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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

THE EFFECT OF CONTRAST AGENT USED DURING VASCULAR IMAGING AND ENDOVASCULAR TREATMENT ON NEPHROPATHY AND PROGNOSIS IN ACUTE STROKE PATIENTS ADMITTED TO THE EMERGENCY DEPARTMENT

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ABSTRACT

INTRODUCTION: The study investigated the incidence of contrast-induced nephropathy in patients with acute ischemic stroke who received recombinant tissue plasminogen activator (rt-PA) and/or endovascular therapy (EVT) after contrast-enhanced computed tomography (CT) angiography and identified potential risk factors for nephropathy.
METHODS: A comparison was made between the groups who received and did not receive contrast material and who developed nephropathy and those who did not, regardless of the use of contrast. Binary logistic regression analysis was used to determine the risk factors for nephropathy.
RESULTS: Of 421 patients, 291 (70.9%) were treated with IV rt-PA, and 119 (29%) received EVT. The number of patients receiving contrast media was 194 (75 in CTA and 119 in EVT). No relationship was found between the use of contrast media and the development of nephropathy (p=0.068) and no difference was found in terms of nephropathy between the treatment options (IV rt-PA/endovascular) (p=0.959). Mortality was higher (41.2% versus 15.7%; p<0.001) and mRS at 3rd months was worse (67.6 vs 46.5%; 25 p=0.018) in the group that developed nephropathy (41.2% versus 15.7%; p<0.001). The major risk factors for developing nephropathy in stroke patients were female gender, hemoglobin elevation, and high NIHS score at admission.
DISCUSSION AND CONCLUSION: There is utility in obtaining baseline creatinine levels to identify patients at risk of contrast-associated acute kidney injury and to establish a diagnosis of contrast-associated acute kidney in patients with subsequent creatinine rises. However, contrast-requiring diagnostic imaging should not be delayed by waiting for the results of the baseline renal function.
Keywords: Acute ischemic stroke, contrast -induced nephropathy, acute kidney injury, endovascular treatment, vascular imaging.

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ACİL SERVİSE BAŞVURAN AKUT İNME HASTALARINDA VASKÜLER GÖRÜNTÜLEME VE ENDOVASKÜLER TEDAVİ SIRASINDA KULLANILAN KONTRAST MADDENİN NEFROPATİ VE PROGNOZ ÜZERİNDEKİ ETKİSİ

ÖZ

GİRİŞ ve AMAÇ: Çalışma, akut iskemik inme hastalarında kontrastlı bilgisayarlı tomografi (BT) anjiyografisinden sonra rekombinant doku plazminojen aktivatörü (rt-PA) ve/veya endovasküler tedavi (EVT) uygulanan kontrast kaynaklı nefropati insidansını araştırmış ve nefropatiye yol açan potansiyel risk faktörlerini tanımlamıştır.
YÖNTEM ve GEREÇLER: Kontrast madde alan ve almayan, nefropati gelişen ve gelişmeyen gruplar arasında kontrast kullanımına bakılmaksızın karşılaştırma yapıldı. Nefropati risk faktörlerini belirlemek için ikili lojistik regresyon analizi kullanıldı.
BULGULAR: 421 hastanın 291'i (%70,9) IV rt-PA ile tedavi edildi ve 119'u (%29) EVT aldı. Kontrast madde verilen hasta sayısı 194 (BTA'da 75, EVT'de 119) idi. Kontrast madde kullanımı ile nefropati gelişimi arasında ilişki bulunmadı (p=0,068) ve tedavi seçenekleri arasında (IV rt-PA/endovasküler) nefropati açısından fark bulunmadı (p=0,959). Nefropati gelişen grupta mortalite daha yüksek (%41.2'ye karşı %15.7; p<0.001) ve 3. ayda mRS daha kötüydü (%67.6'ya karşı %46.5; 25 p=0.018) (%41.2'ye karşı %15.7; p<0.001). İnme hastalarında nefropati gelişimi için başlıca risk faktörleri kadın cinsiyet, hemoglobin yüksekliği ve başvuru anında yüksek NIHS skoru idi.
TARTIŞMA ve SONUÇ: Kontrastla ilişkili akut böbrek hasarı riski taşıyan hastaları belirlemek ve daha sonra kreatinin yükselmeleri olan hastalarda kontrastla ilişkili akut böbrek tanısı koymak için temel kreatinin düzeylerinin elde edilmesinde fayda vardır. Bununla birlikte, kontrast gerektiren tanısal görüntüleme, başlangıçtaki böbrek fonksiyonunun sonuçları beklenerek geciktirilmemelidir.
Anahtar Sözcükler: Akut iskemik inme, kontrast ilişkili nefropati, akut böbrek yetmezliği, endovasküler tedavi, vasküler görüntüleme.

