
Contrast-Induced Nephropathy Among Patients Undergoing Cardiac Catheterization

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To cite this article:

Safauldeen Ahmed Alhajim, Ahmed Sami Jebur. Contrast-Induced Nephropathy Among Patients Undergoing Cardiac Catheterization. *Cardiology and Cardiovascular Research*. Vol. 2, No. 3, 2018, pp. 55-60. doi: 10.11648/j.ccr.20180203.12

Received: August 25, 2018; **Accepted:** September 20, 2018; **Published:** October 17, 2018

Abstract: Contrast-induced nephropathy is an important complication after cardiac catheterization, and is associated with accelerated renal disease, increased costs, mortality rate, need for dialysis and prolonged hospital stay. This study aim is to find its incidence and risk factors. It is a cross-sectional study on 160 patients admitted for diagnostic or therapeutic percutaneous coronary intervention in Basra Cardiac Center, from March to September 2016. Data collected were a complete history, examination, blood pressure, Echo study, fasting blood sugar, lipid profile, blood urea, serum creatinine and estimated glomerular filtration rate, the type and duration of procedure, volume of contrast, and after 48 hours renal function tests were repeated. Contrast-induced nephropathy has developed in 7 (8.3%) men and 5 (6.6%) women; 11 (10.8%) from 102 patients with dyslipidemia (P = 0.03); 8 (22.2%) from 36 with preexisting renal impairment (P = 0.01); 11 (10.9%) from 101 with hypertension (P = 0.02); 9 (13.6%) from 66 diabetic (P = 0.016); 9 (17.3%) from 52 smoker (P = 0.002); 4 (23.5%) from 17 alcohol drinkers (P = 0.026); 11 (11.2%) from 98 with ischemic heart disease (P = 0.02); and 9 (25.7%) from 35 with heart failure (P = <0.001). Also found in 1 (1.6%) from 64 diagnostic procedures; 11 (11.5%) from 96 therapeutic procedures (P = 0.016); 5 (3.7%) from 135 patients received < 300 ml of contrast; and 7 (28%) from 25 received ≥ 300 ml (P = 0.001). In conclusion contrast-induced nephropathy is aggravated by increasing age, diabetes mellitus, heart failure, ischemic heart disease, renal impairment, hypertension, dyslipidemia, smoking and alcohol use. The type of procedure (therapeutic vs. diagnostic), and large volume of contrast agent are important risk factors. Gender had no significant effect.

Keywords: Cardiac Catheterization, Contrast Media, Acute Kidney Injury

1. Introduction

Contrast-induced nephropathy (CIN) is defined as an absolute ($\geq 0.5\text{mg/dL}$) or relative increase ($\geq 25\%$) in serum creatinine at 48–72h after exposure to a contrast agent compared to baseline serum creatinine level, after exclusion of alternative explanation of renal impairment [1]. The incidence of CIN among the general population was found to be (1% - 6%), and increases by 20% or more in selected patients, especially those with previous history of cardiovascular disease [1, 2]. CIN is the third most common cause of renal impairment acquired in hospitals after renal perfusion impairment and nephrotoxic drugs [3]. It is associated with accelerated development of end-stage renal disease, increased costs, mortality rate, need for dialysis and prolonged hospital stay [4]. CIN normally is transient and the

renal function return to baseline within 5-7 days after exposure to contrast agent, less than one third of patients will develop residual renal impairment and dialysis is required in less than 1% of them. The mortality rate in patients with preexisting renal impairment rising to 17% while the rate is around 3.9% without preexisting renal impairment [5]. The pathogenesis of CIN is not so clear, but it is thought to be due to acute tubular necrosis caused by renal vasoconstriction and direct cytotoxicity to the renal tubular epithelium [6]. Many experimental and clinical studies suggest that the osmolality of contrast agent may play a role in the development of CIN [7].

