Original Article

A Study of Estimated Glomerular Filtration Rate in Patients Undergoing Diagnostic or Interventional Coronary Contrast Procedures

Mohammed Shoeb A. Khan, Vinod Kumar K, Anil Kumar R[1], Bipi Prasannan, Vishnudev Urs, V. N. Unni

Departments of Nephrology and [1]Interventional Cardiology, Aster Medcity, Kochi, Kerala, India

Abstract

Introduction: Angiographic procedures are underused in patients with chronic kidney disease (CKD), who present with acute coronary syndromes, due to risk of contrast-induced acute kidney injury (CI-AKI). In this study, we assessed the change in estimated glomerular filtration rate (eGFR) over 3 months following coronary procedures in CKD patients. **Methods:** This observational study was done from July 2017 to January 2019 in patients undergoing elective coronary procedures with an eGFR <60 mL/min/1.73 m². CKD-EPI equation was used to calculate eGFR pre and post coronary procedure at 24, 48, and 72 hours as well as 30, 90 days. AKI was diagnosed and patients were given prophylaxis for CI-AKI as per KDIGO recommendation (intravenous normal saline and oral N-acetyl cysteine). **Results:** Patients studied were 282 (225 males, 57 females) of which 68.1% were diabetics. Mean eGFR was 42.91 ± 10.51 mL/min/1.73 m² and mean hemoglobin was 12.08 ± 1.51 gm/dL. Coronary angiogram (CAG) was done in 174; percutaneous transluminal coronary angioplasty (PTCA) was done in 108. Mean contrast volume in CAG was 55.17 ± 34.45 mL and in PTCA was 156.94±±47.99 mL. CI-AKI was seen in 66 (23.4%) patients. The incidence of CI-AKI increased with severity of underlying CKD. The variability of eGFR at 1 and 3 months after coronary procedures showed no significant change from baseline, even in the patients who developed CI-AKI. **Conclusions:** CI-AKI is self-limiting and has no major detrimental effects on eGFR at 1 and 3 months after contrast exposure.

Keywords: *AKI, contrast, coronary procedure, eGFR*

Introduction

The most important adverse effect of radiocontrast media is contrast-induced acute kidney injury (CI-AKI). The third most common cause of acute kidney injury (AKI) in patients admitted in a healthcare facility is reported to be CI-AKI.[1] The most important risk factor for CI-AKI is preexisting chronic kidney disease (CKD).[2] The risk of CI-AKI increases as the renal function decreases.[3]

The patients with established CKD are at high risk for future cardiovascular events.[4] A coronary intervention invariably requires an intraarterial radiographic contrast, which puts the patient at risk for CI-AKI. The patients known to have CKD who develop an acute coronary syndrome (ACS) have a poor prognosis, with >70% mortality at 2 years.[5] A prospective study has shown that percutaneous coronary intervention (PCI) improved the long-term survival among patients with severe renal dysfunction and ACS.[5] More recent studies have suggested that the risk of AKI due to contrast material is overestimated.[6–8] Such studies are important, considering that angiographic procedures may be underused in the patients with CKD who present with ACSs, presumably because of the concern about precipitating AKI.[9]

This study aims to study the estimated glomerular filtration rate (eGFR) in patients with preexistent CKD, who undergo coronary angiogram (CAG)/angioplasty (PTCA); eGFR at 1 month and 3 months following the procedures.

Materials and Methods

Study design and setting

This prospective single-center observational study was conducted at Aster Medcity, Kochi, Kerala, India, between July 2017 and January 2019, after obtaining institutional ethics committee clearance. All the patients with preexistent CKD who

How to cite this article: Khan MS, Kumar KV, Kumar RA, Prasannan B, Urs V, Unni VN. A study of estimated glomerular filtration rate in patients undergoing diagnostic or interventional coronary contrast procedures. Indian J Nephrol 2022;32:132-7.

