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The Relationship Between the CASTLE (EUROCTO) Score and Contrast-Induced Nephropathy in Patients Undergoing Coronary Chronic Total Occlusion Interventions

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Abstract

Background: Contrast-induced nephropathy (CIN) is still recognized as a major complication in patients undergoing chronic total occlusion (CTO) interventions. The predictive value of CTO complexity scores for CIN remains unclear. The present study investigated whether the CASTLE (EuroCTO) score is associated with the development of CIN in patients treated with CTO-PCI.

Methods: A total of 356 patients undergoing CTO-PCI were retrospectively analyzed and classified according to CIN development. Clinical, angiographic, and procedural characteristics were compared between groups. Missing data were handled using multiple imputation, and independent predictors of CIN were identified through multivariable logistic regression analysis. The predictive performance of CTO scoring systems was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: CIN was observed in 34 patients (9.5%). Individuals who developed CIN were generally older, more frequently diabetic, and had lower left ventricular ejection fraction values. Procedural complexity was greater in the CIN group, reflected by higher CASTLE and J-CTO scores, longer lesion length, and higher contrast volume. In multivariable analysis, the CASTLE score remained associated with CIN (OR: 1.838, 95% CI: 1.354–2.494, p<0.001), whereas the association with the J-CTO score was weaker, and the PROGRESS CTO score was not significant. ROC analysis demonstrated that the CASTLE score showed acceptable discriminative performance (AUC: 0.694, 95% CI: 0.643–0.742), with a cut-off >2 providing a reasonable balance between sensitivity (70.6%) and specificity (63.3%).

Conclusion: The CASTLE (EuroCTO) score showed an association with CIN occurrence in patients treated with CTO-PCI and demonstrated acceptable predictive capability compared with other CTO scoring models. Although the score may contribute to preprocedural risk assessment, the results should be interpreted carefully.

Keywords: Coronary artery disease, Chronic total occlusion; CASTLE score; contrast-induced nephropathy; percutaneous coronary intervention; acute kidney injury

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Koroner Kronik Total Oklüzyon Girişimi Uygulanan Hastalarda CASTLE (EUROCTO) Skoru ile Kontrast Kaynaklı Nefropati Arasındaki İlişki

Öz

Amaç: Kontrast ilişkili nefropati (KİN), kronik total oklüzyon (KTO) girişimlerinde önemli komplikasyonlardan biri olmaya devam etmektedir. KTO lezyon kompleksitesini değerlendirmede kullanılan skorların KİN gelişimini öngörmedeki rolü henüz net değildir. Bu çalışmada, kronik total oklüzyon-perkütan koroner girişim (KTO-PKG) uygulanan hastalarda CASTLE (EuroCTO) skorunun KİN gelişimi ile ilişkisi araştırıldı.
Yöntemler: KTO-PKG uygulanan toplam 356 hasta retrospektif olarak değerlendirildi ve KİN gelişimine göre iki gruba ayrıldı. Gruplar arasında klinik, anjiyografik ve prosedürel özellikler karşılaştırıldı. Eksik veriler çoklu imputasyon yöntemi ile tamamlandı. KİN'in bağımsız belirleyicileri çok değişkenli lojistik regresyon analizi ile değerlendirildi. KTO skorlama sistemlerinin öngörü performansı receiver operating characteristic (ROC) eğrisi analizi ile incelendi.
Bulgular: KİN, 34 (%9,5) hastada gelişti. KİN gelişen hastalar daha ileri yaşta olup diyabetes mellitus sıklığı daha yüksek ve sol ventrikül ejeksiyon fraksiyonu daha düşüktü. KİN grubunda prosedürel kompleksite daha yüksek olup, bu durum daha yüksek CASTLE ve Japanese chronic total occlusion (J-CTO) skorları, daha uzun lezyon uzunluğu ve daha fazla kontrast madde kullanımı ile ilişkiliydi. Çok değişkenli analizde CASTLE skoru, KİN gelişimi ile bağımsız olarak ilişkili bulundu (OR: 1,838; %95 güven aralığı [GA]: 1,354–2,494; p<0,001). J-CTO skorunun ilişkisi daha zayıfken, PROGRESS CTO skoru anlamlı bulunmadı. ROC analizinde CASTLE skorunun orta düzeyde ayırt edici performans gösterdiği saptandı (eğri altında alan [EAA]: 0,694; %95 GA: 0,643–0,742). >2 eşik değeri, duyarlılık (%70,6) ve özgüllük (%63,3) açısından en uygun dengeyi sağladı.
Sonuç: CASTLE skoru, KTO-PKG uygulanan hastalarda KİN gelişimi ile ilişkili bulundu ve diğer KTO skorlama sistemlerine kıyasla daha iyi öngörü performansı gösterdi. CASTLE skoru, işlem öncesi risk değerlendirmesinde yararlı olabilir; ancak bulguların prospektif çalışmalarla doğrulanması gerekmektedir.
Anahtar kelimeler: Koroner arter hastalığı, kronik total oklüzyon, CASTLE skoru, kontrast ilişkili nefropati, perkütan koroner girişim, akut böbrek hasarı.