There are many risk factors for CIN development divided into non modifiable and modifiable, and can be either patient related or procedure related. Older age, diabetes mellitus, preexisting renal failure, and heart failure have all been

identified as important risk factors for developing CIN [5, 8, 9]. On the other hand, the main modifiable risk factor is the volume of contrast media. The risk of CIN was minimal in patients who received a contrast volume of 100 mL or less, although, in the presence of other risk factors even low dose of contrast can cause permanent renal failure especially in patient with underlying renal disease [10]. Other properties of contrast media such as viscosity and ionicity may also share the same risk for CIN [11]. Many medications such as NSAID, diuretics, aminoglycosides, metformin and vancomycin can affect renal function through many mechanisms, so withholding these medications is considered before contrast exposure [2]. The major preventive measure is the intravenous volume expansion before contrast agent administration (0.45% or 0.9% saline, 100 ml/h, 12 hours before and 12 hours after) [12, 38]. The effectiveness of sodium bicarbonate and N-acetylcysteine in CIN prevention is controversial, and there are no recommendations to use them due to insufficient evidence of its efficacy [13, 14]. Statins were studied as potential agents to prevent CIN; one of these studies found a significant reduction in CIN incidence, and better post-procedural creatinine clearance [15]. However, till now there is no overall substantial evidence to support the use of statins before contrast-enhanced interventions [11, 40]. Regarding the use of prophylactic hemodialysis after contrast exposure, there was no benefit of it as shown by three studies [16]. On the other hand, prophylactic hemofiltration appears to be effective in preventing CIN and is associated with improvement of in-

hospital and long-term outcomes [17]. The aim of this study is to find the frequency of CIN among patients undergoing coronary catheterization, and its risk factors.

2. Patients and Methods

A cross-sectional study was carried out on 160 patients {85 male (53.1%), 75 female (46.9%)}, who underwent diagnostic and/or therapeutic PCI, between March 2016 and September 2016, in Basra cardiac center. The inclusion criteria were: age more than 18 years, not on nephrotoxic drugs, and had no acute illness or advanced chronic kidney disease. The exclusion criteria were: the patients who refused to consent, patients who did not have renal function test at the day of the procedure or 48 hours after it, and patients who had other cause for renal impairment.

Before the procedure full history and physical examination elicited. Blood pressure and Echo study results were recorded. Blood sample was taken for serum creatinine, fasting plasma glucose, and lipid profile estimation. GFR was calculated by the CKD-EPI Creatinine 2009 equation [18]. After the procedure, the type and duration of the procedure and the volume of administered contrast agent were recorded, and after 48 hours renal function tests were repeated for each patient. The contrast agent that was used in all procedures was Ultravist® (Bayer Health Care / Germany), each 1 ml contains Iopromide 0.769 g (370mg Iodine/ml). Table 1 shows the characteristics of the patients and of the studied variables.

Table 1. Characteristics of the patients and of the studied variables.

Variables		Men (N=85)	Women (N=75)	Total
Age	<45	47 (29.3%)		
Mean (59±18)	45-65	63 (39.4%)		160 (100%)
	>65	50 (31.3%)		
Dyslipidemia		49 (57.6%)	53 (70.6%)	102 (63.75%)
Preexisting renal impairment		32 (37.6%)	4 (5.3%)	36 (22.5%)
HT		59 (69.4%)	42 (56%)	101 (63.12%)
DM		36 (42.4%)	30 (35.3%)	66 (41.25%)
Current smoker		35 (41.2%)	17 (22.2%)	52 (32.5%)
Alcohol use		15 (17.6%)	2 (2.7%)	17 (10.63%)
IHD		52 (61.2%)	46 (61.3%)	98 (61.25%)
Preexisting HF		31 (36.5%)	4 (5.3%)	35 (21.88%)
Type of procedure	Diagnostic	41 (48.2%)	23 (30.6%)	64 (40%)
	Therapeutic	44 (51.8%)	52 (69.3%)	96 (60%)
Volume of contrast	<300 ml	73 (85.9%)	62 (82.7%)	135 (84.38%)
	> 300 ml	12 (14.1)	13 (17.3%)	25 (15.63%)