INTRODUCTION

Stroke is one of the leading causes of morbidity and mortality in the world. Regarding the change in acute stroke protocols, multimodal computed tomography angiogram (CTA) is required for the assessment of major cerebral vessel occlusion and collateral status. Current guidelines recommended endovascular therapy (EVT) in stroke patients with large vessel occlusion (1). The contrast material applied during both CTA and EVT increases the risk of renal dysfunction.

Contrast-induced nephropathy (CIN) is one of the most common causes of hospital-acquired acute renal function impairment and is associated with increased morbidity and mortality. CIN is defined as a 25% increase in serum creatinine (sCr) from baseline or 0.5 mg/dl increase in absolute sCr value within 48–72 hours of intravenous (IV) contrast administration without an alternative aetiology (2). The use of intra-arterial contrast includes greater risk of CIN than using IV contrast (3). Although CTA is generally well tolerated, CIN is a serious side effect reported in 7%–14.8% of patients receiving contrast media (3-5). Furthermore, CIN can be observed in up to 20%–30% of high-risk groups, including patients with hypertension, hypotension, anaemia, age over 75 years, chronic kidney disease, congestive heart failure, diabetes mellitus (DM), peripheral vascular disease and female gender (6). Majority of the studies on the risk of CIN have investigated patients who underwent computed tomography (CT) with a contrast media or a percutaneous coronary intervention (PCI) (7). However, the incidence of CIN related to the administration of contrast media in CT is controversial due to their designs. In a study, CIN could be detected as a frequent complication after PCI in acute myocardial infarction patients. There is limited evidence about the risk of CIN in acute stroke patients receiving CTA and/or EVT. Therefore, we aimed to determine the incidence of CIN in patients with acute ischaemic stroke who underwent IV recombinant tissue plasminogen activator (rt-PA) and/or endovascular stroke treatment after CTA and delineate the potential risk factors leading to CIN.

METHODS

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the Non-Invasive Clinical Research Ethics Committee of Eskişehir Osmangazi University (Date: 21.04.2020, No: 08). The study center is a tertiary hospital.

This is a retrospective analysis of database included patients who admitted to the emergency department (ED) with acute ischemic stroke and underwent multimodal CTA and/or angiography before the initiation of recanalization stroke treatment, including IV rt-PA and/or EVT, between 2010 and 2017. Acute stroke patients who received IV rt-PA and/or underwent endovascular treatment between 18 and 90 years of age were included in the study. All eligible acute ischemic stroke patients with confirmed large-vessel occlusion (Tandem internal carotid-middle cerebral artery (MCA) occlusion, MCA M1, M2 occlusion, carotid T occlusion, basilar artery occlusion) on non-contrast CT and contrast-enhanced neck–brain CTA were treated with EVT within 8 hours of symptom onset. All patients arrived within 4.5 hours of acute stroke onset, and IV rt-PA was administered (0.9 mg/kg of body weight) until the patient reached the angio-suit (1). Patients who had no proximal major vessel occlusion were treated with IV rt-PA alone. Those who had a contraindication for IV rt-PA underwent only endovascular treatment. Prior to 2017, CTA was not the standard neuroimaging tool, and patients who underwent only IV rt-PA within 4.5 hours of stroke onset after plain CT were included in the study as a control group. CT and CTA were assessed by a stroke and interventional neurologist. Endovascular stroke procedures were performed by two interventional neurologists with at least five years of experience.