INTRODUCTION

Percutaneous coronary intervention (PCI) in the setting of chronic total occlusion (CTO) remains among the most complex procedures performed in interventional cardiology[1]. Currently, the anatomical and structural characteristics of CTO lesions are analyzed using various angiographic scoring systems to facilitate procedural planning and to predict guidewire crossing success and technical outcomes. Among these, the CASTLE (EuroCTO) score is widely used due to its validation across different centers, clinical applicability, and strong predictive value[2–5].

Contrast agents used during coronary angiography (CAG) and CTO-PCI procedures may lead to contrast-induced nephropathy (CIN) because of their potential toxic effects on renal tissue[6]. CIN is associated with serious clinical outcomes, including cardiovascular events and chronic kidney disease (CKD), and may progress to chronic renal failure in approximately one-quarter of affected patients[7]. Moreover, this complication is associated with prolonged hospitalization and a 5- to 10-fold increase in healthcare expenditures and socioeconomic burden[8].

Although scoring systems for assessing procedural complexity in CTO-PCI and models for predicting the risk of CIN have been developed separately, data on parameters that can simultaneously predict both conditions remain limited.

In this study, we evaluated whether the CASTLE score could predict not only procedural complexity but also the development of CIN and explored the relationship between procedural complexity and CIN development.

METHODS

Study Setting and Population

In this retrospective multicenter cohort, patients who consecutively underwent CTO-PCI between January 2020 and December 2025 were systematically evaluated. Following the application of predefined exclusion criteria to 467 CTO cases, data from 356 eligible patients were ultimately evaluated.

All procedures were performed at Mersin Medicalpark Hospital, Hatay Private Defne Hospital, and Antakya Private Academy Hospital. Patients were categorized according to the development of contrast-induced nephropathy (CIN), identified by an increase in serum creatinine levels after contrast exposure. Group 1 comprised patients who developed CIN (CIN+), while Group 2 comprised those who did not (CIN−); comparative analyses were conducted between the groups.

Inclusion and Exclusion Criteria

Patients were considered eligible if they were older than 18 years and had evidence of coronary artery occlusion of at least three months' duration or evidence of collateral circulation. All patients had a diagnosis of chronic coronary syndromes, unstable ischemic symptoms, or non-ST-segment elevation myocardial infarction (MI), with objective evidence of myocardial ischemia documented by non-invasive methods such as exercise testing or myocardial SPECT. In addition, all included patients underwent PCI for CTO during the study period and had a calculable CASTLE score. Patients younger than 18 years and individuals with inadequate visualization of the distal vessel bed were excluded. Those with active or prior malignancy, moderate or severe valvular heart disease, or missing or incomplete clinical, procedural, or imaging data were excluded. Additionally, patients with additional CTOs in other vessels or those requiring complex multivessel CTO strategies were excluded from the study.