Out of 160 patients; 41 (48.2%) male and 23 (30.6%) female underwent diagnostic PCI; 44 (51.8%) male and 52 (69.3%) female underwent therapeutic PCI; 73 (85.9%) male and 62 (82.7%) female were injected with less than 300 ml of contrast agent; while 12 (14.1%) male and 13 (17.3%) female were injected with 300 ml or more. The patients were grouped according to age: < 45 years (47patients, 29.3%), 45-65 years (63patients, 39.4%), and > 65 years (50patients, 31.3%). Mean age was 59±18years, range 40- 71 years. Criteria for dyslipidemia are: LDL-C level of > 140 mg/dl (3.6 mmol/L), HDL-C < 40 mg/dl (1.03 mmol/L), or if the TC was ≥ 200 mg/dl (5.17mmo l/L), or the TG level ≥ 150 mg/dl

(1.69 mmol/L) or on treatment with lipid-lowering drugs. Dyslipidemia was present in 102 patients; 49 (57.6%) male, and 53 (70.6%) female. The Eighth Joint National Committee (JNC8) criteria were used for the diagnosis of hypertension.20 hypertension was found in 101 patients; 59 (69.4%) male, and 42 (56%) female. The diagnosis of IHD was based on resting ECG or exercise ECG records, or Echo study and coronary angiography when available.21 Ninety eight patients had IHD, 52 (61.2%) male, and 46 (61.3%) female. Chronic Kidney Disease is defined as abnormalities of kidney structure or function (GFR less than 60ml/min/1.73m2), present for more than three months.22 Thirty six

patients had pre-existing renal impairment, 32 (37.6%) male, and 4 (5.3%) female. The diagnosis of DM was according to the ADA criteria.²³ Sixty six patients were diabetic, 36 (42.4%) male, and 30 (35.3%) female. Current Smoker is an adult who has smoked 100 cigarettes in their lifetime and presently smokes cigarettes every day (daily) or some days (nondaily).²⁴ Fifty two patients were current smokers; 35 (41.2%) male, and 17 (27.2%) female. Current alcoholics defined as drinking up to 1 drink per day for women and up to 2 drinks per day for men.²⁵ Seventeen current alcoholics found; 15 (17.6%) male, and 2 (2.7%) female. The diagnosis of Heart failure depended on clinical symptoms plus Echo study finding and ejection fraction ratio.²⁶ Thirty five patients had pre-existing heart failure; 31 (36.5%) male, and 4 (5.3%) female.

Statistical Analysis:

Data analysis was done by the use of IBM SPSS statistical software version 22.0 for Windows (SPSS Incorporation, Chicago, Illinois, USA), with many continuous and categorical variables. The mean value \pm SD was used for the description of the continuous variables, the frequencies and percentages for the description of the categorical variables. Chi-Square Test χ^2 is used to test and compare the categorical variables. The study adopts the two-tailed probability values with ($p \leq 0.05$) to be statistically significant.

3. Results

In this study from 160 patients 12 (7.5%) developed CIN, 7 (8.2%) male and 5 (6.6%) female. There was a significant association between age and the development of CIN (P value = 0.02). From 47 patients <45 years, only 1 (4.7%) patient developed CIN and 46 (74%) patients not; from 63 patients 45-65 years old, 3 (1.9%) patient developed CIN and 60 (37.5%) had not; from 50 patients >65 years, 8 (16%) patients developed CIN and 42 (60%) had not (Table 2). Gender had no significant association with CIN development (P value = 0.472); among 85 male patients in this study, 7 (8.2%) patients developed CIN and 78 (91.7%) had no CIN. while among 75 female patients, 5 (6.6%) developed CIN and 70 (93.4%) had not (Table 2). Hypertension was significantly associated with CIN development (P value = 0.02); 101 patients have hypertension, from them 11 (10.9%) developed CIN, and 90 (89.1%) did not; 59 patients had no history of hypertension, from them only 1 (1.7%) developed CIN and 58 (98.3%) did not (Table 2). Diabetes mellitus and CIN were significantly associated (P value= 0.016); from 66 patients with diabetes, 9 (13.6%) developed CIN, and 57 (86.4%) not; from 94 patients with no diabetes, 3 (3.2%) developed CIN and 91 (96.8%) not (Table 2). The presence of IHD was significantly associated with the development of CIN (P value=0.02); 98 patient had history of IHD, from them 11 (11.2%) developed CIN and 87 (88.8%) not; 62 patients had no history of IHD, from them only 1 (1.6%) patient developed CIN and 61 (98.4%) not. (Table 2)