Patients who had a medical history of chronic renal disease, active cancer patients and patients who had a CTA performed outside the facility were excluded from the analyses.

The patients were divided into two groups: Those who received contrast media (during CTA and/or endovascular intervention - group 1) and those who underwent IV rt-PA without CTA (non-contrast media - group 2).

Data Source and Patient Collection: A standard stroke patient management protocol was followed according to the current stroke guidelines (1). Written informed consent was obtained before the procedure (CTA and/or endovascular) from all the patients or from their close relatives. Patient's age, gender, medical history, current smoking status, current alcohol use status, the presence of IV rt-PA treatment, complications after IV rt-PA and/or EVT, admission blood pressure, baseline glucose and laboratory tests (white blood cell (WBC), haemoglobin, platelet, triglyceride, HDL, LDL), length of stay in stroke unit and modified Rankin scale (mRS) at 3rd month were recorded from the database. Baseline stroke severity was assessed with the National Institutes of Health Stroke Scale (8). All sCr and blood urea nitrogen (BUN) values at admission before contrast media administration and at 48 hours after CT/CTA and/or endovascular procedure were recorded from the hospital stroke database. Complete patient history was obtained, and full physical examination was performed by the attending physician and/or the senior emergency medicine residents and stroke team. If there was no history of renal disease, emergency CTA was performed regardless of the creatinine level.

Assessment of CIN: CIN was defined as >25% or 0.5 mg/dl increase in sCr value from baseline within 48 hours (2). According to our institutional protocol, hydration (0.45 normal saline solution at 75 mL/h for both 12 h) pre-catheterization and post-catheterization was done after emergency procedures.

Collection of Blood Samples: Blood samples used to obtain the sCr and BUN values were evaluated using the Roche Cobas 501 biochemistry device by photometric method. Samples were obtained before the use of contrast media during the first admission of patients to the emergency room and 48 hours after hospitalisation in stroke intensive care. The Chronic Kidney Disease Epidemiology Collaboration equation was used to calculate estimated glomerular filtration rate (eGFR) (9).

Neuroimaging Contrast Media: Non-contrast CT (NCCT) and CTA were performed at the time of admission as standard protocols. The axial CT was done with a multi-section scanner (SOMATOM Perspective; Siemens Healthcare) using 130 kV and 280 mAs with a 5 mm section thickness. Continuous axial sections were obtained from the base of the skull to the apex, parallel to the orbit meatal line. After NCCT, CTA was obtained by a helix scanning technique using the same scanner. Following the single bolus IV contrast injection of 70–90 ml non-ionic iodinated contrast media iopamidol (Ultravist™, Bayer Healthcare, Inc.) at 5 ml/sec with a delay of 20–25 seconds after the start of contrast injection, acquisitions were achieved. The imaging was automatically started by the appearance of contrast media in the aorta. The CTA was reconfigured at 0.625 mm intervals to 1.25 mm thickness. A follow-up NCCT was

performed at least 24 hours after symptom onset. 100–200 ml non-ionic iodinated contrast media Ultravist 300 mg/100 mL was used in endovascular treatment.

Statistical Analysis: Patients' demographic features were presented through descriptive statistical information such as number, percentage, and standard deviation (SD). Shapiro-Wilk test was used to check the conformity of the data to normal distribution. Ordinal variables were presented as median values and interquartile ranges (IQRs). Categorical variables were summarised as frequencies and percentages. Mann-Whitney U and Kruskal-Wallis tests were used for determining the factors associated with CIN. Odds ratios were presented with 95% confidence intervals (95% CI). P value of <0.05 was considered statistically significant in all analyses. Binary logistic regression analysis was used to determine the risk factors for CIN. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM-SPSS version 26, Chicago, Illinois, USA).

RESULTS

A total of 421 acute ischaemic stroke patients were included in the study for evaluation. Eleven patients were excluded from the study since creatinine control values could not be obtained at the 48th hour. Four hundred and ten patients, comprising 231 males (56.3%), were included in the final analysis. Their mean age was 63.84±11.52 (18-85) years.

