

The Incidence Of Contrast-Induced Nephropathy Or Radiocontrast Nephropathy

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Abstract

BACKGROUND AND PURPOSE: Most studies of contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN) have been derived from intra-arterial administration of contrast and percutaneous coronary intervention, the results of which may not be easily applicable in radiology, where most contrast administration is via the intravenous route. The purpose of this study is to document the rate of CIN/RCN in patients undergoing computed tomography angiography (CTA) of the head and/or neck, who were given contrast via the intravenous route.

MATERIALS AND METHODS: This is a retrospective study involving a random sample of 594 patients with normal serum creatinine and normal estimated glomerular filtration rate who had CTA of the head and/or neck.

RESULTS: Two hundred and twenty eight patients (38.39%) had a decrease in serum creatinine, 212 patients (35.69%) had no change in serum creatinine, and 154 patients (25.93%) had an increase in serum creatinine after contrast administration. There were 2 patients (0.3%) who had greater than 0.5 mg/dL increase in 48-hour serum creatinine, 40 (6.7%) patients who had 25% or greater increase in serum creatinine, and 2 patients (0.3%) who had greater than 0.5 mg/dL increase serum creatinine and 25% or greater increase in serum creatinine 48 hours after contrast administration.

CONCLUSION: The rate of CIN/RCN is 0.3-6.7% depending on the definition used. CIN/RCN is a rare complication in patients given intravenous contrast. The intravenous administration of contrast for CTA of the head and neck is safe, and may be used in routine evaluation of stroke and trauma.

INTRODUCTION

Contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN) is acute renal failure occurring after contrast administration. An accepted definition of CIN/RCN is increase of serum creatinine of > 0.5 mg/dL or 25% above baseline within 48 hours after contrast administration. The pathophysiology of CIN/RCN is not clear but contrast may have ischemic and direct toxic effect on renal tubular cells. The most important risk factors of CIN/RCN are pre-existing renal insufficiency and diabetes. The incidence of CIN/RCN is highly variable, depending on the patient population, length of patient follow-up, definition of CIN/RCN, type of procedure, type and dose of contrast used, and route of contrast administration (1-11).

Most of the studies of contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN) have been derived from intra-arterial administration of contrast (98.7%) (2), and

percutaneous coronary intervention, the results of which may not be easily applicable in radiology, where most contrast administration is via the intravenous route. Although most studies of CIN/RCN have been based on changes in serum creatinine, serum creatinine is not a reliable measure of renal impairment. Serum creatinine is affected by many factors including age, sex, and ethnicity. Glomerular filtration rate (GFR) or estimated glomerular filtration rate (eGFR) is a more appropriate assessment of renal function because it takes into account age, sex, and ethnicity of the patients (11-19).

Computed tomography angiography (CTA) of the head and neck are routinely used in the evaluation of acute stroke and acute trauma. The intravenous administration of contrast is associated with the risk of contrast-induced nephropathy (CIN) or radiocontrast nephropathy (RCN). The aim of this study is to document the rate of contrast-induced

nephropathy (CIN) or radiocontrast nephropathy (RCN) in patients undergoing CTA of the head and/or neck, who were given contrast via the intravenous route. CIN/RCN is diagnosed by changes in serum creatinine and estimated glomerular filtration rate (eGFR) as determined by the older Modification of Diet in Renal Disease (MDRD) Study and the newer Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. I believe that this is the first time that CIN/RCN has been diagnosed by changes in serum creatinine and estimated glomerular filtration rate (eGFR) as determined by the older MDRD Study and newer CKD-EPI equations.

