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Incidence and risk factors of contrast-induced nephropathy after diagnostic or interventional coronary angiography

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ABSTRACT

Objectives. Contrast-induced nephropathy (CIN) is the third most common cause of acute renal failure that occurred in the hospital. In Turkey, there is not enough data about the frequency of CIN in cardiological interventions. Increased contrast volume and creatinine value are related with CIN. We also investigated the CIN predictors. ***Methods.*** A total of 2604 patients who underwent coronary angiography or percutaneous coronary intervention (PCI) in our hospital were prospectively evaluated in terms of CIN. The definition of CIN includes absolute (≥0.5 mg/dl) or relative increase (≥25%) in serum creatinine at 48-72 h after exposure to a contrast agent compared to baseline serum creatinine values. ***Results.*** CIN was detected in 13.6% (355 patients) of 2604 patients. According to the procedure; CIN rate was 13.3% (280 of 2108 patients) in coronary angiography, 13.08% (50 of 382 patients) in elective PCI and 21.49% (25 of 114 patients) in primary PCI. Compared with each of these three groups patients, CIN rate was significantly higher in primary PCI group than coronary angiography (p=0.009) and elective PCI (p=0.02) groups. In multivariate analysis, age (odds ratio [OR]=1.04; 95% confidence interval [CI], 1.02-1.06; p<0.001), glomerular filtration rate (OR=0.99; 95% CI, 0.98-0.99; p<0.001), contrast volume (OR=1.14; 95% CI, 1.007-1.21; p<0.006), contrast volume to creatinine ratio (OR=1.01; 95% CI, 1.009-1.02; p<0.001), three vessel disease (OR=1.77, 95% CI, 1.24-2.51; p=0.001) were independent predictors of CIN. ***Conclusions.*** In our patient population, the incidence of CIN was found to be 13.6% in cardiological interventions. In emergency interventions, incidence of CIN was increased. We found that contrast volume to creatinine ratio is predictor of CIN.

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Keywords: Contrast-induced nephropathy; coronary angiography; percutaneous coronary intervention; renal failure; contrast media

Introduction

Contrast-induced nepropathy (CIN) is one of the cause of acute kidney injury which developes after use of intravascular contrast agent and which can not be defined by another reason. Today, because of the

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increasing cardiovascular procedures, the use of contrast agent has increased, as well. The actual CIN incidence is not known exactly, the frequency ranges between 1% and 25% in terms of the used CIN definition and preprocedural renal functions [1]. Although the mechanism of CIN development is being complicated, direct toxic effects of contrast agent for the renal cells and developing medullary ischemia and metabolic changes as a result of renal glomerular hemodynamic changes are the basis of pathophysiology. Studies have shown that CIN is the third most common cause of acute kidney injury in hospital [2]. The duration of hospitalization is prolong in patients with CIN because of needing renal replacement therapy. In this group of patients, morbidity and mortality frequency is increasing [2]. The main factors that influence the incidence of CIN are older age, pretreatment decrease in renal function (decreased glomerular filtration rate [GFR], increased creatinine level), heart failure, hypertension, diabetes mellitus, contrast volume, contrast osmolarity and ionic charge of contrast agents [1, 2]. Among the factors, changes may be done only in amount and features of contrast agent but it is not possible to change other risk factors. For this reason, numerous studies have been carried out to prevent and predict CIN. But, apart from hidration, benefit of other treatment modalities is still controversial. The use of contrast agents for diagnosis and treatment along with advances in interventional cardiology is rapidly increasing with each passing day. But, there is not enough study in our country in which cardiological interventions related CIN was evaluated. Therefore, we investigated the incidence of CIN that due to invasive cardiac procedures in our clinic and the predictive value of contrast volume to creatinine ratio.

Methods

Patient Selection

A total of 2604 patients who underwent coronary angiography or percutaneous coronary intervention (PCI) in our hospital were prospectively included in the study between January 2010 and February 2012. Patients with chronic kidney disease and, as a result, to whom hemodialysis or peritoneal dialysis was applied and patients who were given to bypass surgery within 48 hours, patients who were included the study before were excluded from the study. Elective PCI defined as; the patients who coronary angiography performed at least 1 week before. All patients gave written inform consent that was approved by Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee protocol.

Study Patients

The demographic characteristics of the patients were examined and physical examinations were performed. Before the process, patients' biochemical values, risk factors were recorded and blood preassure of each patient was measured. Patients whose sistolic blood pressure (SBP) ≥140 mmHg, or whose diastolic blood pressure (DBP) ≥90 mmHg and patients who use anti-hypertensive medication were accepted as hypertension. Patients were defined as diabetic if fasting blood glucose level was ≥126 mg/dL blood on two consecutive measurements or if they used oral antidiabetics/insulin. In accordance with echocardiographic evaluation, patients whose ejection fraction was below 40% were accepted as systolic heart failure.