Of the 410 patients, 291 (70.9%) were treated with IV rt-PA, and 119 (29%) received endovascular treatment. The total number of patients who received contrast media was 194 (47.31%) (75 patients during CT and 119 patients during angiography). Thirty-four (8.29%) patients met the criteria for nephropathy: 11 of 194 (5.6%) patients who received contrast media (1 IV rt-PA and 10 endovascular treatment) and 23 of 216 (10.6%) patients (underwent IV rt-PA treatment) who did not receive contrast media. As seen in Table 1, no relationship was found between the use of contrast media and the development of nephropathy (p=0.068) and no difference was found in terms of nephropathy between the treatment options (IV rt-PA/endovascular) (p=0.959).

In the comparison of the variables between the contrast and non-contrast groups, age (p<0.001) and DM incidence were lower (p<0.05) and smoking (p<0.005), WBC count (p<0.05) and baseline NIHSS score were higher in the contrast group. However, no difference was found in the other variables (Table 2).

A comparison of renal functions with contrast administration is given in Table 3. According to contrast media administration, there was a difference in the sCr and BUN measurements, but no difference was found in the eGFR. There was a significant difference among sCr, BUN and eGFR in the 48th hour measurements.

Regardless of the use of contrast media, age, gender, comorbidity, habits, laboratory findings, hospital length of stay, admission NIHSS scale and 3rd month mRS had no effect on the development on nephropathy, and a difference was found only in the NIHSS score at first admission to ED (p=0.023) (Table 4) (NIHSS was lower in those who developed nephropathy; 16 versus 18). However, no relationship was found between the contrast and non-contrast groups (p=0.959).

The effects of nephropathy development, contrast media administration and treatment options on clinical management and mortality were examined, and mortality was found to be higher (41.2% versus 15.7%; p<0.001), symptomatic haemorrhage capable of causing a decrease in the NIHSS score of 4 or more points within 36 hours was more frequent (11.8% vs 3.7%; p<0.05) and mRS at 3rd month was worse (3-6) (67.6 vs 46.5%; p=0.018) in the group with nephropathy. In the non-contrast group, mRS after 3 months was worse (p=0.021).

When the endovascular and rtPA treatments were compared with respect to clinical management mortality was higher in the patients who underwent EVT (14.8% versus 25.2%; p=0.012), and dramatic improvement within 24 hours was also higher in the EVT (48.7% versus 37.5%; p=0.035) (Table 5).

Finally, in the multivariate logistic regression analysis conducted to determine the independent risk factors for the development of nephropathy in stroke patients, the significant factors were determined as female gender, lack of contrast administration, haemoglobin elevation, and high NIHS score at admission (Table 6).

Table 1. The relationship between the use of contrast media and the development of nephropathy.

	Contrast n=194 (%)		Non-contrast n=216 (%)		p
	Patient with nephropathy 11 (5.6%)	Patient without nephropathy 183 (94.3%)	Patient with nephropathy 23 (10.6%)	Patient without nephropathy 193 (89.3)	0.068*
rtPA (n=291)	1	74	23	193	
Mechanical thrombectomy (n=119)	10	109	-	-	

*Pearson Chi-Squared test was used.

Table 2. Comparison of patient characteristics and procedural and outcome parameters in with and without contrast exposure.