Received: 17-06-2020
Revised: 17-07-2020
Accepted: 01-06-2021
Published: 11-03-2022

Address for correspondence:
Dr. Vinod Kumar K,
Aster Medcity, Cheranalloor, Kochi – 682 027, Kerala, India.
E-mail: drvinodkumark17@gmail.com

Access this article online

Website: www.indianjnephrol.org

DOI: 10.4103/ijn.IJN_280_20

Quick Response Code:

underwent CAG or coronary angioplasty at Aster Medcity were studied.

Methods

Inclusion criteria:
- Elective coronary contrast procedures.
- Age >18 yrs.
- Patients with an eGFR <60 mL/min/1.73 m^2
- Patients who received prophylaxis for contrast exposure as per our institution protocol.

Exclusion criteria:
- Primary PCI
- CKD stage 5.
- Patients diagnosed to have AKI secondary to any other obvious cause (apart from contrast exposure).
- Patients who underwent coronary artery bypass grafting, within 1 month of coronary procedures.
- History of use of nephrotoxic medications within 7 days of contrast exposure.
- Exposure to another dose of contrast within 72 h of coronary procedure.
- Renal allograft recipients.

Protocol for prophylaxis against CI-AKI:
1. Reduce diuretic dose, if possible.
2. Stop angiotensin-converting enzyme inhibitors or Angiotensin II receptor blockers, 24 h before coronary procedure.
3. Stop Metformin, 24 h before coronary procedure.
4. Administer oral N-acetyl cysteine, 1200 mg, twice daily, 24 h before the coronary procedure and continue for 24 h after the coronary procedure.
5. Administer intravenous normal saline at a rate of 1 mL/kg/h for 6 h, prior to coronary procedure, to be continued during the procedure and for 12 h following the procedure.

Data collection methods

From electronic medical record and investigations done in a laboratory affiliated by National Accreditation Board for Testing and Calibration Laboratories. The eGFR was calculated using the CKD-EPI equation.[10] Serum creatinine before the coronary procedure, as well as the values of serum creatinine on 24 h, 48 h, 72 h, 30, and 90 days after the coronary procedure, was recorded in all the patients. Serum creatinine was measured using the modified Jaffe's method. The patients were reviewed in nephrology OPD with a serum creatinine value for 3 months.

Primary outcomes: Change in eGFR from baseline to 1 month after coronary procedure and incidence of CI-AKI.

Secondary outcomes were in-hospital mortality, mortality within 1 month after coronary procedure, requirement of dialysis after coronary procedure, change in eGFR from baseline to 3 months after coronary procedure, and the risk factors associated with CI-AKI.

Data management and statistical analysis

The statistical analysis was performed by IBM SPSS Statistics 20 version. All categorical variables were described as frequency and percentage. All continuous variables were described as mean ± standard deviation and compared using unpaired *t*-test/paired *t*-test/Mann–Whitney test between groups at various follow-ups. Normality was checked by the rule of thumb method. Pearson's Chi-square test and Fisher's exact test were used to find the association between categorical variables. Pearson's correlation coefficient was used to identify correlations between quantitative variables. *P* value of <0.05 was considered to be statistically significant.

Results

Total number of subjects included were 282. The mean age of the study population was 66.86 ± 9.08 years with males 79.8% (225). The mean eGFR prior to coronary procedure was 42.91 ± 10.51 mL/min/1.73 m^2. Other characteristics are expressed in Table 1. Only CAG was done in 174 (61.7%) and PTCA (CAG and PTCA were done in the same sitting) in 108 (38.3%); the details of coronary procedures are expressed in Table 2.

Three patients died in hospital. After discharge, there was no mortality noted within 3 months of coronary procedure. There were no clinically relevant events in 3 months after coronary procedure.

The incidence of CI-AKI (as per KDIGO definition) was 23.4%. AKI stage 1 was in 51 (18.08%) patients, AKI stage 2 in 12 (4.26%) patients, and stage 3 in only 3 patients requiring dialysis. However, in all three, dialysis could be discontinued within 1 month. In patients undergoing PTCA, the incidence of CI-AKI was 38.8%, and those undergoing CAG only was 13.8%. The incidence of CI-AKI increased as the eGFR decreased. The incidence of CI-AKI in the total studied population and respective stage of CKD is expressed in Table 3.

