Cardiovasc Surg Int 2023;10(2):97-102
http://dx.doi.org/DOI: 10.5606/e-cvsi.2023.1527
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Predictors of contrast nephropathy after percutaneous intervention of chronic total occlusion in patients with chronic coronary syndrome: A single-center study

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Received: April 30, 2023 ***Accepted:*** May 12, 2023 ***Published online:*** July 21, 2023

ABSTRACT

Objectives: This study was planned to determine the predictors of contrast nephropathy developing after percutaneous coronary intervention (PCI) in patients who underwent coronary angiography due to chronic coronary syndrome and were found to have chronic total occlusion (CTO).

Patients and methods: The retrospective observational study included 110 patients with chronic coronary syndrome who were diagnosed with CTO between March 2017 and February 2023. All patients were divided into two groups: 53 patients (29 males, 14 females; mean age: 62.8±10.2 years; range, 42 to 84 years) who developed contrast-induced nephropathy (Group 1) and 57 patients (38 males, 19 females; mean age: 58.8±11.2 years; range, 37 to 79 years) who did not (Group 2).

Results: The mean age of the patients in Group 1 was statistically greater than in Group 2 (p=0.04). In the multivariate regression analysis we performed for the prediction of contrast nephropathy in patients with CTO, chronic renal failure (OR: 0.025; 95% CI: 0.001-0.430, p=0.01), amount of opaque substance (OR: 1.115; 95% CI: 1.031-1.206, p=0.006), left ventricular ejection fraction (OR: 0.683; 95% CI: 0.551-0.847, p=0.001), and glucose (OR: 1.046; 95% CI: 1.014-1.078, p=0.004) were found to be independent predictors of contrast nephropathy.

Conclusion: Our study revealed that baseline high creatinine (underlying chronic renal failure), high blood sugar that increases plasma osmolarity (uncontrolled diabetes mellitus), high amount of opaque material used, and low left ventricular ejection fraction are predictors of post-PCI contrast nephropathy. Paying attention to correctable risk factors before giving opaque material to patients for whom PCI is planned is valuable in terms of reducing kidney damage.

Keywords: Chronic coronary syndrome, chronic total occlusion, contrast nephropathy, predictor.

Atherosclerosis shows a progressive course as a result of inflammation, which causes coronary artery disease and shows systemic involvement.[1] In the 2019 European Society of Cardiology chronic coronary syndrome (CCS) guideline, patients with stable coronary artery disease were defined as CCS, and new protocols were developed for these patients. Coronary angiography (CAG) and percutaneous coronary intervention (PCI) are still the primary options in the diagnosis and treatment of these patients.[1]

Chronic total occlusion (CTO) is a condition that is characterized by complete occlusion of the coronary arteries for at least three months and is encountered in approximately 20% of CAGs (Figure 1). Apart from being detected as a vascular occlusion not associated with infarction in patients with acute coronary syndrome, it can also be seen in patients with CCS. Chronic total occlusion is attempted to be treated with PCI or coronary artery bypass graft, but the results can sometimes be unfavorable.[2-4] The method chosen for treatment is affected by various factors. Factors such as the experience of the operator, selected PCI materials (such as guide catheter, guide wire), location, length, anatomy of coronary occlusion, and presence of calcification are important.[5] Revascularization of CTO takes more time and may cause various complications since it is an area of interventional cardiology with a high level of difficulty.

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Citation:
Yurdam FS, Demir Y, Bakır EO, Başkurt AA. Predictors of contrast nephropathy after percutaneous intervention of chronic total occlusion in patients with chronic coronary syndrome: A single-center study. Cardiovasc Surg Int 2023;10(2):97-102. doi: 10.5606/e-cvsi.2023.1527.

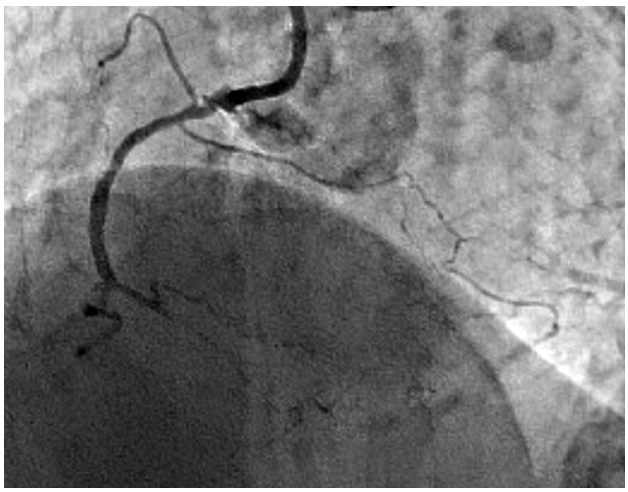

Figure 1. Coronary angiography image of a patient with chronic total occlusion.