Definitions

The definition of CTO was based on the CTO Academic Research Consortium criteria, which refer to a complete interruption of antegrade flow, Thrombolysis in Myocardial Infarction (TIMI grade 0) lasting at least 3 months[9]. Coronary flow was graded using the TIMI classification (grades 0–3)[10].

The CASTLE score was determined using six parameters: previous CABG history, age ≥70 years, blunt stump anatomy, marked vessel tortuosity, lesion length ≥20 mm, and severe calcification. Each component contributed 1 point to the total score, yielding a scale from 0 to 6, with higher values indicating greater lesion complexity and procedural challenge[3].

The Japanese CTO (J-CTO) score was determined using the original scoring system described by Morino et al.[2].

CIN was defined based on the Acute Kidney Injury Network (AKIN) criteria as either an increase in serum creatinine of at least 0.3 mg/dL or a ≥50% rise compared with baseline values after the procedure[11,12]. Renal function indicators, including serum creatinine and estimated glomerular filtration rate (eGFR), were evaluated on the first post-procedural day and again at discharge. The occurrence of CIN and the need for hemodialysis during hospitalization were recorded as renal complications.

Procedural and Clinical Characteristics

Baseline demographic and clinical characteristics, such as age, sex, body mass index (BMI), hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), CKD, smoking history, family history of premature coronary artery disease, current medical therapy, and echocardiographic left ventricular ejection fraction (LVEF), were obtained from

institutional medical records. Renal parameters were assessed before the procedure and re-evaluated during the post-procedural period.

In accordance with current guideline recommendations, all patients received prophylactic measures to reduce the risk of CIN[13]. This protocol consisted of intravenous isotonic saline infusion at a rate of 1.0–1.5 mL/kg/h, initiated approximately 12 hours before angiography and maintained for up to 24 hours after the procedure.

Serum creatinine measurements obtained during the first 24 hours after CTO-PCI were used to evaluate CIN. Because the study data were collected retrospectively and follow-up creatinine measurements beyond the first day were not consistently available in all patients, 48–72-hour renal assessments could not be analyzed systematically.

Angiographic and procedural characteristics included the target vessel location (left anterior descending artery, right coronary artery, or left circumflex artery), as well as the CASTLE and J-CTO scores. Procedural variables, including procedure duration, fluoroscopy time, contrast volume, guidewire type, and the number and total length of implanted stents, were documented. Procedural success was defined as successful antegrade or retrograde recanalization of the target lesion. Procedural complications, including coronary perforation, dissection, no-reflow phenomenon, failed intervention, and in-hospital mortality, were also recorded. Post-procedural outcomes included in-hospital adverse events such as MI, stroke, bleeding, and acute kidney injury, as well as the duration of intensive care unit stay and length of hospitalization. In addition, early post-discharge outcomes within 30 days were evaluated. Clinical and procedural information was obtained from hospital database systems and archived patient records. Approval for the study protocol was provided by the local ethics committee of Mersin University (2026/064; January 21, 2026). The investigation was carried out in line with established principles for ethical conduct in clinical research, as outlined in the Declaration of Helsinki.

Statistical Interpretation

Statistical processing was carried out using R software (version 4.5.2; R Foundation for Statistical Computing, Vienna, Austria). Quantitative variables were summarized as mean ± standard deviation when normally distributed, whereas skewed variables were reported as median and interquartile range. Categorical parameters were expressed as frequencies and percentages. Distribution patterns were evaluated through the Kolmogorov–Smirnov test together with histogram and Q–Q plot assessments.

Comparisons between patients with and without CIN were performed using Student's t-test or the Mann–Whitney U test according to distribution characteristics, while categorical variables were analyzed with chi-square or Fisher's exact tests where appropriate. Missing observations, which accounted for less than 5% of the dataset, were completed using chained-equation multiple imputation. Five separate imputed datasets were generated and combined according to Rubin's methodology.

Variables potentially related to CIN were initially explored with univariable logistic regression, followed by multivariable modeling to identify independent predictors. To minimize overfitting, the events-per-variable ratio was taken into consideration during model construction. Collinearity among covariates was examined using variance inflation factor values, and highly correlated variables were omitted from the final analysis. Results were presented as odds ratios with corresponding 95% confidence intervals.