Variable Patients	Contrast agent (+) (n=194), (%)	Contrast agent (-) (n=216), (%)	p
Age in years*	63 (52-69)	70 (61.25-75)	**< 0.001**
Male (%) **	102 (52.6)	129 (59.7)	0.145
Comorbidities			
DM **	47 (24.2)	78 (36.1)	**<0.05**
HT**	117 (60.3)	146 (67.6)	0.125
AF **	71 (36.6)	69 /(31.9)	0.321
Hyperlipidemi**	86 (44.3)	108 (50)	0.34
Habitat			
Smoker **	89 (45.9)	74 (34.3)	**<0.05**
Alcohol **	10 (5.2)	5 (2.3)	0.12
Laboratory Findings			
White blood cell (x103 cells/mm3) *	9.6 (8.1-11.8)	8.95 (7.36-10.8)	**<0.05**
Platelet (109 /l)**	234 (193-283)	225 (192-271)	0.275
Triglyceride (mg/dl)*	120 (86-172)	127.5 (93-166)	0.279
HDL (mg/dl)* *	42 (34-52)	45 (36-53)	0.159
LDL (mg/dl)**	119.5 (90-145)	116 (93-145)	0.747
Hemoglobin (g/dl)*	13.5 (12.3-14.7)	13.6 (12.2-14.9)	0.891
Baseline glucose*	134.5 (110-175)	128 (108-171)	0.535
Clinical status			
NIHSS baseline*	18 (12-22)	15 (10-18)	**<0.001**
Hospital admission (day)*	8 (5-13.250)	7 (5-11)	0.073
mRS 3 th months*	2 (1-5)	3 (1-5)	0.076

*Median (Q1-Q3), P value derived from t test. **n (percent), P value derived from chi-square test.

Table 3. Comparison of renal functions with contrast administration.

Variable*	Contrast agent (+) (n=194)	Contrast agent (-) (n=216)	p
Baseline creatinine (mg/dl)	0.91 (0.79-1.03)	0.95 (0.78-1.15)	**<0.05**
48.h creatinin (mg/dl)	0.82 (0.68-0.94)	0.95 (0.8-1.14)	**<0.001**
	<0.001	<0.001	
Baseline BUN (mg/dl)	18.05 (13.47-26.2)	34 (26.3-47.75)	**<0.001**
48. h BUN (mg(dl)	15 (11.57-19.57)	18 (12.2-24.59)	**<0.001**
	<0.001	<0.001	
Baseline GFR (mL/min/1.73 m^2)	79.83 66.24-93.7)	77.5 (57.48-92.34)	0.70
48. h GFR (mL/min/1.73 m^2)	92 (76.1-108.26)	74 (58.4-93.96)	**<0.001**
	<0.001	<0.001	

*Median (Q1-Q3), P value derived from t test. **Mann-Whitney U test.

Table 4. Comparison of patients with and without nephropathy.

Variable	Patients with nephropathy (n=34), (%)	Patients without nephropathy (n=376), (%)	p
Age in years, mean (±SD)*	62.5 (±10.5)	63.63 (12)	0.190+
Male (%) **	16 (47.1)	215 (57.2)	0.254++
Comorbidities			
DM **	13 (38.2)	112 (29.9)	0.310++
HT**	23 (67.6)	240 (63.8)	0.657++
AF **	13 (38.2)	127 (33.8)	0.600++
Hyperlipidemi**	18 (52.9)	176 (47.3)	0.529++
Habitat			
Smoker **	13 (38.2)	150 (39.9)	0.850++
Alcohol **	1 (2.9)	14 (13.7)	1.000+++
Laboratory Findings			
White blood cell (x103 cells/mm3) *	9.45 (7.88-11.27)	9.2 (7.71-11.4)	0.436++
Platelet (109 /l)**	245 (189-296)	229 194-275)	0.634++
Triglyceride(mg/dl)*	139 (101-180)	121 (88*166)	0.074++
HDL (mg/dl)* *	42 (32-50)	44 (35-53)	0.261++
LDL (mg/dl)**	115 (88-135)	118 (91-146)	0.373++
Hemoglobin (g/dl)*	14.2 (12.62-15.65)	13.5 (12.3-14.7)	0.113++
Clinical status			
NIHSS baseline*	18 (12-22)	16 (10-20)	**0.023**++
Hospital admisssion (day)*	8 (5-13)	8 (5-12)	0.625++

*Median (Q1-Q3), P value derived from t test.**n (percent)/SD, + Mann-Whitney U test, ++Pearson Chi-squared test, +++Fisher Exact test.

Table 5. Comparison of patient clinical outcome parameters.