MATERIALS AND METHODS

This is a retrospective study of patients who had CTA of the head and/or neck. All patients were given the same amount of contrast (100 ml of Optiray 350) by the intravenous route. A random sample of 594 patients with normal serum creatinine who presented to my institution between July 2008 and October 2009 was undertaken. A waiver was granted by the Institutional Review Board for this study which is compliant with the U.S. Health Insurance Portability and Accountability Act. The inclusion criteria include: (i) baseline serum creatinine on the day of the examination, prior to the examination and follow-up serum creatinine in 48 hours. (ii) No history of acute or chronic renal impairment. (iii) Availability of the necessary demographic information of age, sex, and race. Estimated glomerular filtration (eGFR) was calculated from serum creatinine using the older Modification of Diet in Renal Disease (MDRD) Study and the newer Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations; the details of these equations are beyond the scope of this paper and have been covered elsewhere. Chronic kidney disease is defined as glomerular filtration (GFR) < 60 mL/min/1.73 m² (12-19). Patients with baseline eGFR of 60 mL/min or less were excluded from this study. Data analysis was done using Northwest Analytical Quality Analyst 6.1 statistical software (Portland, Oregon). The results are presented as mean (standard deviation, SD), and t-test ($p = 0.05$) was used for comparisons.

RESULTS

The age range of the 594 patients is 17 - 91 years (mean 48.5, SD = 19.7). There were 378 males (63.4%) and 216 females (36.4%); 514 whites (86.5%) and 80 nonwhites (13.5%) (3 American Indians (0.5%), 74 African Americans (12.5%), and 3 Pacific Islanders (0.5%)). One hundred and sixteen (19.5%) patients had CTA of the head, 274 patients

(46.1%) CTA of the neck, and 204 patients (34.3%) had CTA of the head and neck. The 48-hour fluctuation of serum creatinine is defined as baseline serum creatinine minus 48-hour serum creatinine. The distribution of the 48-hour change in absolute serum creatinine and the 48-hour percent change in serum creatinine are shown in Tables 1 and 2. Two hundred and twenty eight patients (38.39%) had a decrease in serum creatinine, 212 patients (35.69%) had no change in serum creatinine, and 154 patients (25.93%) had an increase in serum creatinine after contrast administration. The range of the baseline serum creatinine is 0.3 - 1.6 mg/dL, with a mean of 0.81 mg/dL (SD = 0.19). The follow-up 48-hour serum creatinine ranged from 0.4 to 1.5 mg/dL, with a mean of 0.78 mg/dL (SD = 0.18). The average 48-hour fluctuation of serum creatinine is -0.02 mg/dL (SD = 0.14), and average 48-hour fluctuation of eGFR is 2.34 mL/min/1.73 m² (SD = 12.51) and 3.33 mL/min/1.73 m² (SD = 20.61) by CKD-EPI and MDRD methods, respectively. The average 48-hour percent fluctuation in serum creatinine is -1.46 % (SD = 16.96).

There is no statistically significant difference in the 48-hour fluctuation of the serum creatinine between whites and nonwhites ($p = 0.62$). However, there is a statistically significant difference in the 48-hour fluctuation of the serum creatinine for all patients ($p < 0.01$), between females and males ($p = 0.02$), young (≤ 49 years) and old (≥ 50 years) patients ($p = 0.01$), and low baseline serum creatinine (≤ 0.9) and high baseline serum creatinine (≥ 1.0) ($p < 0.01$). The reason for these statistically significant differences (which are much less than 0.1 mg/dL) is not clear; however, they are not clinically significant because they may not be detected in routine laboratory testing since serum creatinine is measured in 0.1 mg/dL increments.

DISCUSSION

The majority of the patients (74.08%) had no change or a decrease in serum creatinine whilst 25.93% had an increase in serum creatinine after contrast administration. An accepted definition of CIN/RCN is increase of serum creatinine of > 0.5 mg/dL or 25% above baseline within 48 hours after contrast administration. There were 2 patients (0.3%) who had greater than 0.5 mg/dL increase in 48-hour serum creatinine, 40 (6.7%) patients who had 25% or greater increase in serum creatinine, and 2 patients (0.3%) who had greater than 0.5 mg/dL increase serum creatinine and 25% or greater increase in serum creatinine in 48 hours. In other words, in this study, the rate of CIN/RCN varies from 0.3 – 6.7% depending on the definition used (Table 3), which is

comparable to previous reported incidence of CIN/RCN of 0.37-14.5% in patients without risk factors and 2-37% in patients with risk factors (2, 3, 10, 11, 20-35)

