

# A novel risk prediction tool for contrast-induced nephropathy in patients with chronic kidney disease who underwent diagnostic coronary angiography

M. ÇETIN<sup>1</sup>, F. ACEHAN<sup>2</sup>, H. KUNDI<sup>1</sup>, I.E. YAKICI<sup>1</sup>, B. KATIPOGLU<sup>3</sup>, G. DURAN<sup>1</sup>, B. YAZICI<sup>1</sup>, Z.G. CETIN<sup>1</sup>, I. ATES<sup>2</sup>

<sup>1</sup>Department of Cardiology, Ankara Bilkent City Hospital, Ankara, Turkey

<sup>2</sup>Department of Internal Medicine, Ankara Bilkent City Hospital, Ankara, Turkey

<sup>3</sup>Department of Geriatrics, Gulhane Training and Research Hospital, Ankara, Turkey

**Abstract. – OBJECTIVE:** The incidence of contrast-induced nephropathy (CIN) is higher than 20% in patients with chronic kidney disease. In this study, we sought to define the predictors of CIN and develop a risk prediction tool in patients with chronic kidney disease.

**PATIENTS AND METHODS:** Patients aged 18 years and older who underwent invasive coronary angiography with an iodine-based contrast media between March 2014 and June 2017 were retrospectively analyzed. Independent predictors for CIN development were identified and a new risk prediction tool was created that included these predictors.

**RESULTS:** In total, 283 patients included in the study were divided into those who developed CIN (n=39, 13.8%) and those who did not (n=244, 86.2%). Male gender (OR: 4.874, 95% CI: 2.044-11.621), LVEF (OR: 0.965, 95% CI: 0.936-0.995), diabetes mellitus (OR: 1.711, 95% CI: 1.094-2.677), and e-GFR (OR: 0.880, 95% CI: 0.845-0.917), were identified as independent predictors for the development of CIN in the multivariate analysis. A new scoring system has been designed that can score a minimum of 0 and a maximum of 8 points. Patients with a new scoring system score of  $\geq 4$  were at approximately 40 times higher risk of developing CIN than others (OR: 39.9, 95% CI: 5.4-295.3). The area under the curve value of CIN's new scoring system was 0.873 (95% CI, 0.821-0.925).

**CONCLUSIONS:** We found that four easily accessible and routinely collected variables, including sex, diabetes status, e-GFR, and LVEF, were independently associated with the development of CIN. We believe that using this risk prediction tool in routine clinical practice may guide physicians to use preventive medications and techniques in high-risk patients for CIN.

*Key Words:*

Chronic kidney disease, Contrast-induced nephropathy, Risk prediction.

## Introduction

Contrast-induced nephropathy (CIN) is described as acute renal failure caused by the injection of contrast media (CM), which may arise as a consequence of invasive coronary angiography<sup>1</sup>. In the general population, the incidence of CIN is 2%, but it can be as high as 20-30% in high-risk populations such as patients with chronic kidney disease, diabetes mellitus, congestive heart failure, and elderly individuals<sup>1,2</sup>.

With a prevalence of 10 percent, CIN is the third most prevalent cause of acute renal failure acquired in a hospital setting<sup>3</sup> CIN can result in a long length of stay in the hospital, a rise in the hospital's expenditures, and an increase in the risks of mortality and disability. The use of CM is gaining popularity on daily basis and is developing into an increasingly significant issue<sup>4</sup>.

Even though there is considerable information regarding the epidemiology of CIN, the pathophysiology of the condition is still unknown<sup>5</sup>. Because there is no effective therapy for CIN, it is critical to research CIN risk factors to identify instances that will benefit from preventive measures. Particularly, a considerable number of patients with chronic kidney disease are unable to receive a diagnosis of CIN since the condition is already oliguric<sup>6</sup>.

However, to the best of our knowledge, to date, there is no risk tool to predict CIN in patients

with chronic kidney disease. In the current study, based on the above information and necessity, we sought to define the predictors of CIN in patients with chronic kidney disease. Furthermore, we sought to develop a CIN risk prediction tool for the target population.