Clinical outcome	Contrast exposure (n=194)	Non-contrast (n=216)	p
Mortality (Yes: 73)	36 (18.6%)	37 (17.1%)	0.706*
Dramatic improvement within 24 hours (NIHSS = 0-1 or> 8 reductions in NIHSS)(n=167)	80 (41.2%)	87 (40.3%)	0.844*
Symptomatic hemorrhagea (Decrease in the NIHSS score of 4 or more points within 36 hours) (n=18)	8 (4.1%)	10 (4.6%)	0.803*
mRs at 3rd month (n=198)	82 (42.3%)	116 (53.7)	**0.021***
Clinical outcome	rtPA (n=291)	Mechanical thrombectomy (n=119)	p
Mortality (Yes: 73)	43 (14.8%)	30 (25.2%)	**0.012***
Dramatic improvement within 24 hours (NIHSS = 0-1 or> 8 reductions in NIHSS) (n=167)	109 (37.5%)	58 (48.7%)	**0.035***
Symptomatic hemorrhagea (Decrease in the NIHSS score of 4 or more points within 36 hours) (n=18)	11 (3.8%)	7 (5.9%)	0.346*
mRs at 3rd month (n=198)	139 (47.8%)	59 (49.6%)	0.739*
Clinical outcome	Patient with nephropathy (n=34)	Patient without nephropathy (n=376)	p
Mortality (Yes: 73)	14 (41.2%)	59 (15.7%)	**<0.001***
Dramatic improvement within 24 hours (NIHSS = 0-1 or> 8 reductions in NIHSS)(n=167)	11 (32.4%)	156 (41.5%)	0.299*
Symptomatic hemorrhagea (Decrease in the NIHSS score of 4 or more points within 36 hours) (n=18)	4 (11.8%)	14 (3.7%)	0.052**
mRs at 3rd month (n=198)	23 (67.6%)	175 (46.5%)	**0.018***

*Pearson Chi Squared test, **Fischer Exact test

Table 6. Univariate analysis for determining major risk factors for nephropthy.

	β	Std. Error	Test Statistics	p	OR	95% C.I.for OR	
						Lower	Upper
Sex (Male)	-.914	0.417	4.813	0.028	0.401	0.177	0.907
Contrast	-1.193	0.429	7.736	0.005	0.303	0.131	0.703
Haemoglobin	0.315	0.111	8.110	0.004	1.371	1.103	1.703
NIHSS_baseline	0.122	0.039	10.009	0.002	1.130	1.048	1.219

DISCUSSION AND CONCLUSION

In our study, we investigated the incidence and relationship of CIN in patients who were admitted to our ED with acute ischaemic stroke and who were administered contrast media for CTA and CTA and/or endovascular intervention. Interestingly, it was found that the incidence of nephropathy was lower in the acute stroke treated patients who received a contrast media than in those who did not receive any contrast media (5.67% vs. 10.6%; p=0.068). Based on these data, it was found that the contrast media applied during CTA and CTA+EVT in acute stroke patients included in our study did not pose any risk for CIN.

In some retrospective studies, the incidence of CIN was reported to be between 5% and 13% (10-12). The CIN incidence reported in cohorts of non-stroke patients, including those with pre-existing renal dysfunction or DM who did not undergo a standard pre-hydration protocol, was between 12% and 26% (13,14). Especially in post-PCI studies, this rate varied between 3.3% and 25% (15-18). The same studies also reported that the need for dialysis in patients who underwent PCI and developed nephropathy was between 0.3% and 0.7% (15-18). Mortality in patients requiring dialysis was found to be 45.2% in a study by Gruberg (19). A few studies suggested that the risk of CIN is lower after contrast-enhanced scans when compared with the risk after arterial cardiac catheterisation (20,21). Studies showing the effect of IV contrast media administration on kidney damage are controversial. Two reviews evaluated the relationship between CIN and contrast media, and no difference was found between the contrast media group and the control group. This finding was also confirmed in a meta-analysis CT (22). However, there was considerable heterogeneity among the patients in both studies.