Predictive performances of the CASTLE, J-CTO, and PROGRESS CTO scores were examined through receiver operating characteristic (ROC)

curve analysis, and area under the curve values were calculated for each model. ROC curves were compared with the DeLong approach. The most appropriate threshold value for the CASTLE score was selected according to the highest Youden index. Sensitivity, specificity, and positive/negative likelihood ratios were also calculated for relevant cut-off levels. Calibration performance was evaluated with the Hosmer–Lemeshow goodness-of-fit test, while sensitivity analyses were additionally performed to examine the robustness of the findings. Statistical significance was defined as a two-sided p-value below 0.05.

RESULTS

A total of 356 patients were included in the final analysis, of whom 34 (9.5%) developed CIN. Baseline characteristics are presented in Table 1. Patients with CIN were significantly older (66.1±8.4 vs. 60.0±9.7 years, p=0.001), had a higher prevalence of diabetes mellitus (61.8% vs. 43.5%, p=0.047), and lower left ventricular ejection fraction (44.3±8.2 vs. 49.6±9.6, p=0.002). Other baseline variables were comparable between groups. Procedural and angiographic characteristics are summarized in Table 2. The CASTLE score was significantly higher in the CIN group (2.97±1.19 vs. 2.06±1.22, p<0.001), with higher score categories more frequently observed (p=0.001). The J-CTO score was also higher in patients with CIN (2.41±1.26 vs. 1.97±1.18, p=0.040), whereas the PROGRESS CTO score did not differ significantly (p=0.344). CTO lesion length and contrast volume were significantly greater in patients who developed CIN (both p<0.05). In addition, technical success (77.4% vs. 93.7%, p=0.006) and procedural success (67.7% vs. 88.5%, p=0.003) rates were significantly lower in the CIN group.

Table I: Demographic and baseline data

Variables	CIN - (n=322)	CIN + (n=34)	*p*-value*
Age, years	60.0±9.7	66.1±8.4	0.001*
Gender, female, n (%)	41 (12.7)	7 (20.6)	0.194
BMI, kg/m^2	28.84±5.4	29.3±4.2	0.560
Diabetes mellitus, n (%)	140 (43.5)	21 (61.8)	0.047*
Hypertension, n (%)	211 (65.5)	25 (73.5)	0.446
Family history, n (%)	153 (47.5)	14 (41.2)	0.588
Previous PCI, n (%)	152 (47.2)	14 (41.2)	0.589
Previous CABG, n (%)	143 (44.4)	17 (50.0)	0.533
Previous MI, n (%)	68 (21.1)	9 (26.5)	0.511
Smoking, n (%)	171 (53.1)	16 (47.1)	0.589
Dyslipidemia, n (%)	116 (36.0)	13 (38.2)	0.852
CHF, n (%)	38 (11.8)	6 (17.6)	0.407
PAD, n (%)	14 (4.3)	4 (11.8)	0.081
Prior neurological events, n (%)	18 (5.6)	1 (2.9)	1.000
Creatinine, mg/dL	0.99±0.21	0.97±0.29	0.574
Hb, g/dL	13.68±2.18	13.40±2.10	0.487
Left Ventricular Ejection Fraction, %	49.57±9.58	44.29±8.19	0.002*

Data are shown in n (%), and mean± standard deviation.

** A p-value of <0.05 was considered statistically significant.*

Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; CHF, congestive heart failure; CIN, contrast-induced nephropathy; CTO, chronic total occlusion; Hb, hemoglobin; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention.