Weight and height measurements of patients were made. Body mass index (BMI) were calculated according to body weight (kg)/height of the square (m2). GFR was calculated with Cockcroft-Gault formula; [(140-age) x body weight (kg)] / [72 x serum creatinine] (if women x 0.85) [3]. If serum creatinine values were ≥1.5 mg/dl, intraveneous hydration was performed with 0.9% sodium chloride (1 ml/kg/h) before the procedure in elective coronary angiography and elective PCI cases. The hydration dose was reduced (0.5 ml/kg/h) in patients with heart failure. Drugs of the patients were not modified before the procedure. The contrast volume to creatinine ratio was calculated as; used contrast volume/baseline creatinine level.

Interventional Procedure

All coronary angiography and percutan coronary interventions were performed with transfemoral approach. Over 50% stenosis on coronary angiography was accepted as a lesion. Before the PCI, 10.000 unit bolus heparin was applied to all patients. Conrast dose, angioplasty technique , stent and pharmacological medications which were used during the process were left to preferance of the operator. In all procedure, the non-ionic, low osmolar contrast agent (Omnipaque 350; 350 mgI/mL (iohexol) was used.

Follow-up

Necessity of urgent hemodialysis was decided

accordance to oliguria be longer than 48 hours or failure responce to forced diuresis for 24 hours. Urea and creatinine values were checked between 48-72 hours after the procedure to assess the development of CIN in patients. Early discharged patients were called for checking the biochemical parameters.

Definition of CIN

CIN was defined absolute (≥0.5 mg/dl) or relative (≥25%) increase in serum creatinine at 48-72 hours after exposure to a contrast agent compared to baseline serum creatinine values in the absence of other reasons which cause kidney failure.

Statistical Analysis

Statistical evaluation was performed using the SPSS program (Statistical Package for the Social Sciences ver. 10.0, SPSS Inc, Chicago, Illinois, USA). Numerical variants were defined as mean ± standart deviation and categorical variables were defined as percentage. In the comparision among the groups ; in the variables showing a normal distribution, student t test was used and in the variables not showing a normal distribution Mann-Whitney U test was used. Categorical variables were compared with chi-square test or Fisher's exact chi-square test. Univariate and multivariate logistic regression analyses were used to determine significant predictors of CIN. Receiver operating characteristics (ROC) analysis was used to determine the sensitivity and specificity of contrast volume to creatinine ratio to predict CIN. In all evaluations, $p<0.05$ was accepted statistically significant.

Results

The baseline demographic, echocardiographic, and biochemical characteristics of the study cohort are shown in Table 1. The age of 2604 patients were between 17 and 91 and the mean age was 59.5 years; 34.8% (906) of patients were female and 65.2%

Table 1. Characteristics of patients with and without CIN

	CIN (+) (n=355)	CIN (-) (n=2249)	*p*
Age (year)	60.96±11.25	59.34±11.38	0.01
Gender			
Male	215 (60.7)	1483 (65.9)	0.04
Female	140 (39.4)	766 (34.1)	
BMI (kg/m^2)	28.01±5.58	28.19±5.59	0.57
Hypertension	211 (59.4)	1163 (51.7)	0.007
Diabetes mellitus	79 (22.3)	395 (17.6)	0.03
EF (%)	52.88±11.88	54.54±10.99	0.009
GFR (ml/min)	98.91±34.04	113.34±44.37	<0.001
Urea (mg/dl)	33.99±14.99	34.76±15.63	0.38
Creatinine (mg/dl)	0.95±0.32	0.81±0.38	<0.001
Amount of contrast (ml)	109.05±73.95	99.64±54.75	0.004
Contrast volume to creatinine ratio	148.37±110.41	111.09±66.22	<0.001
Drugs			
ACEI	97 (27.3)	666 (29.6)	0.37
ARB	52 (14.6)	313 (13.9)	0.86
Statin	78 (22.0)	425 (18.9)	0.17
Diuretic	26 (7.3)	130 (5.8)	0.25
Metformin	52 (14.6)	221 (9.8)	0.006
Sulfonylurea	33 (9.3)	143 (6.4)	0.04
Insulin	20 (5.6)	91 (4.0)	0.16
Number of arteries with lesion >50%			
No lesion	107 (30.1)	849 (37.8)	0.001
One artery with lesion	103 (29.0)	670 (29.8)	
2 arteries with lesion	48 (13.5)	311 (13.8)	
3 arteries with lesion	97 (27.3)	418 (18.6)	
Procedure			
Coronary angiography	280 (78.9)	1828 (81.3)	0.03
Elective PCI	50 (14.1)	332 (14.8)	
Primary PCI	25 (7.0)	89 (4.0)	

