practice for ISR in SKD patients.

The most frequently utilized method for PCI is the insertion of a stent, which is associated with potential complications including stent thrombosis and restenosis [5]. As PCI procedures become more complex and involve multiple vessels, ISR is becoming more prevalent. It is associated with various lesions, procedural elements, and clinical aspects, as well as, significantly, patient-specific factors. The demographics include age, female gender, hypertension, diabetes, CHF, renal failure, and stroke or transient ischemic attack (TIA). The mechanisms of ISR are complex. Inflammation and neointimal formation are crucial in revascularization [11]. Hypertension, diabetes mellitus, and hyperlipidemia are linked to heightened inflammation [12].

Research shows that patients with CKD have an increased risk of cardiovascular events, with 50% of CKD stage 4 to 5 patients experiencing cardiovascular disease (CVD) [13]. CVD risk factors associated with CKD encompass both conventional elements such as hypertension and diabetes, and non-conventional factors such as mineral and bone abnormalities, inflammation, oxidative stress, and anemia. Additionally, dialysis-related factors such as the type and frequency of dialysis and dialysate composition are linked to cardiovascular abnormalities in CKD. Conventional risk factors associated with coronary artery disease (CAD) are correlated with atherosclerosis in the early stages of CKD, whereas non-conventional risk factors become increasingly significant as glomerular filtration rate (GFR) declines, ultimately contributing to the formation of fibrocalcific lesions.