## Patients and Methods

### Study Population and Design

In this study, patients aged 18 years and older who underwent invasive coronary angiography with an iodine-based CM between March 2014 and June 2017 were retrospectively analyzed. Patients with chronic kidney disease who had an e-GFR value below 60 ml/min for at least three months

were included in the study. Those with e-GFR  $\geq 60$  ml/min, those who underwent revascularization, those with incomplete data, those who died within 72 hours after the procedure, and those who received maintenance dialysis treatment were excluded from the study. In addition, to reduce the effect of confounding factors, patients with clinical conditions such as sepsis, hypotension and cardiac arrest which can cause impaired renal function were also excluded from the study. Finally, 283 patients eligible for the study were divided into those who developed CIN (CIN group) and those who did not (non-CIN group), and the factors associated with the development of CIN were defined (Figure 1). Then, independent predictors for CIN development were identified and a new scoring system was created that included these predictors.

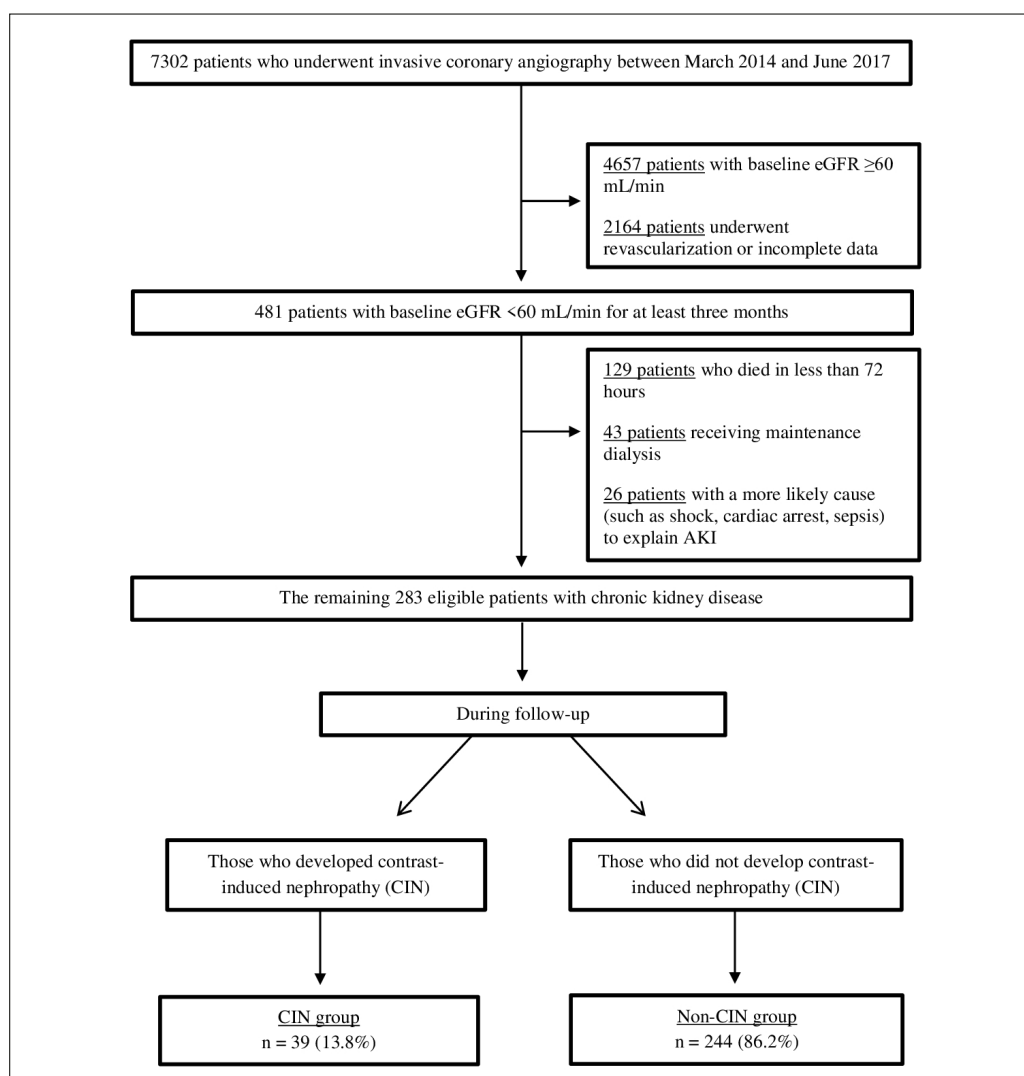


Figure 1. A flow-chart showing the number of included and excluded patients.