Data are given as mean±standard deviation or number (%). ACEI=angiotensin converting enzyme inhibitor, ARB=angiotensin II receptor blocker, BMI=body mass index, CIN=contrast-induced nepropathy, EF=ejection fraction, GFR=glomerular filtration rate, PCI=percutaneous coronary intervention

(1698) of patients were male. In the study patients, mean body mass index was 28.1. In the study group 474 patients (18.2%) were diabetic, 1374 patients (52.8%) were hypertensive and 450 patients (17.3%) had heart failure history. Before the procedure, the mean creatinine values was 0.93 mg/dl and the mean calculated GFR was 100.86.

In admission, 3.3% (86) of patients creatinine value was ≥1.5 mg/dl. Contrast agent was used maximum 650 ml and minimum 20 ml and mean was 100.9 ml. The used contrast volume of the 97 (3.7%) patients were exceeded the threefold of creatinine clearance. Coronary angiography was performed 81% (2108), elective PCI was performed 14.7% (382) and primary PCI was performed 4.4% (114) of the study patients (2604).

CIN was found in 13.6% (355) of 2604 patients. CIN developed in 13.3% (280) of 2108 patients to whom coronary angiography was applied, in 13.1% of 382 (50) patients to whom elective PCI was applied and in 21.9% (25) of 114 patients to whom primary PCI was applied (see Table 1). Twenty-three (0.9%) of the 2604 patients was requiring dialysis due to CIN. CIN rate was 2.6% (67 patients) according to absolute increase of creatinine (≥0.5 mg/dl) and 13.5% (352 patients) according to relative increase of creatinine (≥25%) at 48-72 hours.

When comparing these three groups of patients (coronary angiography, elective PCI, primary PCI) in terms of CIN incidence, primary PCI group CIN incidence was significantly higher than coronary angiography group (p=0.009) and elective PCI group (p=0.02) (Figure 1). The CIN incidence was similar between coronary angiography and elective PCI group (p=0.91) (see Figure 1).

According to baseline characteristics; in CIN developed patients, women gender (p=0.04), hypertension (p=0.007) and diabetes mellitus (p=0.03) were significantly higher than in patients without CIN (Table 1). No significant difference was found in use of angiotensin converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) in both groups (p=0.37 and p=0.86).

The use of metformin (p=0.006), sulfonylurea (p=0.04) and number of arteries with lesion was significantly higher (p=0.001) in CIN group (see Table 1). In CIN patients, the values of left ventricular ejection fraction (p=0.009) and GFR (p<0.001) were significantly lower, age (p=0.01), initial creatinine values (p<0.001), amount of contrast agents (p=0.004) and contrast volume to creatinine ratio (p<0.001) were significantly higher than in patients without CIN (Table 1).

Using a univariate and multivariate regression models, the patients's age, gender, hypertension, diabetes mellitus, ejection fraction, GFR, urea, creatinine, contrast volume, contrast volume to creatinine ratio, medications (drugs), number of arteries with lesion and procedure were included as predictor variables for CIN (Table 2). In univariate