The mean eGFR of the entire study population at 1 month and 3 months after the procedure was 44.6 ± 12.59 and 43.9 ± 13.45 mL/min/1.73 m^2. The improvement was maximum in PTCA group; however, this change in eGFR was not statistically significant [Figure 1]. The patients who developed CI-AKI were separately analyzed. The mean eGFR did not show a progressive worsening, rather a minor improvement in eGFR at 3 months was observed. However, it was not statistically significant [Figure 2].

Comparison of risk factors between the patients who did not develop AKI and those who developed CI-AKI are shown in Table 4. In our study, type 2 diabetes mellitus, congestive cardiac failure, anemia, pre-procedure eGFR, and albuminuira were found to be significant risk factors for the development of CI-AKI. Among the procedure-related

factors, exposure to higher contrast volume was found to be a risk factor.

Discussion

In this prospective observational study, we studied the patients with an eGFR <60 mL/min/1.73 m^2 who underwent coronary procedures after receiving prophylaxis for CI-AKI as recommended by the KDIGO working group. In-hospital mortality was seen in 1.06% of the study population, and the cause of death was ACS and cardiac arrhythmia. No mortality was noted after discharge within 3 months of study follow up for the entire study group. A recent meta-analysis reported that the in-hospital mortality in patients exposed to contrast material to be 2.4%.[11]

The mean age of the population studied was 66.86 ± 9.0 years and 36 patients (12.77%) of the study population were above the age of 75 yrs. Older age is a known risk factor for CI-AKI.[12]

CI-AKI, as per the KDIGO definition of AKI,[13] was seen in 66 patients (23.4%). Very few studies have been done in patients using the KDIGO definition of AKI, exclusively in patients with eGFR <60 mL/min/1.73 m^2 undergoing a coronary procedure. In our study, the incidence of AKI stage 1 was 18.08%, AKI stage 2 was 4.26%, and AKI stage 3 was 1.06%. Only three patients in our study required dialysis for a short period (less than 2 weeks). Tsai *et al.*[14] reported the need for dialysis to be 4.3% and reported that incidence of CI-AKI increased as the baseline preprocedural eGFR decreased. In our study, the incidence of CI-AKI also increased as the stage of CKD progressed. In CKD stage 4, the incidence of CI-AKI was 28.94%. The lower incidence of CI-AKI requiring dialysis in our study group may have been due to rigorous implementation and adherence of CI-AKI prophylaxis with intravenous normal saline and oral N-acetyl cysteine. Other factors contributing to lower severity of CI-AKI in our patients may have been:

1. Exclusion of patients undergoing primary PCI.
2. Higher mean eGFR before the coronary procedure.
3. Lower mean age in our study group.

Table 1: Baseline characteristics of the study population (*n*=282)

Co-morbid Variables	Values
Mean age, in years (standard deviation)	66.86±9.08
Gender	
Male, number (%)	225 (79.8%)
Female, number (%)	57 (20.2%)
Comorbidities: *n* (%)	
Diabetes mellitus	192 (68.1%)
Hypertension	177 (62.8%)
Congestive cardiac failure	66 (23.4%)
Cerebrovascular disease	11 (3.9%)
Chronic liver disease	4 (1.41%)
Current smoker	78 (27.66%)
Mean eGFR, mL/min/1.73 m^2 (standard deviation)	42.91 (±10.51)
Hemoglobin, gm/dL, mean (standard deviation)	12.08 (±1.51)
Proteinuria (Urine protein dipstick) *n* (%)	
Nil	33 (11.7)
Trace or more	249 (88.29)

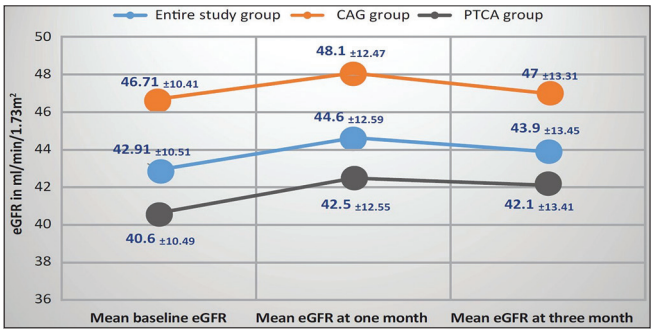

Figure 1: The change in eGFR from baseline to one and three months after coronary procedure in the entire study group