Although the most important instrument used during PCI is the contrast agent (opaque material), one of the undesirable effects is contrast agent-induced nephropathy. It has been suggested that contrast media-induced nephropathy occurs with the synergistic effect of direct renal tubular cell toxicity and renal medullary ischemia. Contrast nephropathy is thought to occur with direct cytotoxicity, cell damage after contrast administration, and histological changes in enzymuria.

The nature of the contrast, associated ions, concentration, and concomitant hypoxia are important for the degree of cellular damage, while the osmolality of the solution appears to be of secondary importance. Contrast injection causes a biphasic hemodynamic change in the kidney, with an initial transient increase followed by a longer-lasting reduction in renal blood flow.[6,7] In previous studies, the reasons that increase contrast nephropathy were examined and clinical conditions to be avoided were explained. The most important thing is the presence of chronic renal failure (CRF), a history of diabetes mellitus (DM), and heart failure.[8] This study aimed to determine the predictors of contrast nephropathy in patients with CCS who underwent PCI for CTO.

PATIENTS AND METHODS

The retrospective observational study included 110 patients with CTO who applied to the cardiology outpatient clinic of the Bakırçay University Çiğli Training and Research Hospital between March 2017 and February 2023 and were diagnosed with CCS with noninvasive tests and underwent CAG. Patients older than 18 years of age and with optimal CAG images were included in the study. Patients with a history of percutaneous transluminal coronary angioplasty with coronary artery bypass graft, those with active infection or severe liver failure, and patients whose kidney function test results could not be obtained were excluded from the study. Demographic data, comorbid histories, routine blood tests and transthoracic echocardiography data of the patients in the study were noted by looking at the hospital data recording system. All patients were divided into two groups: 53 patients (29 males, 14 females; mean age: 62.8±10.2 years; range, 42 to 84 years) who developed contrast-induced nephropathy (Group 1) and 57 patients (38 males, 19 females; mean age: 58.8±11.2 years; range, 37 to 79 years) who did not (Group 2).

Smoking was accepted if the patients were active users according to their verbal expressions. Blood pressure above 140/90 mmHg with repeated measurements or the use of oral antihypertensive drugs was defined as having hypertension, which is one of the comorbidities. A glomerular filtration rate below 60 mL/min for CRF, total cholesterol >200 mg/dL, low-density lipoprotein cholesterol >130 mg/dL or triglyceride >150 mg/dL for hyperlipidemia, and for heart failure left ventricular ejection fraction (LVEF) <50% was taken as the defining criterion. A 25 to 50% increase in serum creatinine levels at 48 h post angiography from baseline is recommended to define contrast nephropathy.[9,10]

Coronary angiography was performed on all patients in the study using the standard Judkins technique. The patients were started with the necessary premedication during PCI. Dual antiplatelet therapy was given at a loading dose for each patient. Coronary angiography images were viewed via the imaging software system, and the presence of CTO in any coronary artery, the presence of calcification in the relevant coronary artery, and the development of collateral circulation were evaluated. The data of the opaque substance used during PCI and the duration of the interventional procedure for these patients, which can be accessed through the hospital information management system, were noted.

Statistical analysis

Data were analyzed using IBM SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Distribution normality analysis of continuous variables was evaluated according to the Shapiro-Wilk test. Normally distributed continuous variables were analyzed with Student's t-test and presented as mean and standard deviation. Nonnormally distributed continuous variables nonnormally distributed were presented as median and interquartile range and analyzed using the Mann-Whitney U test. Categorical variables were reported as number and frequency and assessed using the Pearson chi-square test and Fisher exact test. Logistic regression analysis was performed to estimate the presence of contrast nephropathy. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the patients in Group 1 was statistically greater than in Group 2 (62.8±10.2 years *vs.* 58.8±11.2 years, p=0.04). Among the comorbid