Table II: Procedural Characteristics

Variables	Study Groups		*p*-value*
	CIN - (n=322)	CIN + (n=34)	
Retrograde approach, n (%)	52 (16.2)	7 (21.2)	0.464
CTO Artery, n (%)			0.259
LAD	104 (32.4)	11 (32.4)	
LCx	51 (15.9)	2 (5.9)	
RCA	166 (51.7)	21 (61.8)	
PROGRESS Score	1.32 ± 0.95	1.48 ± 0.97	0.344
CASTLE score	2.06 ± 1.22	2.97 ± 1.19	<0.001
CASTLE score, n (%)			0.001
0	34 (10.6)	0 (0.0)	
1	74 (23.0)	5 (14.7)	
2	96 (29.8)	5 (14.7)	
3	81 (25.2)	14 (41.2)	
4	31 (9.6)	6 (17.6)	
5	5 (1.6)	4 (11.8)	
6	1 (0.3)	0 (0.0)	
PROGRESS score, n (%)			0.484
0	65 (20.6)	4 (12.1)	
1	121 (38.4)	15 (45.5)	
2	96 (30.5)	9 (27.3)	
3	29 (9.2)	4 (12.1)	
4	4 (1.3)	1 (3.0)	
J-CTO score	1.97±1.18	2.41±1.26	0.040
J-CTO score, n (%)			0.155
0	32 (10.0)	1 (2.9)	
1	90 (28.1)	9 (26.5)	
2	87 (27.2)	8 (23.5)	
3	82 (25.6)	8 (23.5)	
4	24 (7.5)	7 (20.6)	
5	5 (1.6)	1 (2.9)	
Stump, n (%)			0.101
Tapered	184 (57.3)	14 (41.2)	
Blunt	137 (42.7)	20 (58.8)	
CTO length, mm	64.0 ± 27.6	76.9 ± 36.9	0.030
Number DES, mean ± SD	1.89 ± 0.85	1.93 ± 1.21	0.830
Dose area product, Gy·cm²	31147 [18344, 53634]	36660 [16324, 43776]	0.794
Fluoroscopy time, min	95.52 ± 54.94	106.35 ± 56.81	0.277
Contrast volume, mL	263.4 ± 110.4	400.9 ± 157.4	<0.001
In CTO bend, n (%)			0.844
0	226 (70.4)	25 (73.5)	
1	95 (29.6)	9 (26.5)	
Complications			
Technical success, n (%)	296 (93.7)	24 (77.4)	0.006
Procedural success, n (%)	278 (88.5)	21 (67.7)	0.003
Dissection, n (%)	2 (0.6)	0 (0.0)	1.000
Bleeding, n (%)			0.708
Minor	5 (1.6)	0 (0.0)	
Major	6 (1.9)	1 (2.9)	
Major vascular complications, n (%)	14 (4.3)	1 (2.9)	0.432
MI, n (%)	3 (0.9)	0 (0.0)	0.616
24-h post-procedural creatinine, mg/dL	0.96 ± 0.22	1.45 ± 0.46	<0.001

Data are shown in n (%), median (interquartile range; 25th-75th percentiles), and mean ± standard deviation.

** A p-value of <0.05 was considered statistically significant.*

Abbreviations: CIN, contrast-induced nephropathy; CTO, chronic total occlusion; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; DES, drug-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention.

The discriminative performance of CTO scoring systems was evaluated using ROC curve analysis (Figure 1). The CASTLE score showed the best discriminative ability among the evaluated scoring systems, with an AUC of 0.694 (95% CI: 0.643–0.742, p<0.001). In contrast, the J-CTO score showed limited discriminative ability (AUC: 0.592, 95% CI: 0.538–0.644, p=0.068), and the PROGRESS CTO score exhibited poor predictive performance (AUC: 0.539, 95% CI: 0.485–0.592, p=0.411).

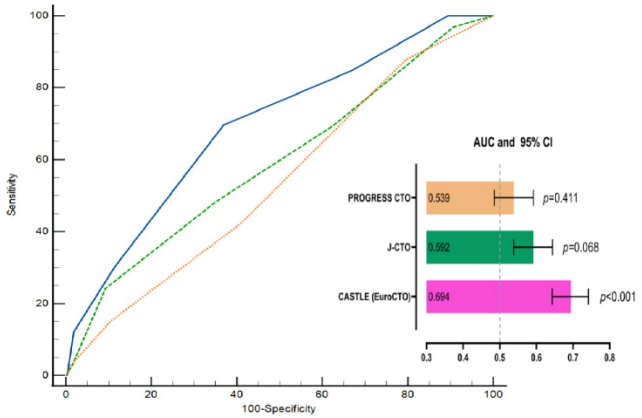

Figure 1. Receiver operating characteristic (ROC) curves comparing the ability of the CASTLE (EuroCTO), J-CTO, and PROGRESS CTO scores to predict CIN.

