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Original Paper

Incidence and Main Determinants of Contrast-Induced Nephropathy following Coronary Angiography or Subsequent Balloon Angioplasty

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Key Words
Coronary artery · Angiography · Angioplasty · Nephropathy

Abstract
Background/Aims: Patient assessment by imaging studies using contrast media is currently replacing open procedures, especially in high-risk patients. However, the use of such contrast media might result in acute events and injuries after the procedure. In the present study, we first determined the incidence of contrast-induced nephropathy (CIN) in a sample of Iranian patients who candidated for coronary angiography and/or angioplasty, and then assessed major risk factors predicting the appearance of CIN following these procedures. ***Methods:*** Two hundred and fifty consecutive, eligible patients scheduled for coronary angiography and/or angioplasty at the Afshar Hospital in Yazd between January 2009 and August 2010 were considered for enrollment. Renal function was measured at baseline and 48 h after the intervention, and CIN was defined by an increase in creatinine of >0.5 mg/dl or 25% of the initial value. The predictive role of potential risk factors was determined in a multivariate model adjusted for comorbidities, preexisting renal impairment, and angiographic data. ***Results:*** CIN following coronary angiography or angioplasty appeared in 12.8% of the cases. A myocardial infarction before the procedure (OR = 2.121, p = 0.036) and a prior history of hypertension (OR = 2.789, p = 0.025) predicted the appearance of acute renal failure following angiography or subsequent angioplasty. A low estimated glomerular filtration rate at baseline slightly predicted CIN after these interventions. ***Conclusion:*** Transient acute renal dysfunction occurred in 12.8% of the patients within 48 h after angiography or subsequent angioplasty and could be predicted by a myocardial infarction before the procedure or by a prior history of systolic hypertension.
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Introduction

Patient assessment by imaging studies using contrast media is currently replacing open procedures, especially in high-risk patients. However, the use of such contrast media might result in acute events and injuries after the procedure [1, 2]. Contrast-induced nephropathy (CIN) refers to an abrupt deterioration in renal function temporally associated with iodinated contrast media administration, with no alternative clinical explanation [3]. It has been suggested that the serum creatinine increase usually peaks between days 3 and 5 of contrast media use, with levels returning to baseline within 1–3 weeks [4]. However, persistent serum creatinine elevation might lead to increased morbidity and even death after diagnostic or interventional procedures. Studies on patients who underwent coronary angiography and/or angioplasty have shown that the risk for early adverse events such as in-hospital cardiac death, need for coronary artery bypass grafting, major adverse cardiac events, need for blood transfusions, vascular surgery of the access site, and prolonged length of stay is significantly higher in patients who developed CIN compared with control subjects [5].

Underlying risk profiles have a major role for adverse events, particularly CIN following coronary angiography or angioplasty. According to recent reports, the incidence of CIN in patients with normal renal function is estimated to be <3%, but it widely varies between 12 and 50%, depending on the underlying risk factors [6–9]. Such risk factors can be related to patient characteristics such as advanced age, preexisting renal dysfunction, diabetes mellitus, systolic hypertension, hypotension, congestive heart failure, and use of nephrotoxic drugs. Procedure- and contrast medium-related risk factors include high total doses of contrast media and their high osmolality, high ionic content, and high viscosity as well as intra-arterial administration of contrast media and <2 days between the use of contrast media and the accomplishment of emergency procedures [10, 11]. Hence, it seems that the incidence of CIN varies in different populations due to the prevalence of these underlying risk profiles. In the present study, we first determined the incidence of CIN in a sample of Iranian patients who candidate for coronary angiography and/or angioplasty, and then assessed major risk factors predicting the appearance of CIN following these procedures.

Methods

Two hundred and fifty consecutive, eligible patients scheduled for coronary angiography and/or angioplasty at the Afshar Hospital in Yazd between January 2009 and August 2010 were considered for enrollment. The main exclusion criteria were a glomerular filtration rate (GFR) <30 ml/min, regular dialysis before angiography/angioplasty, a history of disseminated intravascular coagulation, coagulopathy, bleeding disorders, or acute renal failure secondary to other pathologies such as obstruction. Histories of multiple myeloma or pulmonary edema, pregnancy, administration of theophylline, dopamine, mannitol or fenoldopam, and recent exposure to radiographic contrast media (within 2 days of the study) were also considered as exclusion criteria. In addition, patients who denied research access to their medical records were excluded as well. The sample size was estimated by the Power Analysis and Sample Size for Windows software (PASS 2000). The group size of 220 achieved 90% power to detect a 15.0% prevalence of acute renal dysfunction following cardiac interventions, with a significance level (alpha) of 0.05. Allowing for a 10% dropout rate, the study required 250 patients. The study protocol was approved by the local Ethics Committee and written informed consent was obtained from all patients.