Table 2: Coronary procedure (details)

	n (%)
Type of coronary procedure	
Coronary angiogram (CAG) only	174 (61.7%)
Percutaneous transluminal coronary angioplasty (PTCA)	108 (38.3%)
	Mean in mL (standard deviation)
Volume of contrast used	
Entire population (*n*=282)	94.14 mL (±63.75)
In patients undergoing CAG (*n*=174)	55.17 mL (±34.45)
In patients undergoing PTCA (*n*=108)	156.94 mL (±47.99)
Type of contrast used for coronary procedures *n* (%)	
Iohexol (Low-osmolar contrast)	180 (63.8%)
Iodixanol (Iso-osmolar contrast)	102 (36.2%)
Vascular access used for coronary procedures *n* (%)	
Right radial artery	219 (77.7%)
Right femoral artery	60 (21.3%)
Left femoral artery	3 (1.1%)

4. Early referral to nephrologist.
5. More trans-radial route for coronary procedures.
6. More hemodynamically stable patients.

Incidence of CI-AKI was more in the patients undergoing PTCA when compared to the patients undergoing CAG alone. One of the important factors for this difference could be the lower baseline eGFR and higher contrast volume in PTCA group when compared to the CAG group. We could find a direct relationship between volume of contrast used and development of CI-AKI in patients with CKD (*P* value <0.001).

In our study group, the most used vascular access for coronary contrast procedures was the right radial artery, accounting for 77.7%. A large multicenter study done in 2014, involving 82,225 PCI, demonstrated that the risk for CI-AKI and progression of underlying CKD was lower with trans-radial vascular access compared to transfemoral vascular access.[15]

In our study, we did not find persistent decrease in mean eGFR of the entire study population from baseline to 3 months after coronary procedures. In a recent study, it was reported that only 2% of patients with CKD undergoing coronary procedures develop worsening renal dysfunction over 3 months.[16] In the subgroup analysis of patients who did not develop a CI-AKI, only 0.9% of patients showed lower creatinine clearance compared to baseline.[16] A recent study done in around 21,000 patients undergoing contrast procedures has reported that intravenous contrast material exposure is not an independent risk factor for dialysis or mortality.[7]

In our study, after coronary procedures, we found a mild improvement in the eGFR (3.93%) at 1 month and at 3 months (2.3%). However, the change in eGFR from baseline to 1 month and 3 months after coronary procedures was not statistically significant. Similar findings were also observed in the patients who developed CI-AKI. It is important to highlight that the patients undergoing coronary intervention may have multiple other mechanisms of

Table 3: Incidence of CI-AKI in studied population

	Incidence of CI-AKI, *n* (%)
Total studied population (*n*=282)	66 (23.4%)
Stratification of total population in various CKD stages	
CKD stage 3a (*n*=147)	30 (20%)
CKD stage 3b (*n*=97)	25 (25%)
CKD stage 4 (*n*=38)	11 (28.94%)