Abbreviations: ROC, receiver operating characteristic; CIN, contrast-induced nephropathy; CTO, chronic total occlusion.

In multivariable logistic regression analysis, the CASTLE score remained an independent predictor of CIN (OR: 1.838, 95% CI: 1.354–2.494, p<0.001), while the J-CTO score showed a weaker but significant association (OR: 1.362, 95% CI: 1.011–1.835, p=0.042). The PROGRESS CTO score was not independently associated with CIN (OR: 1.197, 95% CI: 0.825–1.735, p=0.344) (Table 3).

Table III: Binary logistic regression analysis of scores in CTO patients undergoing revascularization

Variable	Covariate Effect		
	OR	95% CI	*p*-value*
CASTLE score (EuroCTO)	1.838	1.354–2.494	<0.001
J-CTO score	1.362	1.011–1.835	0.042
PROGRESS CTO score	1.197	0.825–1.735	0.344

** A p-value of <0.05 was considered statistically significant.*

Abbreviations: CI, confidence interval; OR, odds ratio; CTO, chronic total occlusion; CIN, contrast-induced nephropathy.

The diagnostic performance of the CASTLE score across different thresholds is presented in Table 4 and Figure 2. The Youden index reached its maximum at a cut-off value of >2, indicating the optimal balance between sensitivity and specificity. At this threshold, sensitivity was 70.6%, and specificity was 63.4%. Lower cut-off values resulted in higher sensitivity but reduced specificity, whereas higher thresholds improved specificity at the cost of markedly decreased sensitivity. Notably, a cut-off >4 achieved high specificity (98.1%) but very low sensitivity (11.8%).

Table IV: Diagnostic performance of the CASTLE score at different cut-off values based on ROC curve analysis.

Criterion	Sensitivity (%)	95% CI (Sensitivity)	Specificity (%)	95% CI (Specificity)	+LR	-LR
≥ 0	100.0	89.7 – 100.0	0.00	0.0 – 1.1	1.00	NA
> 0	100.0	89.7 – 100.0	10.6	7.4 – 14.4	1.12	0.00
> 1	85.3	68.9 – 95.0	33.5	28.4 – 39.0	1.28	0.44
> 2	70.6	52.5 – 84.9	63.4	57.8 – 68.6	1.93	0.46
> 3	29.4	15.1 – 47.5	88.5	84.5 – 91.8	2.56	0.80
> 4	11.8	3.3 – 27.5	98.1	96.0 – 99.3	6.31	0.90
> 5	0.0	0.0 – 10.3	99.7	98.3 – 100.0	0.00	1.00
> 6	0.0	0.0 – 10.3	100.0	98.9 – 100.0	NA	1.00

Abbreviations: CI, confidence interval; LR, likelihood ratio; +LR, positive likelihood ratio; −LR, negative likelihood ratio; ROC, receiver operating characteristic; CIN, contrast-induced nephropathy.

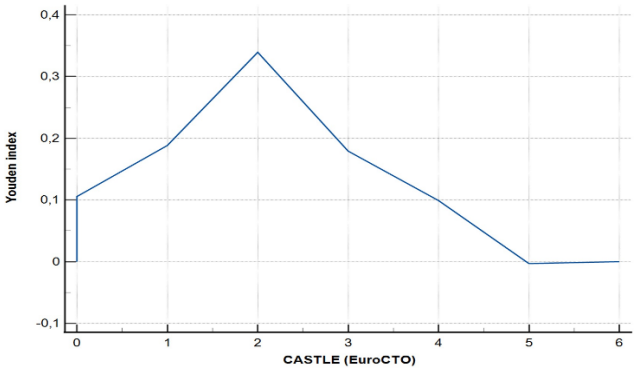

Figure 2. Sensitivity and specificity of the CASTLE (EuroCTO) score across different cut-off values for predicting contrast-induced nephropathy (CIN), demonstrating the optimal cut-off determined by the maximum Youden index.