Patient, disease, and procedural data were recorded prospectively, and a careful history and examination were done to assess comorbid conditions such as diabetes mellitus and hypertension, previous exposure to contrast media and drugs, and hydration status. Procedural variables were also recorded, including the type of procedure (diagnostic, interventional), contrast medium type, contrast dye load, and contrast agent. The study participants received the nonionic, iso-osmolar dimeric contrast medium iodixanol (Visipaque®; GE Healthcare, Oslo, Norway) or the nonionic, low-osmolar monomeric agent iopromide

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Table 1. Clinical and demographic characteristics of the study population

Male gender	176 (70.4)
Age >70 years	42 (16.8)
Angioplasty protocol	59 (23.6)
History of diabetes mellitus	86 (34.4)
History of hypertension	140 (56.0)
History of anemia	64 (25.6)
Left ventricular ejection fraction <45%	52 (20.8)
Nephrotoxic drug use	44 (17.6)
Glomerular filtration rate <60 ml/min	96 (38.4)
Myocardial infarction within 24 h before procedure	35 (13.6)
Contrast medium volume >200 mm^3	26 (10.4)
Type of contrast medium	
Ultravist	187 (74.8)
Visipaque	63 (25.2)

Data are presented as numbers (%).

(Ultravist®; Bayer Schering Pharma, Berlin, Germany) for coronary angiography. All information was recorded in a coded data collection form.

All patients were administered IV fluids (normal saline) before the procedure, except for patients with congestive cardiac failure. Intravenous hydration consisted of 1 ml normal saline per kilogram of body weight per hour, which was started 12 h before contrast agent injection and continued for 12 h after the injection.

Serum creatinine, blood urea nitrogen, sodium, and potassium were measured the day before and 48 h after contrast agent administration. At baseline, estimated GFR (eGFR) was calculated by the level-modified Modification of Diet in Renal Disease equation as follows: (186.3 × serum creatinine 1.154) × (age – 0.203) × (0.742 if female) [12]. Left ventricular ejection fraction was estimated by coronary angiography or echocardiography, if available, and the type and amount of the contrast medium were recorded. Choice of the contrast medium depended on the patient's comorbidity and on the serum creatinine levels before the procedure.

The end point of the study was the peak increase of serum creatinine as a measure of CIN during hospitalization for coronary angiography and/or angioplasty. CIN was defined by an increase in creatinine of >0.5 mg/dl or 25% of the initial value [13].

The results were reported as the means ± standard deviation for the quantitative variables and percentages for the categorical variables. The groups were compared using the χ^2 test or Fisher's exact test if required for the categorical variables. Predictors exhibiting a statistically significant relation with CIN in univariate analyses were taken for multivariate logistic regression analysis to investigate their independence as predictors. ORs and 95% CI were calculated. This study was done with the power of 90%. p values of ≤0.05 were considered statistically significant. All statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, Ill., USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, N.C., USA).

Results

The mean age of the study population (n = 250) was 55.2 ± 12.6 years, 16.8% were older than 70 years, 70.4% were male, and 20.8% had a left ventricular ejection fraction <45%. Diabetes mellitus was found in 34.4%, 56.0% had systolic hypertension, and 13.6% experienced a myocardial infarction within 24 h before the procedure (table 1). Forty-four patients (17.6%) were administered one of the nephrotoxic drugs, including NSAIDs, ACE inhibitors, or metformin. Forty-five patients were administered N-acetylcysteine before the procedure. Ninety-six (38.4%) patients had preexisting renal dysfunction, defined as an eGFR <60 ml/min. The volume of the contrast agent administered during angiography and

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Table 2. Clinical and demographic characteristics in the two angioplasty and isolated angiography subgroups