Although there are studies on kidney damage due to contrast media or other reasons in patients with acute stroke, the results are controversial. Renal dysfunction after acute ischaemic stroke, independent of contrast agent usage, ranged from 2.2% to 28.4%. In a meta-analysis, while kidney damage was 12.9% in acute ischaemic strokes, it was 19% in intracranial haemorrhages. In our study, a lower incidence of nephropathy (5.67%) was found in patients who received contrast media during CTA and endovascular procedures compared to the literature, and nephropathy was observed in a small percentage of the patients. The low CIN incidence observed in this research is parallel to other studies, but none of these studies compared their results with a control group (3,12,23). Furthermore, the incidence of nephropathy in the present study is much lower than the rate of 20–30% reported in previous studies for high-risk patients with chronic renal failure, DM, congestive heart failure, advanced age and previous cardiac interventions (24).

These variations in the reported CIN incidence can be explained by differing definitions, patient populations, contrast doses, administration routes and patient follow-up timing (25,26). The difference of our study from others was that the contrast vs. non-contrast comparison was made between similar patient groups. Nevertheless, none of these patients developed permanent renal failure and none of them had a treatment approach requiring dialysis. On the other hand, the incidence of nephropathy was higher in patients not receiving contrast media. This increase may be related to the severity of the disease, higher NIHSS, age, administered drugs, hemodynamic disorders, intensive care treatment, length of hospital stay, and underlying comorbidities rather than the contrast media used. Furthermore, fluid infusion was given in a more controlled and planned manner to prevent nephropathy in patients receiving contrast media. On the other hand, no renal damage requiring permanent dialysis occurred in any of the patients in the non-contrast nephropathy group. Therefore, when appropriate fluid replacement therapy and standard prophylactic measures are taken in patients receiving contrast media (including the use of low osmolar contrast media, adequate IV hydration), it supports the safety of IV contrast media in acute stroke patients independent of the initial eGFR and possible kidney dysfunction can be prevented.

The best studies on CIN pathogenesis were conducted on animal models. Although contrast media usage was shown to cause CIN, the mechanism is not fully understood (3,27). The cause of CIN has been explained by two theories. The first is medullary hypoxia-induced renal vasoconstriction mediated by changes in nitric oxide, endothelin and / or adenosine owing to a

possible increase in viscosity. The second is the direct outcome of the cytotoxic effects of the contrast media on the tubular cells in CIN (27-30). In our study, haemoglobin elevation was found to be associated with nephropathy, and this was thought to be due to increased viscosity. Contrast-induced acute kidney injury is characterised by a relatively rapid recovery of kidney function. Although this may result in reversible kidney damage, its development may be associated with adverse outcomes. In our study, patients who developed nephropathy had a worse disability in 3 months and the overall mortality was also higher. This observation was likely due to the high NIHSS scores of the patients who developed nephropathy. Although some previous studies have observed serious side effects due to contrast material use in patients with acute stroke, non-ionic contrast material should be used for both imaging and endovascular intervention. Since treatment timings are critical, it is not recommended to wait for sCr measurement results for imaging purposes, especially to avoid delay in the acute period (23). Smith et al. showed that waiting for the baseline sCr level will result in long delays in treating the acute stroke patients, which has been associated with poor outcomes (31). Although DM is stated as a risk, it was not identified as a risk factor for CIN development in the our study (12,23).

This study has limitations due to its retrospective nature. Although there were no CIN cases leading to chronic kidney disease in this study, we cannot reliably estimate the risk of such an occurrence because of the small number of these cases. In addition, the lack of creatine values of the 48th and 96th hour of our patients is the limitation of our study. In such a retrospective study, the inclusion of a larger number of patients will increase the overall reliability of the findings.

As a conclusion, the results of our study show that none of the patients developed renal impairment or required dialysis, although a few patients developed CIN. The independent risk factors for the development of nephropathy in stroke patients were determined as a female gender, haemoglobin elevation, and high NIHSS score at admission.

It is not necessary to wait for creatinine values as it will delay the treatment. If patients with known renal insufficiency are excluded, we think that contrast media administration may be safe in acute stroke patients even if there are risk factors present.

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Ethics

Ethics Committee Approval: The study was approved by Non-Invasive Clinical Research Ethics Committee of Eskişehir Osmangazi University (Date: 21.04.2020, No: 08).
Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.
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