Abbreviations: CIN, contrast-induced nephropathy; CTO, chronic total occlusion.

Consistent with these findings, the diagnostic performance of the CASTLE score improved progressively as score values increased, indicating enhanced specificity-driven discrimination at higher thresholds (Figure 3). In addition, the predicted probability of CIN increased stepwise with higher CASTLE score values, demonstrating a clear dose–response relationship between lesion complexity and CIN risk (Figure 3A). Figure 3B further illustrates the progressive increase in diagnostic performance observed at higher CASTLE score thresholds.

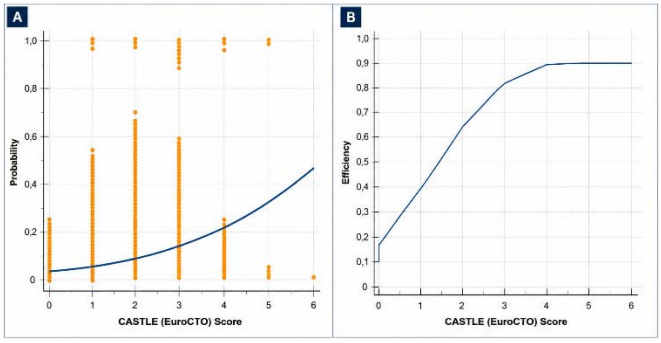

Figure 3. (A) Predicted probability curve demonstrating the relationship between the CASTLE (EuroCTO) score and the risk of CIN. (B) Diagnostic performance of the CASTLE (EuroCTO) score at different score levels for predicting CIN, demonstrating increasing diagnostic performance with higher score values.

Abbreviations: CIN, contrast-induced nephropathy; CTO, chronic total occlusion.

DISCUSSION

The present results demonstrate an association between the CASTLE score and CIN risk in patients undergoing CTO-PCI. Patients with CIN were generally older, had a higher prevalence of DM, and demonstrated lower LVEF values. In addition, patients who developed CIN had higher CASTLE and J-CTO scores, longer CTO lesion length, and greater contrast volume used during the procedure, whereas technical and procedural success rates were lower. These observations indicate that the development of CIN is associated not only with patient-related characteristics but also with lesion complexity and procedural burden.

The stronger association between the CASTLE score and CIN may be explained by the fact that this score incorporates not only lesion morphology but also patient-related clinical risk factors. Indeed, the development of CIN is not solely determined by anatomical difficulty or the amount of contrast used during the procedure, but is also closely related to the patient's baseline clinical status, renal reserve, and hemodynamic vulnerability. Therefore, the CASTLE score may provide a more comprehensive approach for assessing CIN risk in patients undergoing CTO-PCI.

Mehran et al. reported that the prevalence of CIN ranged from 3.3% to 14.5%[14]. In high-risk patient groups, such as those with DM, advanced age, and chronic kidney disease, this rate has been shown to increase to 20%–30%[15–19]. According to a current meta-analysis comprising 120 studies, the overall incidence of CIN was 9.1%[20]. In our study, the incidence of CIN among patients undergoing CTO-PCI was 9.5%, which is consistent with the existing literature. However, the limited availability of serum creatinine measurements beyond the first 24 hours may have led to an underestimation of the true incidence of CIN.

The finding that patients who developed CIN were older and more frequently diabetic supports the role of advanced age and DM as important risk factors for CIN.7 DM may predispose the kidney to nephrotoxic injury through reduced medullary oxygenation, increased oxidative stress, and enhanced inflammatory activity[21]. Similarly, heart failure may also aggravate renal injury by impairing systemic perfusion and contributing to renal congestion. In older individuals, comorbid conditions such as chronic kidney disease, DM, and heart failure frequently coexist, making this patient population more vulnerable to CIN[22–24]. These findings further support that the development of CIN in older patients is related not only to contrast burden but also to the overall burden of accompanying comorbidities.