The mean 48-hour fluctuation in serum creatinine is - 0.02 mg/dL (SD = 0.14). The results of this study suggest that a more appropriate definition of CIN/RCN is absolute increase in serum creatinine of 0.3 mg/dL rather than 0.5 mg/dL. A definition of CIN as 25% increase in serum creatinine may be too permissive; rather a 50% increase in serum creatinine may be more appropriate, which is comparable to prior studies (21-23). The incidence of CIN/RCN 1.2% if it is defined as both an absolute increase in serum creatinine of 0.3 mg/dL and 50% increase in serum creatinine. Using a definition of CIN/RCN as increase in serum creatinine \geq 0.50 mg/dL and increase of serum creatinine of \geq 25%, Jabara et al (20) reported CIN/RCN rates of 3.3% and 10.2%, respectively. Cramer et al (21) reported that the rate of renal impairment in patients given contrast administration was 2.1% and 1.3% in a control group that did not receive contrast, statistically insignificant difference. Heller et al (23) demonstrated renal impairment in 4%, 12%, and 4% of patients who were given high osmolar contrast, low osmolar contrast, and no contrast. Langner et al (34) found that 7% of patients who had contrast had a relative increase of serum creatinine of equal to or greater than 25% compared with baseline, and 12% of control patients who had no contrast had a relative increase serum creatinine of equal to or greater than 25% compared with baseline, statistically insignificant difference. Bruce et al (10) found no significant difference in incidence of presumed contrast-induced kidney injury between patients given iso-osmolar contrast and control group which was not given contrast. Kragha (unpublished data, 2010) (36) in a study of the usual 48-hour background fluctuation of serum creatinine and estimated glomerular filtration rate in patients without renal impairment found that approximately 0.4% had greater than 0.5 mg/dL increase in 48-hour serum creatinine, 8.9% patients had 25% or greater increase in serum creatinine, and 0.4% patients met both criteria.

The wide variation in the published incidence of CIN/RCN may be due to differences in study population, pre-existing disease or risk factors, lack of adequate control groups, timing of follow-up definition, contrast type, dose and route of administration (2, 3, 11, 20-35; Table 4). There appears to be overestimation of the incidence of CIN/RCN in published reports for the aforementioned reasons. Contrast may have no significant role in the elevation of serum creatinine - the

rate of CIN/RCN found in this study may be due to normal background fluctuation of renal function or other confounding factors (2, 3, 10, 11, 20-36).

There is inverse relationship between the elevation of serum creatinine post contrast administration and baseline serum creatinine (linear correlation coefficient of - 0.43). The reason for this finding is unclear and is opposite to the finding of Bruce et al (10) who reported increasing incidence of acute kidney injury with increasing baseline creatinine concentration. However, baseline creatinine accounts for only about 18% of the variance in elevation of serum elevation post contrast administration.

The results of this study may not be applicable to the general population because of (i) it is a retrospective study with selection bias of hospital patients, and (ii) the MDRD Study and CKD-EPI equations underestimate GFR at higher values (12-19). Although a large prospective controlled study may be desirable to demonstrate the very low incidence of CIN/RCN, such a study may be unnecessary because of a very large sample size to needed to demonstrate a statistically significant but clinically insignificant finding (2, 3, 21).

CONCLUSION

The majority of the patients (approximately 74%) had no change or a decrease in serum creatinine whilst approximately 26% had an increase in serum creatinine after contrast administration. The rate of CIN/RCN is 0.3 – 6.7%, depending on the definition used. This low rate of CIN/RCN may be attributed to normal background fluctuation of renal function or other confounding factors, without contrast playing any significant role. In other words, CIN/RCN is a rare complication in acute stroke and acute trauma patients who are given intravenous contrast for CTA of the head and neck. The administration of 100 ml of Optiray 350 (a nonionic contrast) intravenously for CTA of the head and neck is safe, and may be used in routine evaluation of stroke and trauma. In emergency, it may not be necessary to obtain serum creatinine if early diagnosis in acute stroke and trauma is needed because of the low rate of CIN/RCN. Furthermore, evaluation of renal function in patients without significant risks factors for renal impairment after contrast administration may not be necessary. I believe that this is the first time that CIN/RCN has been diagnosed by changes in serum creatinine and estimated glomerular filtration rate (eGFR) as determined by the older MDRD Study and newer CKD-EPI equations.