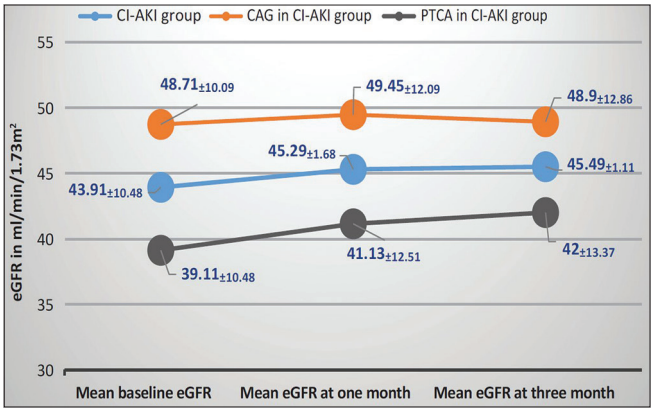

Figure 2: Variability of eGFR in patients who developed CI-AKI over three months

Table 4: Comparison of demographics between AKI group and No-AKI group

	AKI group (*n*=66)	No-AKI group (*n*=216)	*P*
Mean Age, in years (standard deviation)	67.75 (±9.14)	66.62 (±9.07)	0.39
Gender			
Females, number (%)	9 (14)	48 (22)	0.123
Males, number (%)	57 (86)	168 (78)	
Clinical Characteristics			
Diabetes mellitus, number (%)	57 (86.36)	138 (63.89)	<0.05
Systemic hypertension, number (%)	42 (63.6)	135 (62.5)	0.283
Congestive heart failure, number (%)	27 (40.9)	39 (18)	0.01
Transient Hypotension, number (%)	3 (4.5)	18 (8.33)	0.267
Hemoglobin pre procedure in gm/dL (standard deviation)	11.53 (±1.22)	12.23 (±1.55)	<0.05
Mean baseline eGFR in mL/min/1.73 m² (standard deviation)	43.91 (±10.48)	46.37 (±10.24)	0.08
Albuminuria (Dipstick)			
Trace or more, number (%)	63 (95.45)	186 (86.11)	<0.01
Type of coronary procedure			
PTCA, number (%)	42 (63.6)	66 (30.55)	<0.001
CAG, number (%)	24 (36.36)	150 (69.44)	<0.001
Mean volume of contrast used in mL (standard deviation)	128.5 (±68.04)	84.86 mL (±59.36)	<0.001
Vascular access used			
Trans-radial access, number (%)	54 (81.81)	165 (76.39)	0.568
Trans-femoral access, number (%)	12 (18.18)	51 (23.61)	

kidney injury, like hemodynamic instability, neurohormonal activation, venous congestion, inflammation, cardio-renal syndrome, and atheroembolism, which may affect the long-term clinical course.[17] There is a strong possibility that after revascularization there has been a resolution in many of these factors. It is well known that coronary revascularization also leads to sustained improvement in the left ventricular ejection fraction.[18] In our study, patients who benefited the most at 3 months were those who underwent PTCA (Δ eGFR: +1.5 mL/min/1.73 m^2) and probable improvement in cardiac function and better perfusion of kidneys may have contributed improvement in eGFR over 3 months, compared to patients who underwent CAG only (Δ eGFR: +0.29 mL/min/1.73 m^2).

We are moving towards an era in which intravascular contrast administration is not universally considered to be nephrotoxic. It is known that kidney disease is a risk factor for development of cardiovascular disease.[4] The risk for developing de novo coronary artery disease or death increases significantly even after a minor reduction in GFR; therefore, the patients with CKD are likely to derive greater absolute benefits from invasive approach for ACS.[19] However, the patients with kidney disease suffer from therapeutic nihilism due to risk perception of CI-AKI; a large study showed that fewer patients with CKD than without CKD underwent angiography during their hospital stay (25.2% versus 46.8%; $P < 0.0001$); they also showed that angiography rates were lower for CKD patients with diabetes than for those without diabetes (23.6% versus 26.3%; $P < 0.001$).[9] The study also showed that 1 year mortality rate for CKD patients who underwent CAG was 29.8%, PTCA was 25.1%, CABG was 23.4%, and PTCA + CABG was 14.3%, whereas among patients who were considered appropriate to undergo CAG but did not undergo this procedure had a 1 year mortality rate was 47.4%.[9] Renalism (alteration in practice because of an aversion to the risk of radiocontrast-associated nephrotoxicity)[9] must be avoided.

Our study stresses the need to proceed with coronary procedures with recommended prophylaxis for CI-AKI, as the benefits outweigh the risks. A collaborative systematic review has also suggested to consider an early angiographic procedures in CKD as it reduces risk for rehospitalization and reduces risk for death and nonfatal reinfarction.[19]

Limitations

Our findings are based on clinical events from a single center, which limits generalization to the full spectrum of patients at risk for CI-AKI. Among the study population, HbA1C, body mass index, structural abnormalities of kidneys, use of SGLT-2 inhibitors, and number of antihypertensives were not assessed. Proteinuria was not quantified. In addition to enrolling many patients with only mildly reduced eGFR, we excluded subjects with persistent hypotension and patients undergoing emergency procedures.

