

Frequency of Contrast Nephropathy after Intravenous Contrast Computerized Tomography Scan in The Patients Admitted to Emergency Department

Acil Servise Başvuran Hastalarda İntravenöz Kontrast Madde Verilerek Çekilen Tomografi Sonrası Kontrast Madde Nefropatisi Gelişme Sıklığı

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Abstract

Objective	In this study, we aimed to determine contrast nephropathy incidence in patients who admitted to emergency department and got intravenous contrasted computerized tomography scan. (<i>Sakarya Med J</i> 2019, 9(1):22-29)
Materials and Methods	Medical records patients who admitted to the emergency department between October 2013 and October 2014 and underwent intravenous contrasted computerized tomography scan were examined. 142 patients over 16 years old were included in our study. Patient data on demographics, clinical and laboratory findings, previous diagnoses, prognoses and prophylactic treatments were collected and examined.
Results	50,7 % of the patients were female and 49,3 % were male. The mean age was 52,0. 11,2 % of the patients had contrast nephropathy. When the patients were examined separately at 72th and 120th hours, the incidence of radiocontrast nephropathy was found as 9,2 % and 8,5 %, respectively. Women and patients who had diabetes mellitus, low glomerular filtration rate and malignancy were found to have a high risk for contrast nephropathy.
Conclusion	Intravenous contrast usage has increased in emergency departments. Appropriate risk assessment should be made and prophylactic treatment should be administered to the patients with high risk. Also, serum creatinine values should be examined before intravenous contrast administration and should be monitored closely after the exposure.
Keywords	Contrast-induced nephropathy; contrast media; emergency department

Öz

Amaç	Bu çalışmada erişkin Acil Servisine başvuran ve intravenöz kontrast madde verilerek bilgisayarlı tomografi çekilen hastalarda kontrast madde nefropatisi gelişme sıklığının değerlendirilmesi amaçlanmıştır. (<i>Sakarya Tıp Dergisi</i> 2019, 9(1):22-29).
Gereç ve Yöntemler	Ekim 2013 - Ekim 2014 tarihleri arasında acil servise intravenöz kontrast madde verilerek bilgisayarlı tomografi çekildiği tespit edilen hastaların dosyaları, retrospektif olarak tarandı. 16 yaş ve üstü 142 hasta çalışmaya alındı. Bu hastaların demografik, klinik ve laboratuvar verileri, tanıları, klinik sonuçları ve uygulanan profilaktik tedavileri değerlendirildi.
Bulgular	Hastaların %50,7'sinin kadın, %49,3'ünün erkek olduğu ve yaş ortalamasının 52,0 olduğu tespit edildi. Hastaların % 11,2'sinde kontrast madde nefropatisi geliştiği belirlendi. Ayrıca hastalar 72.saat ve 120.saat olarak iki ayrı zaman diliminde değerlendirildiğinde kontrast madde nefropati sıklığı % 9,2 ve % 8,5 olarak tespit edildi. Kadınlarda, diyabeti, malignitesi olanlarda, glomerüler filtrasyon hızı düşük hastalarda kontrast madde nefropatisi gelişimi açısından daha yüksek risk saptandı.
Sonuç	Acil servislere kontrast madde kullanımı hızla artmaktadır. Hastalara doğru bir risk analizi yapılmalı, riskli gruplara gerekli profilaktik tedavi uygulanmalı ve kreatinin düzeyi gerek uygulama öncesi gerekse uygulama sonrası sıkı takip edilmelidir.
Anahtar Kelimeler	Kontrast madde nefropatisi; kontrast madde; acil servis

