Original Article

Contrast-induced nephropathy in urological imaging: A comparison with cardiology interventions

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ABSTRACT

Introduction: Published studies about contrast-induced nephropathy (CIN) mainly focus on cardiac intervention and rarely focus on patients undergoing urological contrast investigations. We aimed to determine the association and effect of intravenous (IV) iodinated contrast material on the incidence of CIN in a group of patients undergoing urology investigation and compare the results with that of cardiology interventions.

Methods: This prospective study was performed in patients undergoing IV contrast studies in Urology and those undergoing coronary interventions, in our institution for 1 year. Association between the occurrence of CIN and the risk factors such as age (≥60 years), sex, diabetes mellitus, hypertension, anemia, left ventricular ejection fraction <40%, estimated glomerular filtration rate (eGFR), and volume of contrast used were studied using Chi-square tests or Fisher exact test and Student's *t*-test.

Results: A total of 339 cases (168 urology and 171 cardiology) were studied. CIN was noted in 8.3% of urology patients whereas it was 29.8% in cardiology patients. In urology patients, statistically significant association was noted between CIN and eGFR <60 ml/min/1.73 m^2 and volume of contrast used. In cardiology patients, statistically significant association ($P < 0.05$) was noted for diabetes, hypertension, eGFR <60 ml/min/1.73 m^2, volume of contrast used.

Conclusion: Although CIN was found to occur with contrast studies, the deleterious effects of contrast in urological procedures were lower than cardiology patients. The association between the occurrence of CIN and patient factors were also different in the two groups.

INTRODUCTION

Contrast-induced nephropathy (CIN) is defined as an increase in serum creatinine (SCr) >25% or ≥0.5 mg/dL from the baseline value, within 48 h of contrast administration in the absence of an alternative cause.[1] CIN is the third most common cause of newly detected acute renal failure in hospitalized patients, the first two causes being surgery and hypotension.[2-5] CIN is believed to resolve within 3 weeks, and the SCr level returns to baseline or new baseline within 1–3 weeks on serial follow-up.[6] CIN is known to increase in-hospital mortality up to 27%.[2,5] Type and volume of contrast material used, route of injection, heart failure (left ventricular ejection fraction <40%), concomitant nephrotoxic drugs, etc., have been proposed to be associated with the risk for CIN.[1,7,8] Preventive measures for high-risk patients include discontinuation of diuretics and nephrotoxic medication in addition to prophylactic intravenous (IV) hydration before and after contrast injection.

Reported incidence of CIN have varied due to inconsistencies in the definition of the condition, as well as differences in the procedure studied, the type and dose of contrast used and patient population in various studies. Rates of CIN in the general population have been estimated to

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be <2%,[7,9] but incidence between 40% and 90% have been quoted in some studies depending on the number of risk factors present.[7,10,11] A large epidemiological study by McCullough *et al*.[3] quoted an overall rate of incidence of 14.5% in patients undergoing radiological procedures with contrast. Guidelines and evidence of CIN have been derived mainly from reports of contrast use in cardiovascular intervention. However, there are few reports on the incidence of CIN in uroradiological imaging, particularly IV pyelogram (IVP), contrast computed tomography (CT) abdomen, contrast enhanced CT abdomen, CT urograms, and renal angiograms. Hence, this study was undertaken to study the incidence of CIN in radiological procedures used for investigations and treatment of urological illnesses, evaluate the association of different risk factors with the incidence of CIN and compare the results with those in cardiology patients undergoing radiological procedures using contrast media.

METHODS

Patients

This was a prospective study in patients undergoing uroradiological imaging using IV contrast injection and those undergoing coronary angiogram/angioplasty in our hospital during 12 months from January 2015. All patients with established chronic kidney disease (CKD), SCr ≥2.5 mg/dl, patients on dialysis and those on long-term diuretics were excluded from the study. Data were obtained through scripted proforma after taking informed consent from the patients. The hospital's ethics committee's approval was obtained. The presence of risk factors such as diabetes mellitus (DM), hypertension, elderly age (≥60 years), anemia (hemoglobin <10 g %), and left ventricular ejection fraction <40% were noted.

Interventions

The renal functions before and after the study were measured. SCr values were obtained using a kinetic colorimetric compensated Jaffe technique, immediately before and 24 h after IV and intra-arterial contrast injection. Prophylactic hydration was given to those cases who had preprocedural SCr values ≥1.5 mg/dl, with normal saline at a dose of 1 mL/kg/h 6 h before the procedure, and continued up to 12 h after the procedure, along with per oral acetylcysteine tablets 600 mg twice daily before and after the procedure continued for 24 h. The SCr evaluated immediately before contrast administration was taken as the baseline value. Patients with detected CIN were followed up for 5 days with daily SCr measurements.