### **Definition and Data Collection**

CIN has been defined by as a serum creatinine increase of  $\geq 25\%$  or  $\geq 0.5$  mg/dL compared to baseline within 24-72 hours after CM exposure<sup>7</sup>, after excluding other possible causes of acute kidney injury. The estimated glomerular filtration rate (e-GFR) values were calculated using the 2009 Chronic Kidney Disease Epidemiology (CKD-EPI) creatinine equation<sup>8</sup>. In this study, patients with structural kidney disease were not considered to have CKD, while only patients with functional renal failure were considered to have CKD. Functional CKD was defined as those with baseline e-GFR values below 60 mL/min/1.73 m<sup>2</sup> for at least three months<sup>9</sup>. According to the KDIGO guideline, patients were classified as stage 3A (e-GFR 45 to 59 mL/min/1.73 m<sup>2</sup>), stage 3B (e-GFR 30 to 44 mL/min/1.73 m<sup>2</sup>), stage 4 (e-GFR 15 to 29 mL/min/1.73 m<sup>2</sup>) and stage 5 (e-GFR <15 mL/min/1.73 m<sup>2</sup>), based on their baseline e-GFR values<sup>10</sup>. Patients who developed CIN were followed up for at least 6 months after coronary angiography. Progression of CKD was defined as a reduction in eGFR greater than 25%, as specified by the KDIGO 2012 guidelines<sup>11</sup>.

Patients' age, sex, CKD stages, left ventricular ejection fractions, comorbidities, Charlson risk scores<sup>12</sup>, invasive treatment approaches, length of hospital stay, needs for hemodialysis treatment, and incidence of CKD progression were recruited from the electronic medical record. In addition, many laboratory results at admission were recorded.

### **Statistical Analysis**

Statistical analysis was conducted using SPSS Statistics Version 26.0 for Windows (IBM Corp., Armonk, NY, USA). The data were evaluated for normality by performing the Shapiro-Wilk test. Numerical variables with a normal distribution were shown as mean  $\pm$  standard deviation, and those without a normal distribution were shown as median (interquartile range). Categorical variables were expressed as numbers and percentages. Comparisons of continuous variables with normal distribution were made with Student *t*-tests, while comparisons of those with non-normal distribution were made with Mann-Whitney U tests and categorical variables were compared with Pearson Chi-square tests. Univariate logistic regression analysis was performed for the development of CIN. Parameters

were found to be significant ( $p < 0.05$ ) in the univariate analysis and some relevant parameters were subsequently included in multivariate stepwise logistic regression analysis and independent predictors of CIN development were identified. In the univariate and multivariate analyses, the odds ratio was calculated with 95% confidence intervals (CIs) for these parameters. Appropriate cut-off values for independent predictors were identified by receiver operating characteristic curve analysis based on Youden's index method. At different cut-off values, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the new scoring system created with independent predictors were calculated and risk analysis was performed. The area under the curve (AUC) values were calculated by receiver operating characteristic curve analysis with 95% CIs to evaluate their performances in distinguishing CIN. Values of *p*-value lower than 0.05 were considered to be significant in the statistical analyses.

## **Results**

### **Comparative Baseline Clinical and Laboratory Findings**

The mean age of the overall population was 71.86 $\pm$ 11.06 years. Of the patients, 57.2% were men and 42.8% were women. Of the total of 283 patients, 113, 115, 52, and 3 were CKD stage 3A, stage 3B, stage 4, and stage 5, respectively. The mean LVEF of the patients was 45.71 $\pm$ 13.27%. The most common comorbid diseases in the sample were hypertension (96.8%) and hyperlipidemia (90.1%), respectively, and atrial fibrillation was significantly less common in the CIN group compared to the non-CIN group (10.3% vs. 25.8%,  $p = 0.034$ ). The median Charlson comorbidity index was significantly higher in the CIN group than in the non-CIN group (5 vs. 4,  $p = 0.003$ ). The median length of hospital stay was 5 (IQR, 4-8) days. The need for hemodialysis developed in 13 (4.6%) patients. Progression of CKD was observed in 7 (2.5%) patients at 6-month follow-up after nephropathy. Hemoglobin, platelet, e-GFR and calcium levels were significantly lower in the CIN group, while urea and creatinine levels were significantly higher. The comparative baseline clinical and laboratory findings are shown in Table I and Table II.