INTRODUCTION

Nowadays, radiological diagnostic methods especially with the spread of iodinated contrast agent (CA) has steadily increased. CA is used in approximately 60 million cases around the world annually.¹ A number of complications accompany these increasing uses. Contrast induced nephropathy (CIN) is the most important of these complications.² CIN is the third most common cause of kidney failure acquired in the hospital is after surgery and hypotension.³ CIN is defined as increase of serum creatinine by 0.5 mg/dL or an increase of 25% or more relative to the baseline value after 48-72 hours of intravenous (IV) CA administration, and a decrease in calculated glomerular filtration rate (eGFR) 25% or more, or a combination of these.⁴

Although the incidence of CIN is unknown, it was found to be up to 50% in patients with a risk factor like chronic renal failure (CRF) in diabetics and 1-2% for those without risk factors. Hypotension, age (75 years), congestive heart failure (CHF), diabetes mellitus (DM), hypertension (HT), CRF, nephrotoxic drug use, proteinuria, anemia, hyperuricemia, hypercalcemia, multiple myeloma (MM), used CA amount and type have been shown to facilitate the development of CIN in various studies. IV fluid administration is the only practical way of preventing the development of CIN.⁵ In addition, a variety of methods such as N-acetylcysteine (NAC), calcium channel blockers, mannitol, angiotensin converting enzyme (ACE) inhibitors, theophylline, fenoldopam and hemodialysis have been used in clinical trials but, debates about the usefulness of these methods are still in progress.

In recent years, diagnostic imaging interventions have frequently been used in emergency departments. Contrast enhanced computerized tomography (CT) is the most common diagnostic imaging intervention which uses CA in the emergency department. On the other hand, it has been determined that half of the physicians do not have known about the risks related to CIN in a study.⁶ Despite the high frequency of contrast-enhanced CT in emergency

departments, there are not enough studies in the literature regarding the rate of CIN in the emergency. For this reason, we planned this study to evaluate the frequency of CIN in emergency department patients who had contrast-enhanced CT. In addition we aimed to determine the association between CIN frequency and demographic variables such as age and sex and pre-contrast treatment. Thus, we targeted to make a contribution to predicting patients at risk in terms of CIN in emergency department.

MATERIALS and METHODS

This is a descriptive and cross sectional study which was carried out on 282 patients who had an IV contrast enhanced tomography in the emergency department of Kahramanmaraş Sutcu Imam University (KSU) between October 20, 2013 and October 20, 2014, with the approval of KSU Medical Faculty Scientific Research Ethics Committee (Decision date:10.11.2014; Decision no:6). The study included 142 patients over the age of 16 who had 72 hours or 120 hours creatinine value after IV CA delivery for emergency diagnostic evaluation in the emergency department. Demographic, clinical and laboratory data, diagnostic and clinical outcomes of these patients, and prophylactic treatments applied to emergency or hospitalized patients were evaluated. 140 patients who had a chronic renal disease requiring dialysis, whose file information was not available from the hospital automation system, died within 72 hours after the contrast was given, or whose creatinine level had not measured at 72 hours or 120 hours after the administration of contrast, were excluded. CIN was defined as an increase of 0.5 mg/dL or or a 25% or higher increase in serum creatinine levels compared to the baseline level observed at 72 hours and 120 hours after administration of IV CA. Basal creatinine levels with a baseline creatinine value of <1.2 mg/dL evaluated as normal, and basal creatinine levels in patients with $\geq 1,2$ mg/dL assessed as abnormal. GFR is calculated based on the "Modification of Diet in Renal Disease" equation. Patients who received 600 mg oral NAC before and after CA administration, given IV sodium bicarbonate infusion before and after CA admini-

nistration, given ≥ 100 mL/h IV serum physiologic (0.9% and 0.45%) for at least 4 hours before CA administration, defined as having received preventive treatment. Statistical analysis was performed using the SPSS 20.0 package program. Mean, frequency and standard deviation values were determined in the analysis of the data. Compliance of normal distribution were analyzed using the Kolmogorov-Smirnov test variable. Chi-square and Studentt-test were used to determine the difference between the two groups. The paired t-test was used to determine the change in repeated measures. Statistically, $p < 0.05$ was considered significant.