For uroradiological imaging, CT urogram, CT abdomen, CT angiograms and IVP, Omnipaque (Iohexol), a low osmolar nonionic monomer, IV, at a dose of 1–1.5 ml/kg was used as a contrast medium. For cardiological intervention such as angiograms and angioplasties also Omnipaque (Iohexol), intra-arterially was used. However, dosage varied depending on the type of lesion studied in the coronary vessels.

End-point

The incidence of CIN and correlation with risk factors were compared in two groups. Association between the occurrence of CIN and the risk factors such as age ≥60 years, sex, DM, hypertension, anemia, left ventricular ejection fraction <40%, estimated glomerular filtration rate (eGFR), and volume of contrast used was studied. To calculate eGFR, we used the CKD epidemiology collaboration formula.[12] MedCalc® statistical software v12.5 (www.medcalc.org) was used for analysis of data. The significance of results was tested using Chi-square tests or Fisher exact test and Student's *t*-test. A statistical $P < 0.05$ was considered statistically significant.

RESULTS

A total of 339 cases (168 urology and 171 cardiology) were included in this study. The age of patients undergoing urological procedures ranged from 22 to 80 years, and those undergoing cardiological procedures ranged from 37 to 80 years. 66% were men in the urology group versus 68.9% in the cardiology group. The other precontrast patient data is given in Table 1.

The mean volume of contrast used in different procedures is given in Table 2. Only 7.14% of patients (12 cases) in

Table 1: Precontrast patient data

Characteristics	Urology cases (*n*=168)	Cardiology cases (*n*=171)
Mean age (years)	50±13.34	59±9.87
Elderly (≥60 years) (%)	28.2	50
Precontrast SCr, mean (mg/dL)	1.04±0.30	0.98±0.28
Incidence of eGFR <60 mL/min/1.73 m^2 (%)	6.60	11.70%
Diabetes mellitus (%)	44.7	70.8
Hypertension (%)	38.8	66.0
Anemia (Hb <10 g%)	7.8	16
Mean contrast volume (mL)	81.3±15.4	105.6±102
Ejection fraction range (%)	48–80	30–76
Ejection fraction <40%	Nil	2.83
Prophylactic hydration and N-acetyl cysteine therapy (%)	7.14	9.35

eGFR=Estimated glomerular filtration rate, Hb=Hemoglobin, SCr=Serum creatinine

Table 2: Volume of contrast used versus type of procedure undergone

Type of procedure	Percentage of cases	Number of cases	Volume of contrast used (mL)
CT urogram	47.02	79	60-120
CT abdomen	11.90	20	80-120
Renal CT angiogram	10.73	18	90-100
IVP	30.35	51	60-80
Coronary angiogram	75.5	130	40-150
Coronary angiogram + angioplasty	24.5	41	100-800

CT=Computed tomography, IVP=Intravenous pyelogram

urology group compared to 9.35% of patients (16 cases) in cardiology group required prophylactic hydration.

An increase in SCr of 25% above the baseline was observed in 8.33% of patients (14 cases) in urology group compared to 29.82% of patients (51 cases) in cardiology group; whereas, an absolute increase of more than 0.5 mg/dL was observed in only 2.38% of patients (four cases) of urology group compared to 5.26% of patients (nine cases) of cardiology group. Only one out of 12 cases who received prophylactic hydration therapy developed CIN in urology group whereas three out of 16 cases in cardiology group developed CIN. All patients who had CIN were followed up with daily SCr which showed a downward trend and none of the patients required dialysis in the urology group, whereas 11 cardiology patients required dialysis.

In urology patients group, no association was noted between the CIN and age ≥60 years, sex, diabetes, hypertension, anemia, and left ventricular ejection fraction <40%. However, significant association existed between CIN and eGFR <60 ml/min/1.73 m^2 and volume of contrast used. In cardiology patient group significant association was noted between CIN and diabetes, hypertension, eGFR <60 ml/min/1.73 m^2, volume of contrast used, and type of procedure done. The associations between CIN and various risk factors in the Urology and Cardiology patient groups are given in Table 3.

DISCUSSION

Reported incidence of CIN has varied due to inconsistencies in the definition of this condition, as well as differences in the type of procedure undertaken, the type and dose of contrast used, and differences in patient populations studied in various reports. The rate of CIN in the general population has been estimated to be <2%,[9] but incidences between 40% and 90% have been reported in some studies, depending on the number of risk factors present.[10,13] In our study, the incidence of CIN was 8.33% in urology patient group, whereas it was 29.82% in cardiology patient group.