**Table I.** Comparative baseline clinical and follow-up findings.

Parameter	Overall n = 283	CIN group n = 39	Non-CIN group n = 244	p-value
Age (years), mean (SD)	71.86 ± 11.06	67.05 ± 12.76	72.63 ± 10.59	0.003
Male gender, n (%)	162 (57.2)	28 (71.8)	134 (54.9)	0.048
CKD GFR stages*				< 0.001
Stage 3A (GFR 45 to 59 mL/min per 1.73 m <sup>2</sup> )	113 (39.9)	4 (10.3)	109 (44.7)	
Stage 3B (GFR 30 to 44 mL/min per 1.73 m <sup>2</sup> )	115 (40.6)	11 (28.2)	104 (42.6)	
Stage 4 (GFR 15 to 29 mL/min per 1.73 m <sup>2</sup> )	52 (18.4)	24 (61.5)	28 (11.5)	
Stage 5 (GFR < 15 mL/min per 1.73 m <sup>2</sup> )	3 (1.1)	0	3 (1.2)	
LVEF, (%)	45.71 ± 13.27	43.51 ± 12.90	46.06 ± 13.32	0.266
Coexisting diseases				
Congestive heart failure, n (%)	115 (40.6)	11 (28.2)	104 (42.6)	0.089
Hypertension, n (%)	274 (96.8)	38 (97.4)	236 (96.7)	1.000
Atrial fibrillation, n (%)	67 (23.7)	4 (10.3)	63 (25.8)	0.034
Hyperlipidemia, n (%)	255 (90.1)	38 (97.4)	217 (88.9)	0.146
Diabetes mellitus, n (%)	174 (61.5)	29 (74.4)	145 (59.4)	0.075
Neurological disease, n (%)	81 (28.6)	11 (28.2)	70 (28.7)	0.951
Pulmonary disease, n (%)	82 (29.0)	9 (23.1)	73 (29.9)	0.382
Chronic liver disease, n (%)	5 (1.8)	2 (5.1)	3 (1.2)	0.141
Malignancy, n (%)	16 (5.7)	0	16 (6.6)	0.140
Charlson comorbidity index, median (IQR)	4 (3-5)	5 (4-6)	4 (2-5)	0.003
Weighted comorbidity classes				0.009
Low (0 points), n (%)	5 (1.8)	0	5 (2.0)	
Medium (1 to 2 points), n (%)	59 (20.8)	3 (7.7)	56 (23.0)	
High (3 to 4 points), n (%)	116 (41.0)	13 (33.3)	103 (42.2)	
Very high (≥ 5 points), n (%)	103 (36.4)	23 (59.0)	80 (32.8)	
Length of hospital stay, median (IQR)	5 (4-8)	7 (3-14)	5 (4-8)	0.078
Serious clinical events				
Need for hemodialysis, n (%)	13 (4.6)	13 (33.3)	-	-
Progression of CKD, n (%)	7 (2.5)	7 (17.9)	-	-

\*Patients were staged according to their baseline e-GFR values.

### Independent Risk Factors for CIN

While many parameters were significantly associated with the development of CIN in the univariate analysis, four parameters, namely male gender (OR: 4.874, 95% CI: 2.044-11.621), LVEF (OR: 0.965, 95% CI: 0.936-0.995), diabetes mellitus (OR: 1.711, 95% CI: 1.094-2.677), and e-GFR (OR: 0.880, 95% CI: 0.845-0.917), were identified as independent predictors for the development of CIN in the multivariate analysis (Table III). Nominal variables were created based on the optimal cut-off value of 45% for LVEF and staging for e-GFR. Then, multivariate regression analysis was repeated using these four parameters (Table IV).

### Stages of Derivation of the New Scoring System

Gender, diabetes mellitus, LVEF and CKD GFR stages were included in the scoring system. In the scoring model, the *B* coefficients of the parameters in multivariate analysis with

nominal variables were rounded to appropriate integers and these integers were assigned as the scores of those parameters (Table V). As a result, a new scoring system has been designed that can score a minimum of 0 and a maximum of 8 points.

### Predictive Values of the New Scoring System Score at Different Cut-Offs

The predictive values of the new scoring system at different cut-offs were evaluated (Table VI). Accordingly, when Youden's index method was taken as a basis, the most appropriate cut-off was 4.5 and the sensitivity, specificity, PPV, and NPV of the new scoring system at this cut-off were 84.6%, 75.4%, 35.5% and 96.8%, respectively. Patients with a new scoring system score of ≥4 were at approximately 40 times higher risk of developing CIN than others (OR: 39.9, 95% CI: 5.4-295.3). None of the patients with a new scoring score of <3 developed CIN (NPV 100% for new scoring score of <3).