RESULTS

The mean age of the patients was 52.0 ± 20.6 (min=18, max=95), and 50.7% (n=72) were female and 49.3% (n=70) were male. CIN has developed at the 72nd hour, in 9 (12.5%) female patients, in 4 (5.7%) male patients. Of the 12 patients who developed CIN at 120th hours, 11 (15.3%) were female and 1 (1.4%) were male. At the 120th hour, a significantly higher CIN development rate was detected in female patients ($\chi^2=8.799$, $p=0.003$). Furthermore, when

these patients are classified according to age groups; it was determined that 56 (39.4%) patients were in the age range of 18-44, 36 (25.4%) were between the ages of 45-64 and 50 (35.2%) were in the age range of ≥ 65 . The distribution and averages of the numerical data of the total 142 patients are summarized in Table 1.

75 patients (52.9%) were found to have accompanying disease. The relationship between illnesses and development of CIN at different time periods is shown in Tables 2 and 3. Especially in DM and malignant patients, it was found that there was a statistically significant difference between the 72nd hour and 120th hour CIN development frequency.

Baseline creatinine values were above ≥ 1.2 mg/dL in 12 (8.5%) of the patients included in the study. Basal creatinine levels in these patients were assessed to be impaired, and all of these patients were found to have received IV 0.9% saline ≥ 100 mL/h for at least 4 hours as a prophylactic therapy before administration of IV CA. There was no statistically significant difference regarding the development of CIN at 72nd hours and 120th hours when only

Table 1. Distribution of numerical data in the study.

	n	minimum	maximum	mean	Std. Deviation
Age	142	18.00	95.00	52.0423	20.65106
SBP	142	60.00	190.00	118.5352	21.38126
DBP	142	30.00	110.00	72.6408	13.25813
Basal BUN	142	3.00	55.00	18.0070	9.12443
Basal Cr	142	0.23	2.00	0.7902	0.28556
72nd BUN	142	4.00	50.00	15.288	9.09881
72nd Cr	142	0.22	2.20	0.7065	0.28981
120th BUN	142	2.00	50.00	15.0563	9.98991
120th Cr	142	0.20	2.00	0.6507	0.27653
Basal GFR	142	40.61	398.16	112.3951	52.94364
72nd GFR	142	25.21	412.08	130.1289	61.34129
120th GFR	142	28.15	498.68	147.6451	77.58696

SBP:Systolic Blood Pressure, **DBP:**Diastolic Blood Pressure, **BUN:**Blood Urea Nitrogen, **Cr:**Creatinin, **hr:**hour, **GFR:**Glomerular Filtration Rate

Table 2. The relationship between additional diseases and the frequency of 72th hour CIN development

Disease		CIN+		CIN-		Total		P value	χ^2
		n	(%)	n	(%)	n	(%)		
DM	+	3	33.7	6	66.7	9	100	0.009	6.754
	-	10	7.5	123	92.5	133	100		
HT	+	6	15.8	32	84.2	38	100	0.097	2.746
	-	7	6.7	97	93.3	104	100		
CHF	+	2	18.2	9	81.8	11	100	0.280	1.168
	-	11	8.4	120	91.6	131	100		
Malignancy	+	5	45.5	6	54.5	11	100	0.000	18.89
	-	8	6.1	123	93.9	131	100		
CAD	+	2	12.5	14	87.5	16	100	0.622	0.243
	-	11	8.7	115	91.3	126	100		
Others	+	5	13.5	32	86.5	37	100	0.285	1.14
	-	8	7.6	97	92.4	105	100		
Total		13	9.2	129	90.8	142	100		

DM:Diabetes mellitus, **HT:**Hypertension, **CHF:**Congestive Heart Failure, **CAD:**Coronary Artery Disease

Table 3. The relationship between additional diseases and the 120th hour CIN development frequency