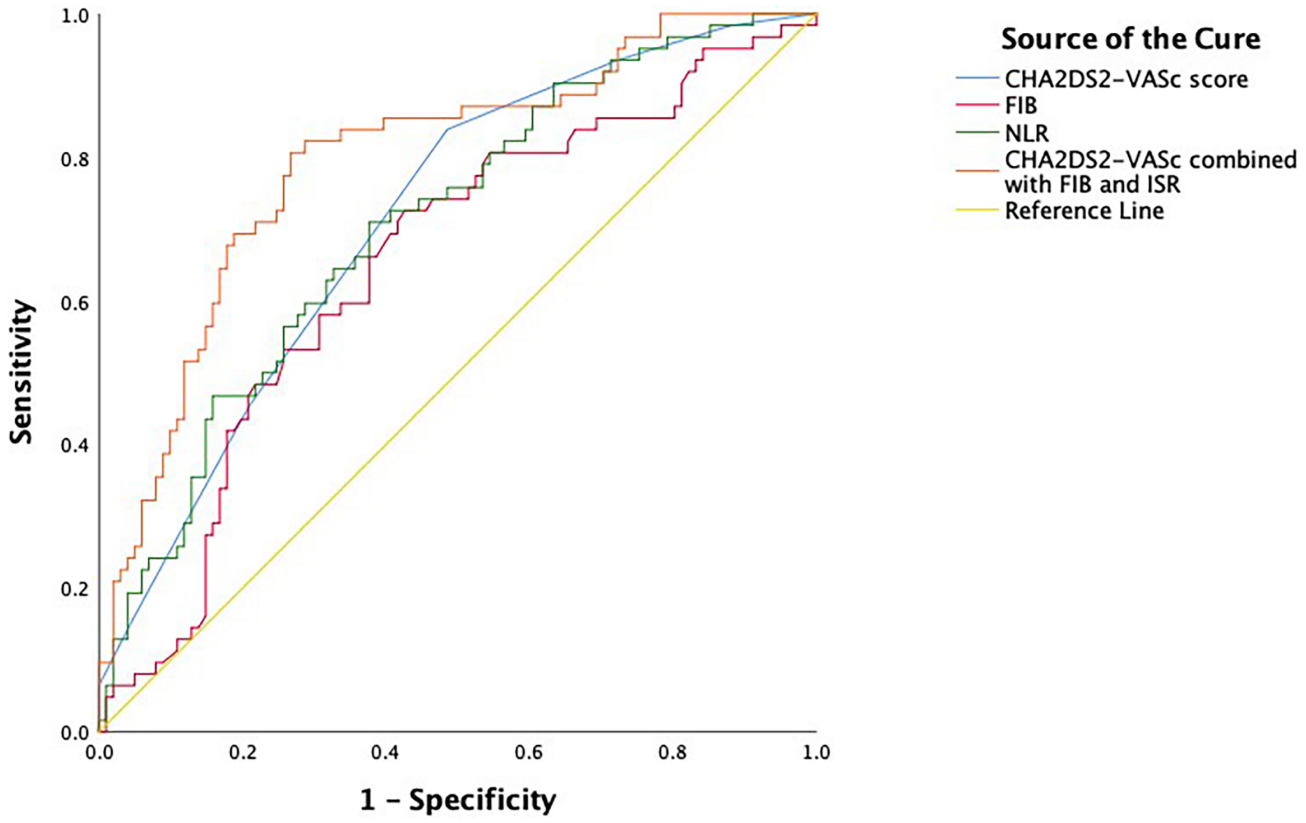

Fig. 2. ROC curves for in-stent restenosis of CHA2DS2-VASc score, FIB and NLR. AUC, indicates area under the curve; CI, confidence interval; ROC, receiver operating characteristic.

Calcification of the coronary arteries is common in CKD patients, with faster progression as kidney function GFR declines [14]. The progression of coronary calcification accelerates as CKD worsens [15]. Calcification of central arterial vessels increases cardiac afterload [16], leading to continuous left ventricular overload subsequently causes maladaptive changes and cardiomyocyte death. This, in turn, results in eccentric hypertrophy, followed by left ventricular dilatation, systolic dysfunction, and reduced ejection fraction [17]. Consistent with this, the study found a significant reduction in LVEF and CHF prevalence in the ISR group.

Hypertriglyceridemia and low levels of high-density lipoprotein (HDL) cholesterol, while most have normal levels of LDL cholesterol. The development of CAD in CKD patients is linked to changes in lipoproteins (such as LDL carbamylation and HDL dysfunction). Risk factors for vascular calcification include aging, inflammation, mechanical stressors (such as shear stress and elastin fatigue), and the possible buildup of microbiome-dependent metabolites (e.g., trimethylamine N-oxide) [16]. The precise mechanism of uremic calcific small arteriopathy is not yet understood. It was previously believed that elevated levels of calcium and phosphorus caused calcification, resulting in uremic calcific small arteriopathy [17]. However, it has been discovered that calcification is a result of active cellular processes triggered by increased calcium and phosphorus concentrations, rather than just passive mineralization [18]. Furthermore, electrolyte imbalances are common in patients with CKD [19] and are associated with a poor prognosis [20]. Serum magnesium levels are often decreased in CKD patients, and magnesium has been found to interfere with the formation of hydroxyapatite crystals, potentially preventing vascular calcification in advanced CKD [21]. In this study, patients in the ISR group, as compared to the non-ISR group, were older and had a higher incidence of prior stroke.

Inflammation plays a crucial role in the pathophysiological process of CKD, which is considered a systemic inflammatory disease with multiple causes [22,23]. Research indicates that CKD patients exhibit more severe coronary plaque inflammation compared to non-CKD patients [24]. There is a progressive increase in proinflammatory circulating mediators as kidney function declines [25]. Proinflammatory processes in CKD patients encompass insulin resistance, oxidative stress due to advanced glycation end product accumulation, metabolic acidosis, reduced cytokine clearance, various infections such as periodontal disease, post-translational modification of blood carrier molecules, and epigenetic factors [22]. Inflammation acting on neoplastic endothelial tissue at the site of coronary stent implantation plays a key role in the progression of ISR

Table 4. Factors associated with the incidence of ISR in both univariate and multivariate logistic regression analysis.

Variables	Univariate			Multivariable		
	OR	95% CI	*p*	OR	95% CI	*p*
Age/years	1.042	1.008–1.078	0.016	1.034	0.980–1.090	0.221
Prior stroke	2.250	1.045–4.842	0.038	0.989	0.285–3.433	0.987
Congestive heart failure	2.866	1.259–6.523	0.012	0.444	0.088–2.247	0.327
LVEF (%)	0.963	0.936–0.992	0.011	0.990	0.941–1.041	0.686
FIB	1.412	1.084–1.838	0.010	1.407	1.007–1.967	0.045
NLR	1.198	1.075–1.335	0.001	1.221	1.022–1.459	0.028
PLR	1.003	1.000–1.006	0.051	0.997	0.992–1.002	0.276
CHA2DS2-VASc score	1.888	1.423–2.504	<0.001	2.111	1.207–3.691	0.009
CHA2DS2-VASc risk score	5.486	1.822–16.525	0.002	1.563	0.256–9.549	0.628

Abbreviations: CI, confidence interval; OR, odds ratio; LVEF, left ventricular ejection fraction; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio.

Table 5. Analyses of ROC curves.