**Table II.** Comparative laboratory results.

Parameter	Overall n = 283	CIN group n = 39	Non-CIN group n = 244	p-value
White blood cell (10 <sup>9</sup> /L)	9.6 (8.0-12.0)	9.0 (7.2-12.0)	9.7 (8.0-11.97)	0.313
Hemoglobin (g/dL)	11.85 ± 2.08	11.14 ± 1.85	11.96 ± 2.09	0.023
Platelet (10 <sup>9</sup> /L)	219 (179-278)	208 (159-248)	222 (181-279)	0.048
Urea (mg/dL)	61 (48-82)	88 (71-102)	59 (46-77)	< 0.001
Creatinine (mg/dL)	1.46 (1.30-1.84)	2.19 (1.69-2.81)	1.42 (1.28-1.65)	< 0.001
e-GFR, CKD-EPI (mL/min)	41 (32-50)	26 (23-35)	42 (35-50)	< 0.001
Uric acid (mg/dL)	7.29 ± 2.03	7.77 ± 1.96	7.19 ± 2.03	0.156
Blood glucose (mg/dL)	154 (113-212)	170 (121-225)	153 (110-207)	0.285
Sodium (mEq/L)	136.36 ± 3.39	135.54 ± 3.37	136.49 ± 3.38	0.105
Potassium (mEq/L)	4.39 ± 0.58	4.49 ± 0.60	4.39 ± 0.58	0.320
Calcium (mg/dL)	8.85 ± 0.53	8.68 ± 0.57	8.88 ± 0.52	0.035
Alanine aminotransferase (U/L)	19 (13-27)	17 (12-30)	19 (14-27)	0.436
Aspartate aminotransferase (U/L)	28 (20-49)	25 (16-41)	28 (20-53)	0.152
Alkaline phosphatase (U/L)	86 (69-112)	97 (72-113)	84 (68-112)	0.228
Gamma-glutamyl transpeptidase (U/L)	26 (19-44)	30 (20-43)	26 (18-46)	0.303
Lactate dehydrogenase (U/L)	266 (232-327)	265 (232-447)	266 (232-323)	0.673
Total bilirubin (mg/dL)	0.3 (0.2-0.5)	0.3 (0.2-0.8)	0.3 (0.2-0.5)	0.674
Total cholesterol (mg/dL)	175 (141-202)	177 (143-212)	175 (141-202)	0.764
Triglyceride (mg/dL)	117 (78-168)	138 (89-183)	113 (77-167)	0.099
LDL-C (mg/dL)	108 (83-135)	107 (84-150)	108 (83-134)	0.818
HDL-C (mg/dL)	37 (31-45)	37 (31-43)	37 (32-45)	0.389
International normalization ratio	1.13 (1.00-1.24)	1.13 (0.99-1.20)	1.13 (1.00-1.25)	0.372
Thyroid stimulating hormone (mU/L)	1.10 (0.64-1.99)	1.02 (0.50-2.02)	1.14 (0.64-1.98)	0.519
Free T4 (ng/dL)	1.00 (0.83-1.20)	1.05 (0.79-1.20)	1.00 (0.86-1.20)	0.873
Free T3 (ng/L)	2.39 (2.10-2.80)	2.24 (2.00-2.47)	2.40 (2.12-2.80)	0.089

### **CIN Discrimination Abilities of the New Scoring System**

The diagnostic ability of the new scoring system in predicting CIN development was identified.

The AUC value of the new scoring system for CIN was 0.873 (95% CI: 0.821-0.925). Figure 2 illustrates the ability of scoring systems to distinguish CIN.