Disease		CIN+		CIN-		Total		P value	χ^2
		n	(%)	n	(%)	n	(%)		
DM	+	3	33.3	6	66.7	9	100	0.006	7.690
	-	9	6.8	124	93.2	133	100		
HT	+	4	10.5	34	89.5	38	100	0.591	0.289
	-	8	7.7	96	92.3	104	100		
CHF	+	2	18.2	9	81.8	11	100	0.227	1.459
	-	10	7.6	121	92.4	131	100		
Malignancy	+	3	27.3	8	72.7	11	100	0.019	5.460
	-	9	6.9	122	93.1	131	100		
CAD	+	0	0	16	100	16	100	0.197	1.664
	-	12	9.5	114	90.5	126	100		
Others	+	5	13.5	32	86.5	37	100	0.198	1.658
	-	7	6.7	98	93.3	105	100		
Total		12	8.5	130	91.5	142	100		

DM:Diabetes mellitus, **HT:**Hypertension, **CHF:**Congestive Heart Failure, **CAD:**Coronary Artery Disease

cases with prophylactic IV fluids an were compared with cases without preventative IV fluid ($\chi^2=1.321$, $p=0.250$) ($\chi^2=1.210$, $p=0.271$). We noticed that 16 (11.2%) of the patients had developed nephropathy after IV CA administra-

tion. In 13 of these 16 patients (81.2%) CIN developed in 72 hours and in 3 (18.8%) in 120 hours (Figure 1).

The incidence of CIN in patients is evaluated in two diffe-

rent time zones, 72nd hours and 120th hours; The prevalence of CIN growth in 72nd hours of 142 patients received in total study was 9.2% (13 patients) and the incidence of CIN growth in 120th hours was 8.5% (12 patients).

Patients were diagnosed as 29 (20.4%) traumatic findings, 22 (15.5%) pulmonary embolism, 12 (8.5%) ileus, 11 (7.7%) biliary pathologies, 9 (6.3%) pancreatitis, 5 (3.5%) appendicitis, 5 (3.5%) acute mesenteric ischemia and in 32 (22.5%) patients were evaluated as normal after imaging.

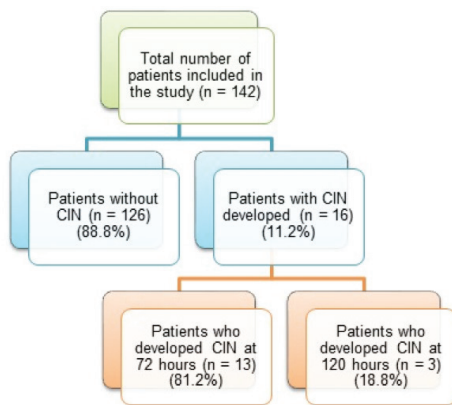


Figure 1. Contrast induced nephropathy (CIN) development frequency flow diagram.

83 of the 142 patients (58.5%) were hospitalized, and 59 (41.5%) were discharged from the emergency service. CIN was found in 8 (9.6%) of the 83 hospitalized patients and in 5 (8.5%) of 59 discharged patients when evaluated regarding 72nd hour CIN development. CIN was found in 5 (6%) of hospitalized 83 patients and 7 (11.9%) of 59 discharged patients when evaluated regarding 120th hour CIN development. There was no statistically significant difference in the evaluation of the clinical outcomes of the patients and the frequency of CIN development at 72nd and 120th hours ($\chi^2=1.520$, $p=0.218$ and $\chi^2=0.056$, $p=0.813$).