Predictor	AUC	Maximum entry index	Sensitivity	Specificity	95% Cl
CHA2DS2-VASc score	0.714	0.354	83.9%	51.5%	0.634–0.793
NLR	0.707	0.334	71.0%	62.4%	0.627–0.788
FIB	0.652	0.300	72.6%	57.4%	0.565–0.739
CHA2DS2-VASc score combined with FIB and NLR	0.797	0.539	80.6%	73.3%	0.725–0.868

Abbreviations: CI, confidence interval; NLR, neutrophil to lymphocyte ratio.

[26]. FIB and NLR are novel prognostic and inflammatory markers in patients with cardiovascular disease. This investigation revealed that the levels of NLR and FIB were notably elevated in the ISR group compared to the non-ISR group. Both FIB and NLR were identified as independent risk factors for ISR in SKD.

The CHA2DS2-VASc score, originally designed for patients with AF, effectively integrates common CKD risk factors, making it a suitable predictor for ISR risk in this population. A higher CHA2DS2-VASc score indicates a greater number of CKD risk factors and an increased susceptibility to ISR. In recent years, numerous studies have demonstrated that the CHA2DS2-VASc score has predictive value for ISR in various patient populations [2,5–7]. Consistently, this research found that the CHA2DS2-VASc score was an independent risk factor for ISR in patients with SKD. The AUC of the CHA2DS2-VASc score was 0.714 (95% CI: 0.634–0.793), with a sensitivity of 83.9% and a specificity of 51.1%.

The study had several limitations. Firstly, it was a single-center, retrospective observational study with a limited sample size, potentially affecting the representativeness of the entire population with the condition. Secondly, the definition of ISR relied on subjective visual assessment by interventional cardiologists rather than more objective measures such as intravascular ultrasound or optical computed tomography. Thirdly, individual demographic characteristics, comorbidities, and medication use of each patient could have influenced the occurrence of ISR. Lastly, the study did not exclude patients with acute inflammatory conditions, which may have affected certain biomarkers.

Conclusions

The combination of CHA2DS2-VASc score, FIB, and NLR can more accurately predict the occurrence of ISR in SKD patients. Further prospective studies are needed to validate these findings.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

YS collected data, created the database and wrote the manuscript. BT analysed data, draw figures and tables, and modified manuscript. JC, KC, YX, QS and ZZ interpreted data and revised the manuscript critically for import intellectual content. QS provided funding support. GL, TL and XZ developed the study concept and design. All authors approved the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study has been granted an exemption from requiring written informed consent by medical ethics committee of the second hospital of Tianjin Medical University. And this study protocol was reviewed and approved by medical ethics committee of the second hospital of Tianjin Medical University, approval number KY2023K161.

Acknowledgment

Not applicable.

Funding

The work was funded by Scientific Research Projects of Tianjin Municipal Education Commission (2020KJ172 to Q.S.), Tianjin Natural Science Foundation (21JCQNJC01620 to Q.S.) and Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-029A).

Conflict of Interest

The authors declares no conflict of interest. TL serves as editorial board member of this journal. TL declares that he was not involved in the processing of this article and has no access to information regarding its processing.

References

[1] Dangas GD, Claessen BE, Caixeta A, Sanidas EA, Mintz GS, Mehran R. In-stent restenosis in the drug-eluting stent era. Journal of the American College of Cardiology. 2010; 56: 1897–1907.

[2] Kurtul A. Usefulness of the CHA2DS2-VASc Score in Predicting In-Stent Restenosis Among Patients Undergoing Revascularization With Bare-Metal Stents. Clinical and Applied Thrombosis/Hemostasis: Official Journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis. 2018; 24: 589–595.

[3] Nakazawa G, Tanabe K, Aoki J, Yamamoto H, Higashikuni Y, Onuma Y, *et al*. Impact of renal insufficiency on clinical and angiographic outcomes following percutaneous coronary intervention with sirolimus-eluting stents. Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions. 2007; 69: 808–814.

[4] Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, *et al*. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. European Heart Journal. 2012; 33: 2719–2747.

[5] Zhao J, Hou L, Zhu N, Huang R, Su K, Lei Y, *et al*. The Predictive Value of the CHA2DS2-VASc Score for In-Stent Restenosis Among Patients with Drug-Eluting Stents Implantation. International Journal of General Medicine. 2023; 16: 69–76.