Characteristics	With angiography (n = 59)	Without angiography (n = 191)	p value
Male gender	9 (15.3)	17 (8.9)	0.215
Age >70 years	3 (5.1)	5 (2.7)	0.403
History of diabetes mellitus	6 (10.2)	10 (5.2)	0.232
History of hypertension	18 (30.5)	6 (3.2)	<0.001
Left ventricular ejection fraction <45%	6 (10.2)	2 (1.1)	0.004
Nephrotoxic drug use	3 (5.1)	7 (3.7)	0.706
Glomerular filtration rate <60 ml/min	7 (11.3)	11 (5.8)	0.160
Myocardial infarction	4 (7.0)	6 (3.2)	0.262
Contrast medium volume >200 mm^3	0 (0.0)	4 (2.1)	0.576

Data are presented as numbers (%).

subsequent angioplasty was >200 mm^3 in 10.4% of the subjects. As expected, CIN following coronary angiography or angioplasty appeared in 12.8% (95% CI: 7.3–28.6) of the cases. None of the patients required transient hemodialysis or developed persistent renal failure. Among those who received N-acetylcysteine, 10.0% experienced CIN, while this complication was observed in 15.6% of the other patients (p = 0.332). Fifty-nine (23.6%) out of 250 patients underwent coronary angioplasty according to these procedure indications. The patients undergoing angioplasty were similar to the other subgroup in terms of sex ratio, mean age, and history of diabetes mellitus; however, systolic hypertension and left ventricular dysfunction were more frequent in the angioplasty group (table 2). Univariate analysis identified five variables that were significantly related to CIN after angioplasty, including a history of diabetes or hypertension, occurrence of a myocardial infarction within 24 h before the procedure, nephrotoxic drug use, and preexisting renal dysfunction (table 3). Larger amounts of a contrast agent or its type were not associated with renal failure following the procedure. When these variables were entered into the multivariate logistic regression model (table 4), two variables (myocardial infarction and a prior history of hypertension) emerged as independent predictors of the outcome with a p value <0.05. A low baseline eGFR slightly predicted CIN following angiography or subsequent angioplasty.

Discussion

CIN is an increasingly common event that warrants careful assessment of affected patients. Prevention of CIN requires careful identification of the factors that increase the risk and affect early and long-term outcome. Regarding the incidence of CIN following percutaneous coronary intervention (PCI), the published reports found various rates. In this study, the incidence of CIN related to angiography or angioplasty was estimated at 12.8%. According to the different definitions of CIN after cardiac procedures, the overall incidence of CIN in the general population was estimated to lie between 1 and 6% [14], but it was higher in those who underwent PCI. In a study by Rihal et al. [7] and based on the Mayo Clinic PCI registry, the incidence of PCI in the general population was 3.3%, and dialysis was needed in 0.3%. However, this rate might rise up to 20% or more in selected patient subsets, especially in patients with underlying cardiovascular disease [3], and even to 50% in high-risk patients

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Table 3. Prevalence of CIN in different risk factor groups

Risk factors	Prevalence	p value
Gender		
Male	26 (14.8)	0.150
Female	6 (8.1)	
Age		
>70 years	8 (19.0)	0.184
≤70 years	24 (11.5)	
Angioplasty procedure		
Positive	8 (13.6)	0.786
Negative	23 (12.0)	
History of diabetes mellitus		
Positive	16 (18.4)	0.047
Negative	16 (9.8)	
History of hypertension		
Positive	24 (17.1)	0.021
Negative	8 (7.3)	
Myocardial infarction within 24 h before procedure		
Positive	10 (28.6)	0.003
Negative	22 (10.2)	
Left ventricular ejection fraction		
>45%	24 (13.1)	0.531
≤45%	8 (15.4)	
GFR		
>60 ml/min	14 (9.1)	0.026
≤60 ml/min	18 (18.8)	
Nephrotoxic drug use		
Positive	10 (22.7)	0.030
Negative	22 (10.7)	
Contrast medium volume		
>200 mm^3	4 (15.3)	0.412
100–200 mm^3	18 (13.6)	
<100 mm^3	10 (11.4)	
Type of contrast medium		
Ultravist	26 (15.5)	0.348
Omnipack	6 (9.5)	

Data are presented as numbers (%). p values ≤0.05 were considered significant.