DISCUSSION

The use of diagnostic tests in emergency departments has increased and the use of CA has also increased considerably. CIN is a condition with high incidence, morbidity,

and mortality, and has recently been a highly clinical and researched clinical problem particularly at risk. The number of studies on the frequency of CIN associated with CA use in emergency services is very few. In a recent study on the frequency of CIN development due to contrast-enhanced CT imaging in emergency surveillance patients, CIN frequency was 11%, in another retrospective study involving 198 patients with acute stroke pre diagnosis with IV contrast enhanced CT angiography CIN frequency was 2.9%, and another frequency of 4.5% in another study conducted in emergency services.^{7,8,9} In our study, we found the CIN development frequency to be 11.2%. Also, we determined these rates as 9,2% and 8,5% when the patients were evaluated in two separate time periods, 72nd hours and 120th hours respectively. We have found that the frequency of CIN development is similar to other studies in the literature. In addition, the majority of CIN was observed in the first 72 hours, consistent with the literature. However, in this study, CIN can be seen even in 120th hours, and most of the studies in the literature are not followed up after 72 hours, which is a big disadvantage in terms of detecting CIN that can develop after this hour. Patients with a high risk of developing complications should be correctly identified so that management and preventive measures of CIN patients can be taken. Many studies to date have revealed many of the risk factors that cause CIN. The most important of these risk factors is pre-existing kidney disease.⁵ Other important risk factors are; type, amount and frequency of administration of CA, HT, cardiogenic shock and hypotension, decreased intravascular volume and dehydration, sepsis, myocardial infarction (MI), anemia and nephrotoxic drugs, renal involvement DM, CRF (Stage 4).^{5,10,11,12}

Although there is no definite age limit for a significant increase in CIN, many studies in the literature show that over 75 years of age have an increased risk for CIN development.^{5,11,13,14} Studies in the literature have shown that CIN is more common in female patients.^{15,16} Increased CIN frequency in women was found to be associated with older

age, impaired basal renal function, and more common risk factors such as HT and DM.¹⁷ In our study, we found that the frequency of CIN development in female gender was higher supporting the literature. In many previous studies, the use, frequency, type, osmolarity, and route of administration of CA have been shown to be an important risk factor for the development of CIN.^{18,19,20,21,22} In this study, we found that all patients were using a single non ionized low osmolar CA and that the sole route of administration was an IV route and 100 mL of CA was given to the patients. For this reason, we did not conduct a comparison study on the amount, type and type of CA. Preexisting kidney disease story is the most critical risk factor that plays a role in the development of CIN.⁵ Patients with a serum creatinine clearance of less than 50 mL/min/1.73m² and eGFR less than 60 mL/min have been found to have an increased risk of CIN.²³ In our study, patients with CRF were not included in the study and therefore were not evaluated for risk factors. We have also found eGFR over 60 mL/min in majority of patients. Despite not finding a statistically significant difference between CIN development frequency and eGFR in our study, we found that the frequency of CIN development in our study was directly proportional to the decrease in eGFR as it is in other literature studies performed. In a previous study by Çavuşoğlu et al., they found that patients with serum creatinine levels of 1.4-1.9 mg/dL had a five-fold increase in CIN compared to patients with a serum creatinine level below 1.2 mg/dL.¹⁰ When we evaluated patients regarding baseline serum creatinine levels in our study, we found that creatinine levels were below 1.2 mg/dL in all CIN patients. Although this finding is controversial in the literature, we attributed this to the treatment of prophylactic fluid with creatinine values of 1.2 mg/dL and above, which we have applied. Although diabetic nephropathy is seen as a definite risk factor for CIN development, DM patients without nephropathy are considered as risky.¹¹ As we have seen in our study, we found that the frequency of CIN development was high in patients with diabetes. This finding is consistent with the literature and supports that diabetes is a significant risk fa-