Conclusion

CI-AKI risk following coronary procedures increases with decline in baseline eGFR. CI-AKI is usually self-limiting.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis 2002;39:930–6.
2. Mehran R, Dangas GD, Weisbord SD. Contrast-associated acute kidney injury. N Engl J Med 2019;380:2146–55.
3. Mehran R, Nikolsky E. Contrast-induced nephropathy: Definition, epidemiology, and patients at risk. Kidney Int 2006;69(Suppl 100):11–5.
4. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, *et al*. Kidney disease as a risk factor for development of cardiovascular disease: A statement from the American Heart Association Councils on kidney in cardiovascular disease, high blood pressure research, clinical cardiology, and epidemiology and prevention. Hypertension 2003;42:1050–65.
5. Keeley EC, Kadakia R, Soman S, Borzak S, McCullough PA. Analysis of long-term survival after revascularization in patients with chronic kidney disease presenting with acute coronary syndromes. Am J Cardiol 2003;92:509–14.
6. McDonald RJ, McDonald JS, Bida JP, Carter RE, Fleming CJ, Misra S, *et al*. Intravenous contrast material-induced nephropathy: Causal or coincident phenomenon? Radiology 2013;267:106–18.
7. McDonald RJ, McDonald JS, Carter RE, Hartman RP, Katzberg RW, Kallmes DF, *et al*. Intravenous contrast material exposure is not an independent risk factor for dialysis or mortality. Radiology 2014;273:714–25.
8. Bruce RJ, Djamali A, Shinki K, Michel SJ, Fine JP, Pozniak MA. Background fluctuation of kidney function versus contrast-induced nephrotoxicity. Am J Roentgenol 2009;192:711–8.
9. Chertow GM, Normand SLT, McNeil BJ. "Renalism": Inappropriately low rates of coronary angiography in elderly individuals with renal insufficiency. J Am Soc Nephrol 2004;15:2462–8.
10. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, *et al*. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.
11. Mcdonald JS, Mcdonald RJ, Comin J, Williamson EE, Katzberg RW, Kallmes DF. Frequency of acute kidney injury following intravenous contrast medium administration : A systematic review and meta-analysis. Radiology 2013;267:119–28.
12. David T. G. Wymer, David C. Wymer Imaging. In: Comprehensive Clinical Nephrology. Elsevier Saunders; 2019. p. 69.
13. Kidney Disease Improving Global Outcomes (KDIGO). Clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012;2:1–138.

14. 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. J Am Coll Cardiol 2014;7:1–9.
15. Kooiman J, Seth M, Dixon S, Wohns D, LaLonde T, Rao SV, *et al*. Risk of acute kidney injury after percutaneous coronary interventions using radial versus femoral vascular access insights from the blue cross blue shield of michigan cardiovascular consortium. Circ Cardiovasc Interv 2014;7:190–8.
16. Maioli M, Toso A, Leoncini M, Gallopin M, Musilli N, Bellandi F. Persistent renal damage after contrast-induced acute kidney injury: Incidence, evolution, risk factors, and prognosis. Circulation 2012;125:3099–107.
17. Solomon R, Barrett B. Follow-up of patients with contrast-induced nephropathy. Kidney Int 2006;69(Suppl 100):S46–50.
18. Perry RA, Singh A, Seth A, Flint EJ, Hunt A, Murray RG, *et al*. Sustained improvement in left ventricular function after successful coronary angioplasty. Heart 1990;63:277–80.
19. Charytan DM, Wallentin L, Lagerqvist B, Spacek R, De Winter RJ, Stern NM, *et al*. Early angiography in patients with chronic kidney disease: A collaborative systematic review. Clin J Am Soc Nephrol 2009;4:1032–43.