Table 1
Demographic, clinical, and angiographic characteristics

	Contrast nephropathy (+) (n=53)			Contrast nephropathy (–) (n=57)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			62.8±10.2			58.8±11.2	0.04
Sex							
Male	29	55		45	67		0.16
Smoking	21	40		27	40		0.94
Hypertension	24	45		21	31		0.11
Diabetes mellitus	24	45		18	27		0.03
Heart failure	29	55		15	22		0.001
Chronic renal failure	11	20		5	7		0.03
Hyperlipidemia	12	23		16	24		0.87
Drugs							
Oral antidiabetics	22	41		16	24		0.04
Insulin	3	6		4	6		0.63
Betablocker	10	19		5	7		0.06
Calcium channel blocker	7	13		8	12		0.83
RAS blocker	23	43		21	31		0.17
Statin	12	23		16	24		0.87
Diuretic	12	23		7	10		0.06
Angiographic findings							
Interference artery							0.09
Right coronary artery	17	32		31	46		
Circumflex artery	13	24		32	48		
LAD artery	23	43		4	6		
Presence of calcification	13	24		7	10		0.05
Duration of PCI (min)			81±20			65±18	**0.001**
Opaque amount (mL)			242±33			200±22	**0.001**
Collateral development	28	52		32	48		0.58

SD: Standard deviation; RAS: Renin angiotensin system; LAD: Left anterior descending; PCI: Percutaneous coronary intervention.

diseases, DM (45% *vs.* 27%, p=0.03) and CRF (20% *vs.* 7%, p=0.03) were significantly higher in Group 1 than in Group 2. Among the angiographic findings of the patients, the duration of coronary intervention (81±20 min *vs.* 65±18 min, p=0.001) and the amount of opaque material used (242±33 mL *vs.* 200±22 mL, p=0.001) were higher in Group 1 than in Group 2. Demographic, clinical, and angiographic characteristics of the patients are shown in detail in Table 1.

Looking at the laboratory analysis results, fasting blood glucose [177 (108-254) mg/dL *vs.* 109 (92-127) mg/dL, p=0.001] and 48th h creatinine [1.23 (1.15-1.36) mg/dL *vs.* 0.93 (0.83-1.05) mg/dL, p<0.001] values were higher in Group 1 than in Group 2. Only two patients who developed contrast nephropathy during follow-up after PCI required acute hemodialysis. Left ventricular ejection fraction measured by echocardiography was significantly lower in Group 1 than in Group 2 [40% (34-50%) *vs.* 50% (50-55%), p<0.001]. Laboratory analysis results of the patients are given in Table 2.

In the univariate regression analysis performed for the prediction of contrast nephropathy in patients with CTO, age [odds ratio (OR): 1.035; 95% confidence interval (CI): 1.000-1.071, p=0.051], DM (OR: 0.444; 95% CI: 0.207-0.953, p=0.04), CRF (OR: 0.308; 95% CI: 0.100-0.951, p=0.04), oral antidiabetic use (OR: 2.262; 95% CI: 1.033-4.952, p=0.04), duration of PCI (OR: 1.045; 95% CI: 1.023-1.068, p<0.001), amount of opaque substance (OR: 1.058; 95% CI: 1.036-1.080, p<0.001), LVEF (OR: 0.852; 95% CI: 0.799-0.909, p<0.001), and glucose (OR: 1.024; 95% CI: 1.013-1.035, p<0.001) were defined as markers of contrast nephropathy. In multivariate regression analysis, CRF (OR: 0.025; 95% CI: 0.001-0.430, p=0.01), amount of opaque substance (OR: 1.115; 95% CI: 1.031-1.206, p=0.006), LVEF (OR: 0.683; 95% CI: 0.551-0.847, p=0.001), and glucose (OR: 1.046; 95% CI: 1.014-1.078, p=0.004) were found to be independent predictors of contrast nephropathy (Table 3).

Table 2
Laboratory results of patients

	Contrast nephropathy (+) (n=53)			Contrast nephropathy (–) (n=57)			
Variables	Mean±SD	Median	IQR (Q1-Q3)	Mean±SD	Median	IQR (Q1-Q3)	*p*
LVEF (%)		40	34-50		50	50-55	**<0.001**
Glucose (mg/dL)		177	108-254		109	92-127	**0.001**
Urea (mg/dL)		37	31-42		34	27-42	0.33
Creatinine (mg/dL)		0.85	0.77-1.04		0.85	0.77-0.97	0.52
Creatinine 48th h (mg/dL)		1.23	1.15-1.36		0.93	0.83-1.05	**<0.001**
Sodium (mEq/L)		139	135-140		138	137-140	0.62
Potassium (mEq/L)		4.3	4.1-4.6		4.4	4.1-4.6	0.63
Calcium (mg/dL)		9.2	8.8-9.5		9.2	8.9-9.5	0.92
Total cholesterol (mg/dL)		152	130-205		168	135-210	0.24
Trygliceride (mg/dL)		139	96-211		146	107-240	0.40
HDL (mg/dL)		43	38-48		43	35-48	0.35
LDL (mg/dL)		73	57-111		86	669-132	0.06
Hemoglobin (mg/dL)		14	12.6-14.8		14.4	12.7-15.2	0.09
Thrombocyte (10^9/L)	243±79			244±66			0.93
White blood cell (10^9/L)	9.12±2.72			9.12±2.46			0.98
Neutrophil (10^9/L)	6.05±2.49			5.71±2.34			0.44

SD: Standard deviation; IQR: Interquartile range; Q: Quartile; LVEF: Left ventricle ejection fraction; HDL: High density lipoprotein; LDL: Low density lipoprotein.