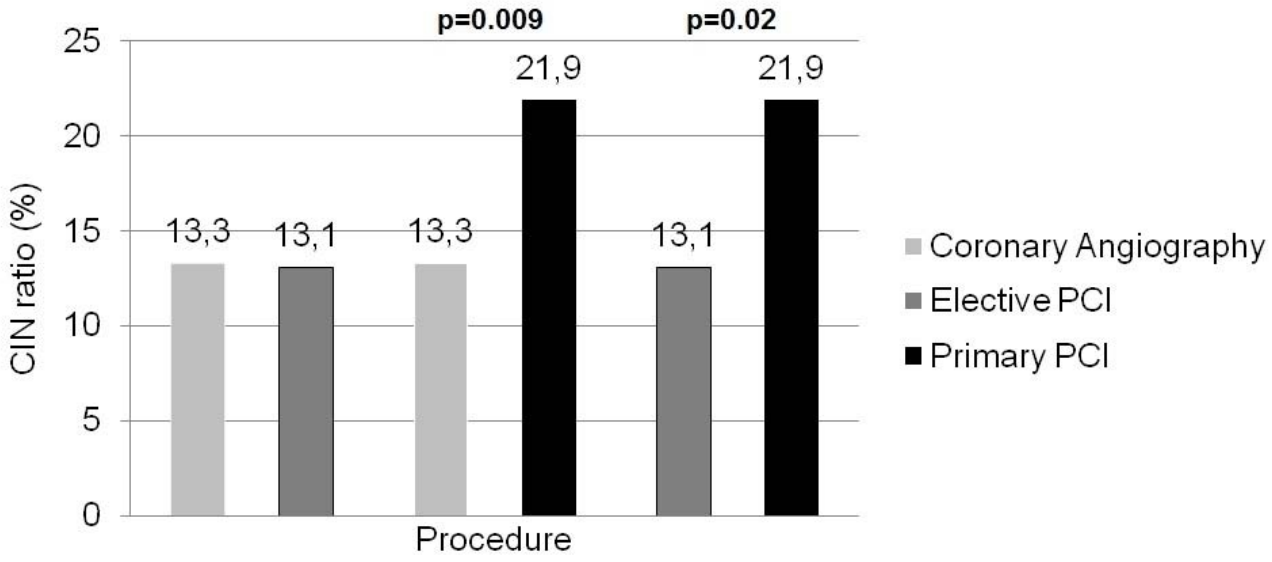

Figure 1. Comparison of the CIN incidence. CIN=contrast-induced nepropathy, PCI=percutaneous coronary intervention

Table 2. Univariate and multivariate analysis of CIN predictors

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age	1.01 (1.003-1.02)	0.01	1.04 (1.02-1.06)	<0.001
Gender	1.26 (1.002-1.58)	0.04	1.04 (0.77-1.40)	0.78
Hypertension	1.36 (1.09-1.71)	0.007	0.92 (0.71-1.19)	0.56
Diabetes mellitus	1.34 (1.02-1.76)	0.03	1.03 (0.66-1.61)	0.88
EF	0.98 (0.97-0.99)	0.009	0.99 (0.97-1.001)	0.08
GFR	0.98 (0.97-0.99)	<0.001	0.99 (0.98-0.99)	<0.001
Urea	0.99 (0.98-1.004)	0.38		
Creatinine	1.90 (1.84-1.95)	<0.001	1.30 (0.66-2.57)	0.43
Amount of contrast	1.002 (1.001-1.004)	0.005	1.14 (1.007-1.21)	<0.001
Contrast volume to creatinine ratio	1.005 (1.004-1.006)	<0.001	1.01 (1.009-1.02)	<0.001
ACEI	1.11 (0.87-1.43)	0.37		
Statin	0.82 (0.63-1.08)	0.17		
Diuretic	1.28 (0.83-1.99)	0.25		
Metformin	1.57 (1.13-2.18)	0.006	0.87(0.53-1.44)	0.59
Sulfonylurea	1.50 (1.01-2.24)	0.04	0.95(0.57-1.59)	0.86
Insulin	1.41 (0.86-2.32)	0.17		
Number of arteries with lesion				
1-0	1.22 (0.91-1.62)	0.17	1.06 (0.74-1.52)	0.73
2-0	1.22 (0.85-1.76)	0.27	1.14 (0.74-1.74)	0.54
3-0	1.84 (1.36-2.48)	<0.001	1.77 (1.24-2.51)	0.001
Procedure				
Coronary angiography – Primary PCI	1.83 (1.15-2.90)	0.02	1.49 (0.85-2.61)	0.16
Coronary angiography – Elective PCI	0.98 (0.71-1.35)	0.91	0.82 (0.53-1.26)	0.38

ACEI=angiotensin converting enzyme inhibitor, CI=confidence interval, CIN=contrast-induced nepropathy, EF=ejection fraction, GFR=glomerular filtration rate, OR=odds ratio, PCI=percutaneous coronary intervention

analysis; age, gender, hypertension, diabetes mellitus, ejection fraction, GFR, creatinine, contrast volume, contrast volume to creatinine ratio, metformin, sulfonilurea, three vessel coronary artery disease and procedure were significant predictor of CIN. In multivariate analysis, age (odds ratio [OR]=1.04; 95% confidence interval [CI], 1.02-1.06; $p<0.001$), GFR (OR=0.99; 95% CI, 0.98-0.99; $p<0.001$), contrast volume (OR=1.14; 95% CI, 1.007-1.21; $p<0.006$), contrast volume to creatinine ratio (OR=1.01; 95% CI, 1.009-1.02; $p<0.001$), three vessel disease (OR=1.77, 95% CI, 1.24-2.51; $p=0.001$) were independent predictors of CIN (see Table 2)

According to ROC analysis, the area under the curve (AUC) of the contrast volume to creatinine ratio for CIN was 0.625 (95% CI, 0.59-0.65; p<0.001) for all the study groups, was 0.618 (95% CI, 0.58-0.65; $p<0.001$) for coronary angiography group, was 0.713 (95% CI, 0.64-0.78; $p<0.001$ for elective PCI group, was 0.58 (95% CI, 0.44-0.71; $p=0.22$) for primary PCI group (Figure 2).