Table 4. Multivariate logistic analysis

Variable	p value	OR	95% CI
Male gender	0.239	0.589	0.198–1.458
Age >70 years	0.321	0.659	0.254–1.017
Diabetes mellitus	0.069	1.255	0.653–3.446
Hypertension	0.025	2.789	1.236–5.878
Myocardial infarction	0.036	2.121	1.040–6.587
Anemia	0.089	1.259	0.825–2.235
Left ventricular ejection fraction <45%	0.785	1.445	0.354–2.147
Nephrotoxic drug use	0.123	1.444	0.235–2.457
Glomerular filtration rate <60 ml/min	0.066	0.235	0.056–1.139
Contrast medium volume >200 mm^3	0.996	0.234	0.021–2.114
Type of contrast medium	0.326	0.243	0.110–1.565

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[6–9]. It should be considered, however, that renal deterioration after angiography usually occurs transiently, and persistent renal failure requiring dialysis or other clinically severe renal events are rarely reported [15–17].

As previously mentioned, underlying risk factors affecting renal failure following cardiac procedures are frequently related to the patient's condition, contrast media use, and even technical and procedural factors. These factors have been shown to compromise medullary oxygen sufficiency as well as alter renal protective mechanisms. Some prevalent patient-related risk factors are advanced age, preexisting renal insufficiency, diabetes mellitus, hypotension, hypertension, congestive heart failure, and the concomitant use of nephrotoxic drugs. The most common procedure- and contrast medium-related risk factors are potentially associated with the dosage, viscosity, and osmolarity of contrast media [10, 11]. In the study by Mehran and Nikolsky [3], the variables with which the risk for CIN after PCI was assessed were hypotension, intra-aortic balloon pump use, congestive heart failure, a serum creatinine level >1.5 mg/dl, age >75 years, anemia, diabetes mellitus, and contrast medium volume. The risk factors for CIN were classified into modifiable factors (such as volume depletion, anemia, blood loss, nephrotoxic medication, low serum albumin, volume, osmolarity, or iconicity of contrast media) and nonmodifiable factors (such as age, patients' medical history and risk factors, emergency PCI, intra-aortic balloon pump insertion, or previous renal transplantation) [18]. In the present study, the two cardiovascular risk factors that emerged as determinants of CIN following angiography or angioplasty were a myocardial infarction before the procedure and a prior history of hypertension. Some cardiac risk factors such as anterior myocardial infarction were associated with an increased risk for CIN as they reduce renal perfusion [19, 20]. In a study by Roghi et al. [21] using a similar logistic regression analysis, acute renal failure was associated with left ventricular ejection fraction, hypertension, and prior coronary bypass surgery. With respect to the important role of hypertension, this indicator can be associated with advanced atherosclerosis of the aorta and suggests that atheroembolization of the kidney during PCI may also be an important cause of acute renal failure [22].

We could not confirm any effective role of contrast medium type or volume in inducing renal failure following cardiac interventions in our survey. This might be due to the low dosage and volume of these agents, i.e. only one-fifth of the patients received a volume >100 ml and only 10.4% of them received a contrast medium volume >200 ml. McCullough et al. [23] showed that the risk for CIN is minimal if patients receive <100 ml contrast media during procedures or if the contrast medium volume used is <5 ml/kg/serum creatinine. Although Kane et al. [24] demonstrated a significant rise in the incidence of CIN with an increased volume of contrast media, Mekan et al. [25] adversely found that the contrast media-induced reduction in renal function was not significantly higher with a higher volume of contrast media (>100 ml). In summary, to demonstrate a relationship between the volume of contrast media and the risk of CIN following angiography or angioplasty, further investigation is needed, especially with larger sample sizes.

A general limitation of our study is that the retrospective design did not allow the researchers to examine random effects of the contrast medium type on the appearance of CIN. As mentioned in the Methods section, all available predictors exhibiting a statistically significant role for CIN in univariate analyses were also used for multivariate analysis to investigate their independence as predictors. As seen in table 2, most variables had a borderline multivariate p value of <0.15. This shows that the results might be different in studies with greater sample sizes or studies that consider more of the probable indicators. Thus, performing further studies with larger sample sizes to confirm the obtained results is recommended.

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Conclusion

In conclusion, we showed that transient acute renal dysfunction occurred in 12.8% of the patients within 48 h after angiography or subsequent angioplasty and could be predicted by a myocardial infarction before the procedure or a prior history of systolic hypertension.

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Disclosure Statement

None of the authors has conflicts of interest to disclose.