**Table III.** Parameters predicting the development of CIN.

Parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	0.959 (0.931-0.987)	0.004		
Male gender	2.090 (0.995-4.387)	0.051	4.874 (2.044-11.621)	< 0.001
LVEF	0.986 (0.961-1.011)	0.266	0.965 (0.936-0.995)	0.024
Congestive heart failure	0.529 (0.252-1.111)	0.092		
Atrial fibrillation	0.328 (0.112-0.961)	0.042		
Diabetes mellitus	1.407 (0.961-2.061)	0.079	1.711 (1.094-2.677)	0.019
Charlson comorbidity index	1.103 (0.983-1.237)	0.096		
Hemoglobin	0.827 (0.702-0.975)	0.024		
Platelet	0.995 (0.991-1.000)	0.070		
Urea	1.024 (1.014-1.035)	< 0.001		
Creatinine	5.161 (2.842-9.371)	< 0.001		
e-GFR, CKD-EPI	0.903 (0.872-0.936)	< 0.001	0.880 (0.845-0.917)	< 0.001
Uric acid	1.140 (0.950-1.368)	0.158		
Sodium	0.925 (0.842-1.017)	0.107		
Calcium	0.505 (0.267-0.958)	0.036		
Triglyceride	1.002 (0.998-1.007)	0.321		
Free T3	0.380 (0.126-1.150)	0.087		



**Table IV.** Multivariate regression analysis for CIN with dichotomous variables of independent predictors.

Parameter	B coefficient	Standard error	OR (95% CI)	p-value
Male gender	1.898	0.497	6.671 (2.521-17.652)	< 0.001
Presence of diabetes mellitus	0.531	0.236	1.701 (1.071-2.700)	0.024
LVEF ≤ 45 percent	1.414	0.463	4.111 (1.660-10.178)	0.002
CKD GFR stages				
Stage 3A	Ref	Ref	Ref	Ref
Stage 3B	1.561	0.629	4.764 (1.388-16.353)	0.013
Stage 4 or 5	4.043	0.677	56.985 (15.128-214.654)	< 0.001

CIN, contrast-induced nephropathy; OR, odds ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; CKD, chronic kidney disease; GFR, glomerular filtration rate.

**Table V.** Components of the new scoring system.

Parameter	Score				
	0 points	1 point	2 points	3 points	4 points
Gender	Female		Male		
Diabetes mellitus	Absent	Present			
LVEF	> 45 percent	≤ 45 percent			
CKD GFR stages	Stage 3A		Stage 3B		Stage 4 or 5

Minimum score: 0, Maximum score: 8. LVEF, left ventricular ejection fraction; CKD, chronic kidney disease; GFR, glomerular filtration rate.

### Discussion

In the current study, we found that male status, diabetes mellitus, low e-GFR, and low LVEF were independently associated with the development of CIN in patients with chronic kidney disease who underwent coronary angiography. We have also provided a CIN risk prediction model based on these four variables. We believe that using this risk prediction tool derived from four

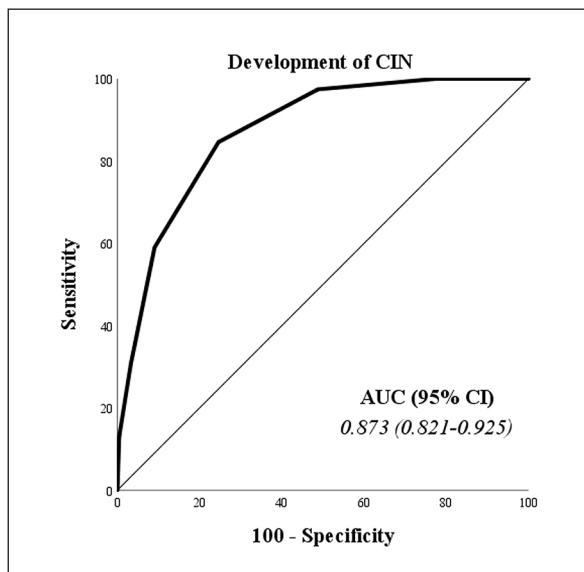
easily accessible and routinely collected variables in routine clinical practice may guide physicians to use preventive medications and techniques in high-risk patients.

Chronic kidney disease has a medical component, but it also has social, economic, and psychological effects on the patients. A patient's chance of acquiring CIN is about 10 times higher if they already have chronic kidney disease<sup>13-15</sup>. The most significant initiating risk fac-