Discussion

In this study, we found that; the CIN frequency that developed as related to interventional cardiological processes was 13.6%, the CIN incidence according to process was 13.3% in patients who underwent coronary angiography, 13.1% in elective PCI and 21.9% in patients who underwent primary PCI. In multivariate analysis, we showed that age, GFR, contrast volume, three vessel coronary artery disease and contrast volume to creatinine ratio were significant independent predictors of CIN.

The incidence of CIN with a retrospective analysis of 7320 patients was found as 14.8% (1069 patients) [4]. The risk factors of CIN has been found as age, diabetes mellitus, hypertension, peripheral vascular disease, ejection fraction less than 40%, multivessel PCI requirement, the presence of hypotension before, after and at the time of procedure [4]. When assessed by multivariate analysis it was found that most of these parameters is an independent risk factor for CIN. In our study, we found the overall incidence of CIN as

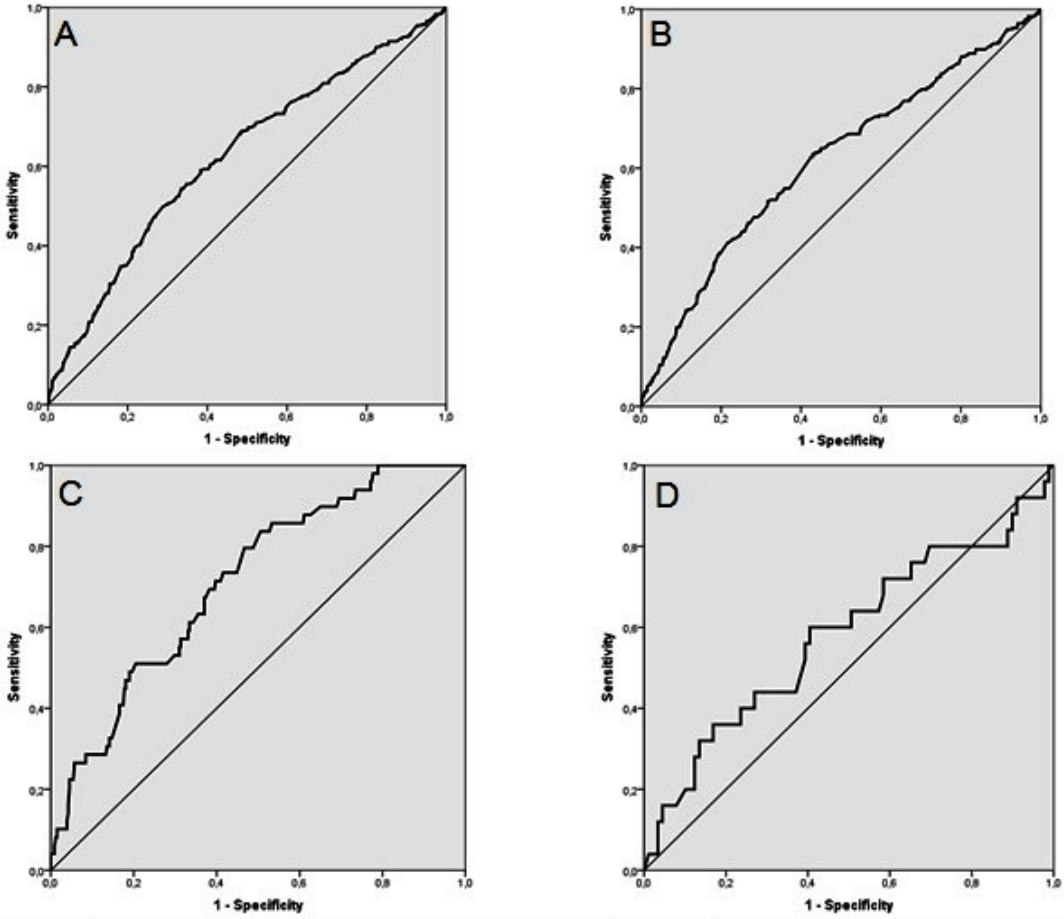

	Figure	AUC	P value	95% CI		Figure	AUC	P value	95% CI	
				Lower bound	Upper bound				Lower bound	Upper bound
Contrast volume / Creatinine	A	0.625	<0.001	0.59	0.65	B	0.618	<0.001	0.58	0.65
	C	0.713	<0.001	0.64	0.78	D	0.580	0.22	0.44	0.71

Figure 2. ROC and AUC of the study population including all of the study population (A), coronary angiography group (B), elective PCI group (C) and primary PCI group (D). AUC=the area under the curve, PCI=percutaneous coronary intervention, ROC=receiver operating characteristics

13.6%. In multivariate analysis age, GFR, contrast volume, three vessel disease and contrast volume to creatinine ratio were independent predictors of CIN.