References

1 Laville M, Juillard L: Contrast-induced acute kidney injury: how should at-risk patients be identified and managed? J Nephrol 2010;23:387–398.
2 Gopalan PD: Contrast-induced acute kidney injury. S Afr J Anaesth Analg 2011;17:193–195.
3 Mehran R, Nikolsky E: Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int 2006;100:11–15.
4 Nikolsky E, Aymong ED, Dangas G, Mehran R: Radiocontrast nephropathy: identifying the high-risk patient and the implications of exacerbating renal function. Rev Cardiovasc Med 2003;4:7–14.
5 Dangas G, Iakovou I, Nikolsky E: Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol 2005;95:13–19.
6 McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW: Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med 1997;103:368–375.
7 Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR Jr: Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation 2002;105:2259–2264.
8 Lautin EM, Freeman NJ, Schoenfeld AH, Bakal CW, Haramati N, Friedman AC, Lautin JL, Braha S, Kadish EG: Radiocontrast associated renal dysfunction: incidence and risk factors. AJR Am J Roentgenol 1991;157:49–58.
9 Parfrey P, Griffiths SM, Barrett BJ, Paul MD, Genge M, Withers J, Farid N, McManamon PJ: Contrast material-induced renal failure in patients with diabetes mellitus, renal insufficiency, or both: a prospective controlled study. N Engl J Med 1989;320:143–149.
10 Toprak O, Cirit M: Risk factors for contrast induced nephropathy. Kidney Blood Press Res 2006;29:84–93.
11 Solomon R, Dauerman HL: Contrast-induced acute kidney injury. Circulation 2010;122:2451–2455.
12 Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D: A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461–470.
13 Solomon R, Deray G: How to prevent contrast-induced nephropathy and manage risk patients: practical recommendations. Kidney Int 2006;69:51–53.
14 Parfrey P: The clinical epidemiology of contrast-induced nephropathy. Cardiovasc Intervent Radiol 2005;28:3–11.
15 Gussenhoven MJ, Ravensbergen J, van Bockel JH, Feuth JD, Aarts JC: Renal dysfunction after angiography: a risk factor analysis in patients with peripheral vascular disease. J Cardiovasc Surg 1991;32:81–86.
16 Lautin EM, Freeman NJ, Schoenfeld AH, Paul MD, Genge M, Withers J, Farid N, McManamon PJ: Radiocontrast-associated renal dysfunction: incidence and risk factors. AJR Am J Roentgenol 1991;157:49–58.
17 Rudnick MR, Goldfarb S, Wexler L, Ludbrook PA, Murphy MJ, Halpern EF, Hill JA, Winniford M, Cohen MB, VanFossen DB: Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: a randomised trial. The Iohexol Cooperative Study. Kidney Int 1995;47:254–261.
18 Shoukat S, Gowani SA, Jafferani A, Dhakam SH: Contrast-induced nephropathy in patients undergoing percutaneous coronary intervention. Cardiol Res Pract 2010;2010:649164.

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19 Dangas G, Iakovou I, Nikolsky E, Aymong ED, Mintz GS, Kipshidze NN, Lansky AJ, Moussa I, Stone GW, Moses JW, Leon MB, Mehran R: Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol 2005;95:13–19.
20 Marenzi G, Lauri G, Assanelli E, Campodonico J, De Metrio M, Marana I, Grazi M, Veglia F, Bartorelli AL: Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. J Am Coll Cardiol 2004;44:1780–1785.
21 Roghi A, Savonitto S, Cavallini C, Arraiz G, Angoli L, Castriota F, Bernardi G, Sansa M, De Servi S, Pitscheider W, Danzi GB, Reimers B, Klugmann S, Zaninotto M, Ardissino D; Atherosclerosis, Thrombosis and Vascular Biology Study Group and the Italian Society for Invasive Cardiology Investigators: Impact of acute renal failure following percutaneous coronary intervention on long-term mortality. J Cardiovasc Med 2008;9:375–381.
22 Keeley EC, Grines CL: Scraping of aortic debris by coronary guiding catheters: a prospective evaluation of 1,000 cases. J Am Coll Cardiol 1998;32:1861–1865.
23 McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW: Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med 1997;103:368–375.
24 Kane GC, Doyle BJ, Lerman A, Barsness GW, Best PJ, Rihal GC: Ultra-low contrast volumes reduce rates of contrast-induced nephropathy in patients with chronic kidney disease undergoing coronary angiography. J Am Coll Cardiol 2008;51:89–90.
25 Mekan SF, Rabbani MA, Azhar-Uddin M, Ali SS: Radiocontrast nephropathy: is it dose related or not? J Pak Med Assoc 2004;54:372–374.

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