Table 1

Change of serum creatinine (mg/dL) after IV contrast administration.

Change in serum creatinine (mg/dL)	Percent
-0.5	0.2
-0.4	1.2
-0.3	3.5
-0.2	11.3
-0.1	22.2
0	35.7
0.1	18.4
0.2	6.1
0.3	0.8
0.4	0.3
0.5	0.2
0.6	0
0.7	0.2

Table 2

Frequency of percent change in serum creatinine after contrast administration.

Range of percent change in serum creatinine	Percent
-31 to -40	2.4
-21 to -30	8.4
-11 to -20	22.4
-1 to -10	5.2
0	35.7
1-10	2.4
11-20	16.0
21-30	5.1
31-40	0.8
41-50	1.0
51-60	0.3
61-70	0.2
71-80	0
81-90	0
91-100	0
>100	0.2

Table 3

Rate of contrast induced nephropathy (CIN) depending on definition.

Definition	Rate of contrast induced nephropathy (%)
[1] Absolute increase in serum creatinine	
>/= 0.25 mg/dL	1.5
>/= 0.50 mg/dL	0.3
[2] Percent increase in serum creatinine	
>/= 25%	6.7
>/= 50%	1.5
[3] A combination of #1 and #2 above	
>/= 0.25 mg/dL + >/= 25%	1.5
>/= 0.25 mg/dL + >/= 50%	1.2
>/= 0.50 mg/dL + >/= 25%	0.3
>/= 0.50 mg/dL + >/= 50%	0.3
[4] Decrease in estimated GFR	
>/= 25%	
CKD-EPI	1.7
MDRD	6.7
>/= 50%	
CKD-EPI	0.2
MDRD	1.0

Table 4a

Incidence of contrast-induced (CIN) or radiocontrast nephropathy (RCN).

AUTHOR	TYPE OF STUDY	SAMPLE SIZE	INCIDENCE OF CIN (NUMBER)	INCIDENCE OF CIN (%)
Dittrich et al (18)	CT perfusion, CTA	162	3	2
Jabara et al (14)	Percutaneous coronary intervention	275		3.3 – 10.5
Josephson et al (19)	CT perfusion, CTA	1075	4	0.37
Krol et al (20)	CTA	224	7	3
Rihal et al (21)	Percutaneous coronary intervention	7586	254	3.3
McCullough et al (22)	Percutaneous coronary intervention	1826		14.5
Davidson et al (23)	Cardiac catheterization	1144		6
Cramer et al (15)	CT	193 study subjects 233 control subjects		2.1 1.3
Heller et al (17)	CT	292 patients given high osmolar contrast 187 patients given low osmolar contrast 405 patients not given contrast	12 23 16	4 12 4
Langner et al (28)	CT perfusion	100 study patients 100 control patients	7 12	7 12
Schwab et al (29)	Coronary angiography	283 low risk patients 160 high risk		10.2 8.2

Table 4b

		patients		
Harris et al (16)	CT	101 patients with renal insufficiency	7 out of 50 given ionic contrast 1 out of 51 given nonionic contrast	14 2
Gruber et al (24)	Percutaneous coronary intervention	439 patients with renal insufficiency	161	37
Barrett et al (25)	CT	166 patients with renal insufficiency	6	4
Becker & Reiser (26)	CT	100 patients with renal failure	9	9
Alamattine et al (27)	Radiological procedures	809 patients with various risk factors	58	7
Gleeson & Bulugahapiti (1)	Review of literature			0-90
Katzberg & Barrett (3)	Review of literature			< 1-30
Murphy et al (5)	Review of literature			3-100
Schrader (6)	Review of literature			0.6-50
Goldenberg & Matetzky (7)	Review of literature			3.3-26
McCullough et al (8)	Meta-analysis	Patients with diabetes, chronic renal failure		1.4-5.5
Weisbord & Palevsky (9)	Review of literature			5 - >50

CT: Computed tomography
CTA: Computed tomography angiography
%: Percentage

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