The main mechanism by which contrast media lead to the development of CIN is the disruption of the balance between oxygen supply and oxygen consumption in the renal medulla[21]. Iodinated radiocontrast agents reduce medullary pO_2 to very low levels, such as 15–20 mmHg, thereby inducing a marked hypoxic stress response; this effect is further amplified particularly in patients with comorbidities due to impairment of the regulatory mechanisms that preserve medullary oxygenation[25]. Experimental studies have shown that suppression of prostaglandin and nitric oxide synthesis abolishes the vasodilatory response in the outer medulla, deepens medullary hypoxia, and leads to acute kidney injury[26]. In addition, contrast agent–induced endothelial cell injury and microcirculatory impairment also contribute to this process and play an important role in the pathogenesis of CIN[27]. In patients who developed CIN, the higher contrast volume observed may have contributed to the association between the CASTLE score and CIN. Since patients with higher CASTLE scores generally undergo more complex CTO-PCI procedures and are exposed to greater amounts of contrast media, part of the predictive value of the CASTLE score may be mediated through increased contrast use. In this context, since longer lesions generally reflect more complex CTO procedures, the relationship between lesion length and CIN may, at least in part, be explained by increased procedural complexity and the accompanying contrast burden.

In addition, the lower technical and procedural success rates observed in patients with CIN may indicate that these cases represented more complex and challenging interventions. This finding supports the possibility of a shared underlying mechanism between procedural difficulty and CIN development.

Although the J-CTO score was significantly associated with CIN, the CASTLE score showed a stronger relationship, and a threshold value of >2 provided acceptable discriminative performance for risk stratification. This may be explained by the CASTLE score, which incorporates both clinical (e.g., age) and angiographic variables, whereas CIN development is influenced not only by lesion complexity but also by patient-related factors[22–24,28].

From a clinical perspective, the CASTLE score may serve as a supportive tool for identifying patients who could be at higher risk of CIN and procedural complexity. For high-risk patients, careful preprocedural planning, limiting contrast volume, and applying appropriate preventive strategies may be particularly beneficial.

Limitations

Several limitations should be acknowledged when interpreting the present findings. First of all, its retrospective design limits causal inference. Another limitation is that the evaluation of CIN was based on serum creatinine measurements obtained within the first 24 hours after the procedure. Since CIN may develop within 48–72 hours following

contrast exposure, the incidence of CIN in our study may have been underestimated. Third, contrast type, hydration strategies, and the use of nephroprotective agents were not standardized across centers, which might introduce confounding. Although data were analyzed cumulatively to minimize intercenter variability, procedural techniques and operator experience could still influence outcomes. Additionally, GFR rather than serum creatinine might have provided a more accurate assessment of renal function. Finally, due to the relatively limited number of CIN events, extensive multivariable adjustment for potential confounders, including contrast volume, was not feasible; therefore, residual confounding cannot be excluded.

CONCLUSION

This study indicates that the CASTLE (EuroCTO) score is associated with CIN occurrence in patients undergoing CTO-PCI. Higher CASTLE values were accompanied by an increased likelihood of CIN, while a threshold above 2 provided a reasonable balance for risk discrimination. Nevertheless, considering the retrospective observational nature of the study and the moderate predictive capacity observed, these findings should be interpreted cautiously. The CASTLE score may contribute to preprocedural risk evaluation and support preventive planning in complex CTO procedures. Additional prospective multicenter research is warranted to validate these observations and better establish the clinical relevance of the score.

Ethics Committee Approval: Approval for the study protocol was provided by the local ethics committee of Mersin University (2026/064; January 21, 2026). The investigation was carried out in line with established principles for ethical conduct in clinical research, as outlined in the Declaration of Helsinki.

Conflict of Interest: The author(s) declare that there is no financial conflict of interest related to this article.

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