Dyslipidemia and development of CIN were statistically

significant (P value=0.03); 102 patients had dyslipidemia, 11 (10.8%) developed CIN and 91 (89.2%) did not; while 58 patient had no dyslipidemia, only 1 (1.7%) developed CIN and 57 (98.3%) did not (Table 2). Heart failure was significantly associated with the development of CIN (P value= <0.001); 35 patients had heart failure, 9 (25.7%) developed CIN and 26 (74.3%) had no CIN; 125 patients had no heart failure, 3 (2.4%) developed CIN and 122 (97.6%) had not (Table 2). Preexisting renal impairment was significantly associated with CIN development (P value=0.01); from 36 patients 8 (22.2%) developed CIN and 28 (97.8%) had not; from 124 patients without preexisting renal impairment, 4 (3.2%) developed CIN and 120 (96.8%) had not (Table 2).

Table 2. Association between presence of CIN and characteristics of patients.

Variables	Presence of CIN		P	
	Yes	No		
Age in Years	<45	1 (2.1%)	46 (97.9%)	0.02
	45-65	3 (4.7%)	60 (74%)	
	>65	8 (16%)	42 (60%)	
Gender	Males	7 (8.3%)	78 (91.7%)	0.472
	Females	5 (6.6%)	70 (93.4%)	
HTN	Yes	11 (10.9%)	90 (89.1%)	0.02
	No	1 (1.7%)	58 (98.3%)	
DM	Yes	9 (13.6%)	57 (86.4%)	0.016
	No	3 (3.2%)	91 (96.8%)	
IHD	Yes	11 (11.2%)	87 (88.8%)	0.02
	No	1 (1.6%)	61 (98.4%)	
Dyslipidemia	Yes	11 (10.8%)	91 (89.2%)	0.03
	No	1 (1.7%)	57 (98.3%)	
Preexisting HF	Yes	9 (25.7%)	26 (74.3%)	<0.001
	No	3 (2.4%)	122 (97.6%)	
Preexisting renal impairment	Yes	8 (22.2%)	28 (97.8%)	0.01
	No	4 (3.2%)	120 (96.8%)	

CIN development was significantly affected by smoking (P value = 0.002); from 52 smokers, 9 (17.3%) developed CIN and 43 (82.7%) did not; 108 patients were not smoker, from them 3 (2.7%) patients developed CIN and 105 (97.3%) patients had not (Table 3). CIN development and alcohol use were significantly associated (p value=0.026); from 17 alcohol users, 4 (23.5%) developed CIN and 13 (76.5%) did not; 143 patients were non-alcohol user, 8 (5.6%) developed CIN and 135 (94.4%) had not (Table 3).

Table 3. The association between smoking and alcohol use on CIN development.

Variables	Presence of CIN		P	
	Yes	No		
Smoking	Yes	9 (17.3%)	43 (82.7%)	0.002
	No	3 (2.7%)	105 (97.3%)	
Alcohol use	Yes	4 (23.5%)	13 (76.5%)	0.026
	No	8 (5.6%)	135 (94.4%)	

Type of the procedure significantly affected the development of CIN (p value= 0.016); 64 patient underwent diagnostic coronary interventional procedure, 1 (1.6%)

developed CIN and 63 (98.4%) did not; while 96 patients underwent therapeutic coronary interventional procedure, 11 (11.5%) developed CIN and 85 (88.5%) did not (Table 4). The volume of contrast agent and the development of CIN

were significantly associated (P value= 0.001); 135 patients received < 300 ml, 5 (3.7%) developed CIN and 130 (96.3%) did not; 25 patients received ≥ 300 ml, 7 (28%) developed CIN and 18 (72%) not (Table 4).

Table 4. The association between the procedure type and volume of contrast on CIN.