[6] Rachoin JS, Wolfe Y, Patel S, Cerceo E. Contrast associated nephropathy after intravenous administration: what is the magnitude of the problem? Renal Failure. 2021; 43: 1311–1321.

[7] Yilmaz S, Akboga MK, Aras D, Topaloglu S. Evaluation of the Predictive Value of CHA_2DS_2-VASc Score for In-Stent Restenosis. Angiology. 2018; 69: 38–42.

[8] Yu H, Dai J, Fang C, Jiang S, Mintz GS, Yu B. Prevalence, Morphology, and Predictors of Intra-Stent Plaque Rupture in Patients with Acute Coronary Syndrome: An Optical Coherence Tomography Study. Clinical and Applied Thrombosis/Hemostasis: Official Journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis. 2022; 28: 10760296221146742.

[9] Okura H, Takagi T, Yoshida K. Therapies targeting inflammation after stent implantation. Current Vascular Pharmacology. 2013; 11: 399–406.

[10] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976; 16: 31–41.

[11] Okura H, Takagi T, Yoshida K. Therapies targeting inflammation after stent implantation. Current Vascular Pharmacology. 2013; 11: 399–406.

[12] Alfonso F, Byrne RA, Rivero F, Kastrati A. Current treatment of in-stent restenosis. Journal of the American College of Cardiology. 2014; 63: 2659–2673.

[13] Stevens PE, O'Donoghue DJ, de Lusignan S, Van Vlymen J, Klebe B, Middleton R, *et al*. Chronic kidney disease management in the United Kingdom: NEOERICA project results. Kidney International. 2007; 72: 92–99.

[14] London GM, Guérin AP, Marchais SJ, Métivier F, Pannier B, Adda H. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2003; 18: 1731–1740.

[15] Bundy JD, Chen J, Yang W, Budoff M, Go AS, Grunwald JE, *et al*. Risk factors for progression of coronary artery calcification in patients with chronic kidney disease: The CRIC study. Atherosclerosis. 2018; 271: 53–60.

[16] Guérin AP, London GM, Marchais SJ, Metivier F. Arterial stiffening and vascular calcifications in end-stage renal disease. Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2000; 15: 1014–1021.

[17] Little WC. Heart failure with a normal left ventricular ejection fraction: diastolic heart failure. Transactions of the American Clinical and Climatological Association. 2008; 119: 93–99; discussion 99–102.

[18] Sarnak MJ, Amann K, Bangalore S, Cavalcante JL, Charytan DM, Craig JC, *et al*. Chronic Kidney Disease and Coronary Artery Disease: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2019; 74: 1823–1838.

[19] Ellis CL, O'Neill WC. Questionable specificity of histologic findings in calcific uremic arteriolopathy. Kidney International. 2018; 94: 390–395.

[20] Shaker JL, Deftos L, Feingold KR, Anawalt B, Boyce A, Chrousos G, *et al*. Calcium and Phosphate Homeostasis. Endotext: South Dartmouth (MA). 2018.

[21] Floege J. Magnesium in CKD: more than a calcification inhibitor? Journal of Nephrology. 2015; 28: 269–277.

[22] Dhondup T, Qian Q. Electrolyte and Acid-Base Disorders in Chronic Kidney Disease and End-Stage Kidney Failure. Blood Purification. 2017; 43: 179–188.

[23] Sakaguchi Y, Hamano T, Obi Y, Monden C, Oka T, Yamaguchi S, *et al*. A Randomized Trial of Magnesium Oxide and Oral Carbon Adsorbent for Coronary Artery Calcification in Predialysis CKD. Journal of the American Society of Nephrology: JASN. 2019; 30: 1073–1085.

[24] Zoccali C, Vanholder R, Massy ZA, Ortiz A, Sarafidis P, Dekker FW, *et al*. The systemic nature of CKD. Nature Reviews. Nephrology. 2017; 13: 344–358.

[25] Amdur RL, Feldman HI, Dominic EA, Anderson AH, Beddhu S, Rahman M, *et al*. Use of Measures of Inflammation and Kidney Function for Prediction of Atherosclerotic Vascular Disease Events and Death in Patients With CKD: Findings From the CRIC Study. American Journal of Kidney Diseases: the Official Journal of the National Kidney Foundation. 2019; 73: 344–353.

[26] Campean V, Neureiter D, Varga I, Runk F, Reiman A, Garlichs C, *et al*. Atherosclerosis and vascular calcification in chronic renal failure. Kidney & Blood Pressure Research. 2005; 28: 280–289.