In retrospective analysis on a large group of patients to whom PCI has been applied, it has shown that, similiar to our study, factors such as age, amount of contrast agent, high level of serum creatinine, diabetes mellitus, peripheral vascular disease, heart failure, hypertension, reference as acute myocardial infarction (MI) increase incidence of CIN, hospitalization and mortality [5, 6]. The score systems in recent studies showed that age, low GFR, low ejection fraction, hypertension, diabetes mellitus and contrast volume were predictors for CIN [7, 8].

Patients with CIN were older than patients without CIN (60.96±11.25 vs. 59.34±11.38; p=0.01). Some studies reported that 70 years and older is an independent risk factor for CIN [9]. In another study, compared with younger patients, elderly patients (>60 age) was significantly higher incidence of CIN (4% to 17%) [10]. Older age associated with sodium and water loss depending on the decrease in renal mass, function and perfusion. In addition lost in kidney functions related to age, the presence of multivessel disease, calcification, requires a greater amount of contrast agent due to tortuosity and embolic events can be accounted as factors that increase risk of CIN devolopment.

In our study, we found the value of basel serum creatinine higher and GFR values lower in CIN patients (p<0,001). The relationship between CIN and creatinine and GFR values is an expected data [4, 9].

The development of acute kidney injury is common after exposure to contrast patients with impaired renal function. Rihal *et al.* [5] have identified the value of the baseline serum creatinine as an independent predictor for CIN development. Hall *et al.* [11] had compared patients whose baseline serum creatinine is above 2.0 mg/dl and patients whose serum creatinine is 1.2 mg/dl and below and they have shown that incidence of CIN has increased 30 times in group with high creatinine. The creatinine clearance is an independent predictor for the development of CIN requiring dialysis after cardiac interventions.

Another well-defined risk factor for CIN is diabetes mellitus. In our study, diabetes mellitus frequency was found in a higher rate in CIN developed patients compared to those CIN hasn't developed (22.3% vs. 17.6%; p=0.03). Clinically serious CIN development was generally seen in diabetic patients who have kidney failure [5]. In our study in univariate analysis diabetes mellitus was a predictor of CIN however in multivariate analysis it was not. Our study diabetic population creatinine value was not different from non-diabetic population (0.95±0.37 vs. 0.93±0.33; p=0.69). This result may be related with this point. Parfery *et al.* [12] had shown that CIN frequency in diabetic patients whose have normal renal functions, in the absence of other risk factors is comparable with healty society.

Many studies revealed clearly that there is a significant positive correlation between the amount of contrast agent and the development of CIN [13]. In our study, patients with CIN has received a greater amount of contrast agent too (109.5±73.95 vs. 99.64+54.75; p=0.004) and ın multivariate analysis contrast volume was an independent predictor.

We evaluate the adjusted contrast amount according to creatinine value (contrast volume/baseline creatinine) and found that the contrast volume to creatinine ratio was significantly higher in the CIN group (111,09±66,22 vs. 148,37±110,41; p<0,001). The contrast volume to creatinine ratio was independent predictor for the development of CIN in univariate and multivariate analysis. In recent studies calculate the maximum allowable contrast volume according to creatinine level and showed that the incremental use of contrast beyond the maximum allowable contrast volume is associated with an increased risk of CIN [14]. These studies results support our trial findings. The contrast volume according to creatinine level is one of the most important factor for CIN.

According to ROC analysis; the contrast volume to creatinine ratio had reasonable AUC for predicting the CIN. In subgroup ROC analysis for the CIN prediction of contrast volume to creatinine ratio showed that the AUC value was the highest level in elective PCI group; however it was not reach the significant p value in the primary PCI group. This point could explain with the few number of patients in primary PCI group. Indeed; the contrast volume to creatinine ratio was higher in CIN group of primary PCI patients (170.49±88.16 vs. 201.74±115.57; p=0.14).

Incidence of CIN has been seen higher (21.9%) in our patients with primary PCI can be associated with hemodynamic theory which takes place in CIN pathophysiology. Primary PCI patients are processed without preservative evaluations; renal perfusion is impaired as a result of developing acute cardiac failure. After undergoing primary PCI, the risk of CIN development is higher when compared to elective patients, even in patients with normal renal functions [9]. In the randomized controlled clinical trial done by Marenzi *et al.* [15], CIN was developed as 19% in patients who applied primary PCI and this value is higher than expected general incidence. In our study, as well, incidence of CIN in patients whose applied primary PCI was higher than general incidence (13.6% vs. 21.9%). In univariate analysis primary PCI was a significant predictor for CIN however in multivariate analysis it was not. Narula *et al.* [16] showed that GFR is the most important factor for CIN in patients with primary PCI (according to propencity score analysis). In our study GFR levels significantly higher in primary PCI group than other patients (100.16±35.05 vs. 90.96±40.59; p=0.01). This result could be explain with this point.