Table 3
Logistic regression analysis

	Univariate logistic regression			Multivariate logistic regression		
Variables	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.035	1.000-1.071	0.051	-		
Diabetes mellitus	0.444	0.207-0.953	0.04	0.580	0.001-303.622	0.86
Chronic renal failure	0.308	0.100-0.951	0.04	0.025	0.001-0.430	0.01
Oral antidiabetic use	2.262	1.033-4.952	0.04	6.635	0.011-4001.272	0.56
Duration of PCI	1.045	1.023-1.068	<0.001	1.013	0.938-1.094	0.74
Opaque amount	1.058	1.036-1.080	<0.001	1.115	1.031-1.206	0.006
LVEF	0.852	0.799-0.909	<0.001	0.683	0.551-0.847	0.001
Glucose	1.024	1.013-1.035	<0.001	1.046	1.014-1.078	0.004

OR: Odds ratio; CI: Confidence interval; PCI: Percutaneous coronary intervention; LVEF: Left ventricle ejection fraction.

DISCUSSION

The main finding of our study is that a history of CRF, excess contrast material used, low LVEF, and high plasma glucose level are predictive of contrast nephropathy in patients with CCS who underwent PCI for CTO. It has been shown in previous studies that the most important predisposing factor in the development of contrast nephropathy is the presence of underlying CRF. Persistence of damage to kidney function after contrast nephropathy has been associated with the degree of CRF. Even if hemodialysis is not needed most of the time, contrast can cause permanent damage in 30% of patients affected by nephropathy.[8-11] In a retrospective study by Lewy et al.,[12] mortality and length of hospital stay were found to be significantly higher when the group that developed contrast nephropathy was compared to the control group, and this result was found due to the findings of acute kidney failure. Again, in the long-term follow-up results of Guzel et al.[13] in patients with CTO, mortality was higher in the group with contrast nephropathy after PCI. The most important measure to avoid contrast nephropathy is to use the least amount of contrast material possible. In previous meta-analyses, the increase in the amount of contrast material used and the use of opaque materials with high osmolarity increased the risk of nephrotoxicity.[14,15]

In previous studies, intravenous fluid administration at least 2 h before and after the procedure to patients with subclinical dehydration before contrast administration has been shown to reduce contrast nephropathy.[16,17] Based on this data, we can conclude that the higher blood osmolarity of patients with higher fasting plasma glucose may lead to contrast nephropathy. In addition, hyperglycemia itself can increase oxidative stress as a result of free oxygen radicals, resulting in both adverse effects on the pathophysiology of DM and damage to the renal tubular system.[18]

Shacham et al.[19] investigated the effect of left ventricular systolic function on acute kidney injury in patients with acute myocardial infarction (AMI) and showed that the prognosis is poor in older patients with impaired renal function and low LVEF. Wang et al.[20] found a higher risk of developing contrast nephropathy in patients with low ejection fraction in their study of the relationship between contrast nephropathy and LVEF after CAG in patients with heart failure. In our study, LVEF was found to be lower in the group with contrast nephropathy.

The main limitations of the study were that it was a single-center study and retrospective in design. In addition, data on hemodynamic variability during the angiography procedure, whether patients were hydrated with intravenous fluid before the procedure, and long-term follow-up results were lacking.

In conclusion, a high creatinine value at baseline (underlying CRF), high blood sugar that increases plasma osmolarity (uncontrolled DM), high amount of contrast agent used, and low LVEF are predictors of contrast nephropathy in patients with CCS who underwent PCI for CTO. Paying attention to the risk factors that can be corrected before the administration

of contrast material to patients is valuable to reduce renal damage.

Ethics Committee Approval: The study protocol was approved by the Bakırçay University Non-Invasive Clinical Ethics Committee (date: 08.03.2023, no: 2023/905). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: Written informed consent was not obtained as this study was retrospective.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Collected study data, wrote the main manuscript, and prepared the tables: F.S.Y.; Performed statistical analyses the article: A.A.B.; Reviewed the article: Y.D., E.O.B.; All authors have read and approved the final article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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