**Table VI.** The ability of the new scoring system to predict CIN at different cut-offs.

Cut-off value	No (%) of patients over the cut-off	OR (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
0.5 point	277 (97.9)	Non-calculated*	100.0	2.5	14.1	100.0
1.5 points	261 (92.2)	Non-calculated*	100.0	9.0	14.9	100.0
2.5 points	228 (80.6)	Non-calculated*	100.0	22.5	17.1	100.0
3.5 points	157 (55.5)	39.9 (5.4-295.3)	97.4	51.2	24.2	99.2
4.5 points†	93 (32.9)	16.9 (6.7-42.2)	84.6	75.4	35.5	96.8
5.5 points	45 (15.9)	14.5 (6.7-31.4)	59.0	91.0	51.1	93.3
6.5 points	20 (7.1)	13.1 (4.9-34.9)	30.8	96.7	60.0	89.7
7.5 points	6 (2.1)	35.7 (4.0-315.1)	12.8	99.6	83.3	87.7

\*When the new scoring score was below 3, OR could not be calculated because no patient developed CIN. †Optimal cut-off based on Youden's index. OR, odds ratio; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.



**Figure 2.** Performance of the new scoring system in predicting the development of CIN.

tor for the development of CIN was found to be pre-existing renal insufficiency in a prospective trial<sup>15</sup> involving 1,144 patients who had coronary angiography. Another study<sup>4</sup> found that of 378 patients who had coronary angiography, 2% developed CIN; however, this risk increased to 30% in those with a baseline creatinine level greater than 1.5 mg/dl. Therefore, a specific focus should be placed on patients with GFRs <60 ml/min since they are more likely to develop CIN. In light of this information, in this study it was decided to study patients with chronic kidney disease. In addition, since many patients with chronic kidney disease are already oliguric, it is hard to interpret CIN in this population. As a result, the CIN risk prediction tool created for the current study may encourage doctors to pay more attention to identifying patients who are at high risk for CIN.

It has been demonstrated in several previous studies<sup>16-18</sup> that having diabetes, being male, and having heart failure are risk factors for the development of CIN in a patient who underwent coronary angiography. For each baseline GFR provided in individuals with CKD, diabetes has been reported to have twice the probability of developing CIN<sup>16</sup>. Additionally, prediabetes was observed to increase the incidence of CIN, and multivariate analysis of the database of 8,357 individuals revealed diabetes to be a 1.6 odd ratio independent risk factor for CIN<sup>17,18</sup>. In a prior study<sup>19</sup> with 386

patients, it was shown that individuals with decreased LVEF had a considerably greater (~2.5) risk of CIN than those with patients with higher LVEF of more than 45%. In addition, a recent meta-analysis<sup>20</sup> of studies providing sex-stratified incidence of CIN demonstrates that the male sex is associated with higher risk of CIN.

However, in addition to providing support for the current literature, our study also adds information. Notably, in this study, we also assigned scores based on how significant these factors were in determining the likelihood of CIN.

### Limitations

There are several limitations to the current study. First, it is not a randomized control study. Second, our approach might not apply to patients who had revascularization because we only included diagnostic patients. In addition, the CM amount was not available; however, since we only included patients who underwent only diagnosed coronary angiography, we assume that the amount of CM was similar in the study population. Last, we were not able to validate our model in a different cohort.

### Conclusions

To the best of our knowledge, this is the first study that provides a risk prediction tool in patients with chronic kidney disease who underwent diagnostic coronary angiography. We found that four easily accessible and routinely collected variables, including sex, diabetes status, e-GFR, and LVEF, were independently associated with the development of CIN in patients with chronic kidney disease who underwent coronary angiography. We believe that using this risk prediction tool derived from four variables in routine clinical practice may guide physicians to use preventive medications and techniques in high-risk patients for CIN. Future studies should be done to validate our provided risk prediction tool.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### Funding

The authors did not receive support or funding from any organization for the submitted work.

### Informed Consent

Not applicable due to the retrospective nature of the study.

### Ethics Approval

This study was conducted following the Declaration of Helsinki and was approved by the Scientific Research Evaluation Commission of Ankara Numune Training and Research Hospital with the decision number E-18-1855 dated 21/03/2018.

### Authors' Contribution

Mustafa Cetin is the principal author of this study and designed the study with resource acquisition, data collection and processing data, data analysis and interpretation, writing-original draft preparation, and editing. All the authors conceived the idea for the article, framing the hypothesis, designed the methods to generate results, data collection and processing data, data analysis and interpretation, writing-original draft preparation, critical review, and edited together. All authors have read and approved the paper.