One of another factors which create risk for CIN development is low EF of left ventriculi. In various studies, it has been shown that ejection fraction less than 40% is an independent risk factor for CIN. In our study, too, it has been found that patients whose ejection fraction was below 40% had a higher CIN incidence than above 40% (16.7% vs. 12,9%; p=0,02).

In patients with low ejection fraction have reduced renal perfusion and use a large number of pharmacological agents, explain the increase in the risk of developing CIN.

While in our study CIN incidence in 1374 hypertensive patients was found as 15.4% (211 patients) , the rate in 1230 patients without hypertension was found as 11.7% (144 patients). CIN incidence in hypertensive patients was statistically significant higher (p=0.007). Consistently high glomerular filtration pressure in hypertensive patients impairs renal function. Hypertensive nephropathy causes a reduction in the number of the functioning nephrons. The risk of CIN increases in patients with hypertension. Also, excessive activation of renin-angiotension system and the reduction of NO release are disturbed the renal autoregulation which predispose to the development of CIN. In the studies, hypertension was found to be an independent risk factor for CIN [17]. According to our study, in univariate analysis hypertension was a risk factor for CIN; however, in multivariate analysis it was not. Mehran *et al.* [7] showed similir results with us, according to univariate analysis hypertension was a risk factor for CIN but in multivariate model it was not.

In our study, the number of female patients have been much more in CIN developed group (39.4% vs. 34.1% p=0.04). In retrospective analysis by Iakovou *et al.* [17], women gender has been found to be an independent risk factor for CIN. Ovarian hormones may lead to an increased risk for CIN in women by affecting renin-angiotensin system and renal blood flow. We also found multivessel disease with increasing incidence of CIN. This may be related to the use of high volumes of contrast media for visualisation the coronary lesion and already compromised renal vessels due to atherosclerosis [13].

We found that the use of oral antidiabetic, especially metformin, is more frequent in patients with CIN. In univariate analysis, sulfonilurea and metformin were predictor for CIN; however in multivariate analysis they were not. As a result of decrease in renal functions following contrast media exposion, metabolism of metformin affected so may lead to increased accumulation in the body and adverse effects. Following contrast application, there is an increase in lactic acidosis risk in patients who use metformin. Lactic acidosis also cause development of CIN. However the metformin adverse effect dependent on renal function. In patients with normal renal function metformin did not increase the CIN risk. Guidelines recommend that this medication should not be taken for 48 hours by the patients who have a high risk in terms of CIN [18].

In the analysis of 7741 patients whose PCI applied, CIN which requires dialysis had developed in 51 patients (0.66%) [19]. A great deal of patients who requires dialysis are women, diabetic, patients with CRF and they have low ejection fraction and history with previous PCI or CABG. In-hospital morbidity (non-Q MI, CK-MB elevation, pulmonary edema and vascular complications) was significantly higher in patients who need dialysis. In our study, CIN that require dialysis has been found in 0.9% patients.

In our patients we used non-ionic, low osmolar contrast agent (iohexol). The contrast agent characteristics affect the CIN incidence. The iso-osmolar, non-ionic contrast agent has low CIN risk and this agent should use especially in patients with preexisting renal insufficiency or those at high risk for CIN is debatable. However the data is not accurate which contrast agent is the ideal agent about the CIN protection in patients with normal kidney function [20].

Recently, one of the trial showed that baseline chronic kidney disease, acute MI presentation, prior heart failure, prior cardiac arrest, prior cardiovascular disease, cardiogenic shock, anemia, age, contrast volume and diabetes mellitus are independent factors associated with acute kidney injury in patients with PCI [21]. Most of these factors were defined as risk predictor for CIN after PCI and a risk score was identified for CIN [7]. These studies result and the indentified risk score was support our study finding. Contrast volume to creatinine ratio was evaluated for CIN in our study. To the best of our knowledge, our study is the first study in literature which evaluate the contrast volume to creatinine ratio for prediction of CIN. These two parameters (creatinine and contrast volume) are accurate value of the patients. They do not need any formula such as GFR. Our findings could guide for new trials in different patients group.

There are important increases morbidity and mortality in patients with CIN [2]. But in our country there is not enough data showing the incidence of CIN is caused by the interventional cardiology procedures.

The exact evaluation incidence of CIN is highly difficult. Since in many clinics patients are discharged a few hours or a day after the interventional procedures, it can't be evaluated whether CIN is developed or not in early discharged patients. As the studies are in selected groups or search for the effects of the treatment regime, it is not possible for incidence of CIN to be evaluated exactly.