ctor for CIN development. Studies by Mehran et al., Rihal et al. have shown that HT is a risk factor for CIN development.^{15,5} Marenzi et al. have not considered HT as a risk for CIN in their study.²⁴ We did not detect a significant CIN development in patients with HT in our study. Hypertension is known to cause renal dysfunction and decrease GFR, which may lead to CIN. Studies have reported that CHF has a definite risk of developing CIN.^{5,11} Mainly, <50% of the left ventricular ejection fraction is considered significant for CIN development.¹¹ In our study, we did not find any significant risk of developing CIN in patients with CHF. In the literature, many studies on CHF have been performed on a group of patients with cardiac problems and coronary intervention. We think that this is the reason why our work is not meaningful because we added all the patients who applied to the emergency service and performed IV CA during imaging to the study. Some drugs may pose a risk for the development of CIN. Since we do not have data on medicines registered in patients' files because of the retrospective nature of the study we conducted, we were not able to assess whether there was a relationship between these drugs and the frequency of CIN development concerning risk. There are also risk factors such as malignancy, coronary artery disease (CAD), decreased intravascular volume and dehydration, hypotension, hyperuricemia, liver insufficiency, MM, hyperlipidemia, single kidney regarding CIN development. In our study, we found that there was a significant risk increase in patients with malignancy from these risk factors. In patients with CAD, we could not detect a substantial increase in risk for CIN development.

Since CIN does not have a valid treatment method, the primary strategy should be to prevent the development of nephropathy.²⁵ Although there have been numerous experimental and clinical trials to date to avoid CIN, there has still been no traditional practice except for IV fluid treatment. However, the length of time and the amount of the solution to be administered remains uncertain. In some studies, it is recommended to apply normal saline

at 1-1.5mL/kg/min for 6-12 hours (without heart failure), starting 3-12 hours before the procedure to provide 150 cc urine output for 6 hours after the procedure.²⁶ In our study, we found that patients were treated with IV fluid prophylactically, and we found that there was no statistically significant difference in CIN development between both treated and untreated cases at both time points. Although this result suggests that IV fluid hydration is useless to be protected from CIN, IV hydration is a frequent application with oral intake restriction in many patients with emergency services. Hydration is performed in different amounts and durations according to the complaints of the patients. For this reason, it is wrong to make a particular comment unless a randomized prospective study is performed.

The CIN frequency was 11.2% in the patients who were admitted to the adult emergency department of the KSU Medical Faculty Hospital and who were given CT with IV CA. Although 8.5% of CIN is observed within the first 72 hours, it is particularly useful to have at least 120 hours of follow-up time for risky patients, since CIN at 120th hours is not negligible. Since CIN does not have adequate treatment, the primary strategy should be to prevent CIN. For this reason, a risk analysis should be performed towards the disease, the necessary prophylactic treatment should be applied to these risk groups, and the creatinine level should be monitored before application or after application. The frequency of CIN development is significantly higher in patients with DM and malignancies, and these two diseases should be questioned especially in patients who will take CA. Although we did not find a statistically significant difference between baseline creatinine level and CIN development, we concluded that this was related to the prophylactic fluid treatment given to all patients with high baseline creatinine (1,2 mg/dL and above). Also, as GFR calculated in patients decreases, CIN development is increased, so it is useful to figure GFR values of patients before treatment, even by the emergency departments' laboratories.

The most critical prophylactic treatment to prevent CIN is IV hydration. Much of the other treatment modalities are still controversial. In our study, we found that isotonic fluid infusion was given prophylactically to all patients with a high baseline creatinine value and that none of these patients developed CIN. For this reason, as in the literature, infusion of IV fluid, especially at risk and high baseline creatinine value, should be given prophylactically. The best way to protect patients from CIN is never to use the CA. IV contrast usage has increased in emergency departments. In many patients, the risk of CIN can be ignored for some reasons, such as the fact that life-threatening illness, and necessary imaging tests are performed without evaluating renal function. In addition to taking the existing diseases into account, it should not be forgotten that the hydration is needed to prevent the development of CIN. Appropriate risk assessment should be made and prophylactic treatment should be administered to the patients with high risk. Also, serum creatinine values should be examined before intravenous contrast administration and should be monitored closely after the exposure. Instead of long-term treatment protocols in CIN prophylaxis, fast and easy treatment protocols should be established which also take into account the time and patient intensity in emergency department.

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