Table 3: Association of risk factors with contrast-induced nephropathy

Risk factor	Urology		Cardiology	
	Association	*P*	Association	*P*
Age ≥60 years (%)	17.24	0.1815	24.52	0.6613
Sex (male:Female) (%)	7.35:11.43	0.7266	27.39:30.30	0.9948
Diabetes (%)	15	0.1187	38.67	<0.05
Hypertension (%)	12	0.5309	40	<0.05
Anemia (%)	0	0	58.82	0.2164
Left ventricular ejection fraction <40%	0	0	100	0.6788
<60 mL/min/1.73 m^2 (%)	25	<0.05	35	<0.05
Mean contrast volume (mL)	87.77	<0.05	172	<0.05

eGFR=Estimated glomerular filtration rate

Reduced renal mass, function, and perfusion associated with advancing age could be risk factors for CIN in old age observed in our study. Selistre Lda *et al*.[14] also showed that significant association existed between elderly age and CIN. Toprak[6] concluded that females were affected by CIN more than males. Our study also confirmed that females were more affected in both groups; however, the association was not statistically significant.

Lasser *et al*.[15] showed that incidence of CIN in patients with diabetes varies from 5.7% to 29.4%. Parfrey *et al*.[16] concluded that diabetes that could represent a true risk factor for CIN only when a coexisting alteration in renal function was present. In fact, the risk of CIN in patients with diabetes who had normal renal function and no concomitant predisposing factors seemed to be similar to that in healthy controls. DM with renal impairment has been identified as an independent risk factor for contrast nephropathy.[17,18] In our study, CIN was noted in 15% of urology patient group when compared to 38.67% of cardiology patient group with DM.

Conen *et al*.[19] showed that CIN developed in 2% of hypertensive patients compared to 0.4% of patients without hypertension undergoing cardiac interventional examinations. Hypertensive patients frequently have DM and/or chronic nephropathy, which makes it difficult to isolate the role of alterations in blood pressure *per se* in the pathophysiology of CIN. Cochran *et al*.[13] concluded that roles of hypertension, peripheral vascular disease, hyperuricemia, hypercholesterolemia, and proteinuria were neither clear nor well established, although their presence should probably be still taken into account when risk-stratifying patients. In our study, CIN occurred in 12% of patients of urology group compared to 40% patients of cardiology group with hypertension. This might be due to the association of hypertension, and other risk factors were more common in the cardiology case group studied.

It is well established that a higher volume of contrast is associated with a higher risk of CIN. Manske *et al*.[20] in their study, inferred that even relatively low doses of contrast (<100 mL) could result in permanent renal failure resulting in increased need for dialysis in patients with CKD. Cigarroa *et al*.[21] concluded that with each 100 mL increment, in contrast, volume resulted in a 30% increase in the risk of CIN. In our study, also CIN occurred more in cardiology group, wherein more volume of contrast was used compared to the urology group. Gleeson *et al*.[8] in his review, quoted that intra-arterial route of contrast was more nephrotoxic than IV route. In our study also, CIN cases were more in cardiology group probably due to intra-arterial contrast.

Tepel *et al*.[22] and Hall *et al*.[23] stated that in patients with CKD, the incidence of CIN could be relatively high and

ranged from 14.8% to 55%, depending on the underlying conditions, whereas, in patients with a GFR >60 mL/min, the risk of CIN was only 2%. Davidson *et al*.[24] reported a low risk of CIN in patients with normal renal function, but high risk in those with preexisting azotemia (SCr >1.2 mg/dL) in a study on patients undergoing cardiac catheterisation. In our study also, cases with precontrast eGFR <60 ml/min/1.73 m^2, 25% of urology patients compared to 35% in cardiology patients were associated with CIN.

European Society of Urogenital Radiology guidelines[25] on the safe use of iodinated contrast media state that coexisting pathologies such as congestive heart failure, a low left ventricular ejection fraction, and hypotension of hypovolemic shock, could contribute to prerenal acute renal failure by reducing renal perfusion, thus enhancing the ischemic insult of contrast agents. Selistre Lda *et al*.[14] in their study also, showed that heart failure was one of the independent risk factor for CIN. In our study, all patients in the cardiology group who had left ventricular ejection fraction <40% had CIN, compared to none in urology cases had an ejection fraction <40%.

Although gender did not show a significant association, in both cardiology and urology groups, incidence of CIN was more in females than male patients. This may be explained by the possible gender-specific renal response to contrast agent, also differential gender specific responses of platelet function, influence of ovarian hormones in renal failure and smaller body surface area in females.[26]

Limitation of our study: The risk factors often coexist, cardiology and urology groups are heterogeneous, making it difficult to exactly match the cardiac and urologic patient cohorts. This makes it difficult to ascribe a specific cause as a reason of CIN in a given patient. Furthermore, the spectrum of risk factors would depend on the referral pattern/clinical practice of a particular institution.

CONCLUSION

In our study, eGFR and volume of contrast were statistically significant risk factors for CIN in both groups, but in cardiology group, diabetes and hypertension were also statistically significant independent risk factors. Left ventricular ejection fraction, gender, age (≥60 years) did correlate with the incidence of CIN but not significant statistically. Intra-arterial administration of large volumes of contrast could be the major factor precipitating CIN in cardiology patients, especially in the setting of coexistent pathologies such as DM, hypertension, and reduced left ventricular ejection fraction.

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