The Limitations of the Study

First; our study population include different patients group such as coronary angiography group, primary PCI group and elective PCI group however the groups were not similar size. Second; we did not use creatinine clearance value based on 24-h urine collection during a true baseline clinical condition, and our GFR calculation is subject to limitations due to the formula used and the possibility that patients may not be at their true baseline condition before interventional procedure, because of dehydration or cardiac illness.

Conclusions

Incidence of CIN which was developed as related to cardiological interventions in our clinic was defined to be similar to data throughout the world. Incidence of CIN was seen to increase in emergency interventions. Identified risk factors for CIN was found to increase the incidence of CIN in our society, as well. We found that contrast volume to creatinine ratio is predictor of CIN especially in elective PCI group.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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References

[1] Lakhal K, Ehrmann S, Chaari A, Laissy JP, Regnier B, Wolff M, et al. Acute Kidney Injury Network definition of contrast-induced nephropathy in the critically ill: incidence and outcome. J Crit Care 2011;26:593-9.

[2] Finn WF. The clinical and renal consequences of contrast-induced nephropathy. Nephrol Dial Transplant 2006;21[Suppl 1]: i2–i10.

[3] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41.

[4] Dangas G, Iakovou I, Nikolsky E, Aymong ED, Mintz GS, Kipshidze NN, et al. Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol 2005;95:13-9.

[5] Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation 2002;105:2259-64.

[6] Lekston A, Kurek A, Tynior B. Impaired renal function in acute myocardial infarction. Cardiol J 2009;16:400-6.

[7] Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;44:1393-9.

[8] Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, Glazier S, et al. Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. Am J Cardiol 2004;93:1515-9.

[9] Marenzi G, Lauri G, Assanelli E, Campodonico J, De Metrio M, Marana I, et al. Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. J Am Coll Cardiol 2004; 44:1780-5.

[10] Kohli HS, Bhaskaran MC, Muthukumar T. Treatment-related acute renal failure in the elderly: a hospital-based prospective study. Nephrol Dial Transplant 2000;15:212-7.

[11] Hall KA, Wong RW, Hunter GC, Camazine BM, Rappaport WA, Smyth SH, et al. Contrast- induced nephrotoxicity: the effects of vasodilator therapy. J Surg Res 1992;53:317-20.

[12] Parfrey PS, Griffiths SM, Barrett BJ, Paul MD, Genge M, Withers J, et al. Contrast material induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. N Engl J Med 1989;320:143-9.

[13] Baker CS, Wragg A, Kumar S, De Palma R, Baker LR, Knight CJ, et al. A rapid protocol for the prevention of contrast-induced renal dysfunction: The RAPPID Study. J Am Coll Cardiol 2003;41:2114-8.

[14] Brown JR, Robb JF, Block CA, Schoolwerth AC, Kaplan AV, O'Connor GT, et al. Does safe dosing of iodinated contrast prevent contrast-induced acute kidney injury? Circ Cardiovasc Interv 2010;3:346-50.

[15] Marenzi G, Assanelli E, Marana I, Lauri G, Campodonico J, Grazi M, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med 2006;354:2773-82.

[16] Narula A, Mehran R, Weisz G, Dangas GD, Yu J, Genereux P, et al. Contrast-induced acute kidney injury after primary percutaneous coronary intervention: results from the HORIZONS-AMI substudy. Eur Heart J 2014;35:1533-40.

[17] Iakovou I, Dangas G, Mehran R, Lansky AJ, Ashby DT, Fahy M, et al. Impact of gender on the incidence and outcome of contrast-induced nephropathy after percutaneous coronary intervention. J Invasive Cardiol 2003;15:18-22.

[18] Toprak O. Contrast-induced nephropathy. In: Baskot BG, ed. What should we know about prevented, diagnostic, and interventional therapy in coronary artery disease. Rijeka, Croatia: InTech; 2013, pp.321-48.

[19] Gruberg L, Mehran R, Dangas G, Mintz GS, Waksman R, Kent KM, et al. Acute renal failure requiring dialysis after percutaneous coronary interventions. Catheter Cardiovasc Interv 2001;52:409-16.

[20] Eng J, Wilson RF, Subramaniam RM, Zhang A, Suarez-Cuervo C, Turban S, et al. Comparative effect of contrast media type on the incidence of contrast-induced nephropathy: a systematic review and meta-analysis. Ann Intern Med 2016;164:417-24.

[21] Tsai TT, Patel UD, Chang TI, Kennedy KF, Masoudi FA, Matheny ME, et al. Contemporary incidence, predictors, and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions. Insights From the NCDR Cath-PCI Registry. J Am Coll Cardiol Intv 2014;7:1-9.