Variables		Presence of CIN		P
		Yes	No	
Type of procedure	Diagnostic	1 (1.6)	63 (98.4%)	0.016
	Therapeutic	11 (11.5%)	85 (88.5%)	
Volume of contrast	< 300	5 (3.7%)	130 (96.3%)	< 0.001
	> 300	7 (28%)	18 (72%)	

4. Discussion

In this study, the incidence of CIN was 7.5% in patients who underwent coronary interventional procedures, which is similar to other studies [2, 27]. This result was lower than the study by Pérez-Topete et al in which the incidence was 14.2 % [8]. Also our result is higher than that shown by Rihal et al that was only 3.3 % [5]. This can be due to use of prophylactic measures before the procedure and sample size of each study. The presence of CIN shown to be significantly increased with increasing age of the patient with prevalence increased from (2.1%) in patients under 45 years old to (16%) in patients above 65 years old. This result was similar to other studies, and it is due to many factors including reduction of GFR and decrease in renal tubular function and concentration ability [10, 28]. Gender had no significant effect on the incidence of CIN; (8.3%) in males and (6.6%) in females. This is supported by other studies like that by Marenzi et al [29]. Hypertension has significantly increased the risk of CIN, and this can be due to effect of high blood pressure on the arteries around the kidneys which lead to vasospasm, narrowing and hardening of these arteries, and this is similar to a study by Bartholomew et al [30]. There was significant increase in CIN prevalence in diabetic patients (13.6%), and this result supported by other studies that show incidence of CIN between 5.7 % -29.4%, mainly due to the decrease in GFR and multiple vascular complications in these patients [31, 35]. dyslipidemia significantly increased the risk of CIN, this was supported by the study of Liu et al who studied 3632 patients. This is because LDL-C is associated with endothelial dysfunction, inflammation, and vasoconstriction, which are involved in the pathophysiology of CIN [32].

Preexisting HF shown to significantly increase the risk of CIN development in this study, which can be due to low renal perfusion [5, 30, 33]. IHD also was significantly increased the incidence rate of CIN in this study, since 11 out of the 12 patients who developed CIN had a history of IHD, sharing the same underlying mechanism with HF that lead to reduced renal perfusion [34, 35]. This study show significant association between preexisting renal impairment and prevalence of CIN, prevalence of CIN after PCI was increased with decreasing GFR [36]. Smoking also significantly increased the frequency of CIN in this study,

because smoking can increase blood pressure, activation of the sympathetic nerve, the renin-angiotensin, and the endothelin systems as well as alteration of intra renal hemodynamics [37]. This result differs from other study which found that smoking was not a significant risk factor for CIN development [30].

Type of the procedure was also important. Therapeutic procedure significantly increases the prevalence of CIN development more than diagnostic procedure. This can be attributed to the volume of contrast agent in these procedures, as therapeutic intervention take longer duration that needs larger volume of contrast agent; this is supported by a study of Kane et al [10]. Similarly, in a retrospective study of nearly 104 patients who underwent diagnostic or therapeutic PCI, those with duration of procedure more than 90 minutes shown a higher risk of CIN development, also shown that use of more than 200 ml of contrast media was associated with further risk for development of CIN [10], and other studies correspond to these findings [30, 33, 39].

Alcohol use was shown to have significant increase in the risk of CIN; (23.5%) of alcohol users developed CIN. This can be due to the renal tubular dysfunction that results from alcohol consumption which includes: increase urinary excretion of calcium, magnesium, and phosphate; incomplete renal tubular acidosis, and impaired urine-concentrating ability [37]. No other studies found that show a positive correlation between alcohol use and CIN development.

5. Conclusion

CIN is an important complication that can develop in patients undergoing cardiac catheterization, and it is aggravated by increasing age, presence of DM, HF, IHD, renal impairment, HTN, dyslipidemia, smoking and alcohol use. Also the type of procedure (therapeutic vs. diagnostic), and large volume of contrast agent are important risk factors for CIN development. There was no significant association between gender and development of CIN. So we recommend proper patient selection, appropriate type and low dose of contrast, and adequate hydration by IV normal saline to prevent CIN.

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