### ORCID ID

Mustafa Cetin: 0000-0001-7542-6602; Fatih Acehan: 0000-0001-8469-0907; Harun Kundi: 0000-0002-0303-9619; Ilyas Emre Yakıcı: 0000-0003-1137-6233; Bilal Katipoglu: 0000-0002-7235-7979; Gulsah Duran: 0000-0001-6849-0593; Batıkan Yazıcı: -0003-1137-6233; Zehra Guven Cetin: 0000-0001-7140-1010; Ihsan Ates: 0000-0003-2858-6229.

### Availability of Data and Materials

The data and materials generated/analyzed in the present study are available from the corresponding author upon request.

## References

- 1) McCullough PA, Adam A, Becker CR, Davidson C, Lameire N, Stacul F, Tumlin J. Risk Prediction of Contrast-Induced Nephropathy. *Am J Cardiol* 2006; 98: 27-36.
- 2) Muntner P, Whelton PK, Coresh J, Klag MJ, Pernerger T. Exposure to Radiologic Contrast Media and an Increased Risk of Treated End-Stage Renal Disease. *Am J Med Sci* 2003; 326: 353-359.
- 3) Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: A prospective study. *Am J Med* 1983; 74: 243-248.
- 4) Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR. Incidence and Prognostic Importance of Acute Renal Failure After Percutaneous Coronary Intervention. *Circulation* 2002; 105: 2259-2264.
- 5) Detrenis S, Meschi M, Musini S, Savazzi G. Lights and shadows on the pathogenesis of contrast-induced nephropathy: state of the art. *Nephrol Dial Transplant* 2005; 20: 1542-1550.
- 6) Trivedi HS, Moore H, Nasr S, Aggarwal K, Agrawal A, Goel P, Hewett J. A Randomized Prospective Trial to Assess the Role of Saline Hydration on the Development of Contrast Nephrotoxicity. *Nephron Clin Pract* 2004; 93: 29-34.
- 7) Section 4: Contrast-induced AKI. *Kidney Int Suppl* (2011) 2012; 2: 69-88.
- 8) Levey AS, Stevens LA, Schmid CH, Zhang Y (Lucy), Castro AF, Feldman HI, Kusek JW, Eggers P, Lente F van, Greene T, Coresh J. A New Equation to Estimate Glomerular Filtration Rate. *Ann Intern Med* 2009; 150: 604.
- 9) Chapter 1: Definition and classification of CKD. *Kidney Int Suppl* (2011) 2013; 3: 19-62.
- 10) Summary of Recommendation Statements. *Kidney Int Suppl* (2011) 2013; 3: 5-14.
- 11) Chapter 2: Definition, identification, and prediction of CKD progression. *Kidney Int Suppl* (2011) 2013; 3: 63-72.
- 12) Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987; 40: 373-383.
- 13) Jacobson HR. Chronic renal failure: pathophysiology. *Lancet* 1991; 338: 419-423.
- 14) Maddox TG. Adverse reactions to contrast material: recognition, prevention, and treatment. *Am Fam Physician* 2002; 66: 1229-1234.
- 15) Davidson CJ, Laskey WK, Hermiller JB, Harrison JK, Matthai W, Vlietstra RE, Brinker JA, Kereiakes DJ, Muhlestein JB, Lansky A, Popma JJ, Buchbinder M, Hirshfeld JW. Randomized Trial of Contrast Media Utilization in High-Risk PT-CA. *Circulation* 2000; 101: 2172-2177.
- 16) Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB, Dangas G. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention. *J Am Coll Cardiol* 2004; 44: 1393-1399.
- 17) McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute Renal Failure After Coronary Intervention. *Am J Med* 1997; 103: 368-375.
- 18) Toprak O, Cirit M, Yesil M, Bayata S, Tanrısev M, Varol U, Ersoy R, Esi E. Impact of diabetic and pre-diabetic state on development of contrast-induced nephropathy in patients with chronic kidney disease. *Nephrol Dial Transplant* 2007; 22: 819-826.
- 19) Shacham Y, Leshem-Rubinow E, Gal-Oz A, Topilsky Y, Steinvil A, Keren G, Roth A, Arbel Y. Association of Left Ventricular Function and Acute Kidney Injury Among ST-Elevation Myocardial Infarction Patients Treated by Primary Percutaneous Intervention. *Am J Cardiol* 2015; 115: 293-297.
- 20) Neugarten J, Golestaneh L. Female sex reduces the risk of hospital-associated acute kidney injury: a meta-analysis. *BMC Nephrol* 2018; 19: 314.