RISK OF CONTRAST-INDUCED NEPHROPATHY AFTER REPEATED CONTRAST MEDIUM ADMINISTRATION

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Keywords: *contrast-induced nephropathy, contrast medium administration, renal function*

Abstract: *The strategy of non-invasive coronary computed tomography angiography (CCTA) and subsequent invasive coronary angiography (ICA) has risks owing to repeated contrast medium administration (CMA) and the possibility of contrast-induced nephropathy (CIN). To assess CIN development, we retrospectively evaluated changes in the serum creatinine (sCr) level and estimated glomerular filtration rate (eGFR) (baseline, 24 hours after CMA, and 48 hours after the second CMA) in patients with repeated CMA. The study included 17 patients, and 7 (41.2%) had prior impaired renal function. The mean CCTA and ICA contrast medium volumes were 114.11 ± 7.75 ml and 129.7 ± 19.24 ml, respectively. The sCr level was higher and eGFR was lower at 48 hours after the second CMA than at baseline ($p \leq 0.05$). However, CIN did not occur. Repeated CMA is not associated with CIN development at 48 hours after the second CMA, even in patients with prior impaired renal function.*

INTRODUCTION

The rapid evolution of cardiovascular imaging during the last few decades has resulted in an increase in the use of intra-venous/intra-arterial iodinated contrast agents. Conventional invasive coronary angiography (ICA) is the gold standard approach for the evaluation of coronary artery disease (CAD), and non-invasive coronary computed tomography angiography (CCTA) is frequently used to exclude CAD in patients with low-to-intermediate pre-test probability. However, the strategy of CCTA and subsequent ICA in the case of positive findings has some risks owing to repeated contrast exposure and the possibility of subsequent contrast-mediated renal injury. Contrast-induced nephropathy (CIN) was first described in the 1950s (1), and it remains one of the leading causes of hospital-acquired acute renal injury.(2) Several studies have mentioned the incidence of CIN after single administration of radiocontrast medium.(3,4) However, in real life, repeated contrast medium administration (CMA) is not infrequent.

PURPOSE

The present study aimed to assess the change in renal function after two consecutive imaging procedures involving intra-venous and intra-arterial CMA in order to evaluate CIN development. To our knowledge, the risk of CIN development after CCTA followed by ICA has not been investigated previously.

MATERIALS AND METHODS

We reviewed the records of patients admitted to our institution for CCTA followed by ICA between January and December 2015.

Renal function was evaluated according to changes in the serum creatinine (sCr) level and eGFR 24 hours after each CMA and 48 hours after the last CMA compared with baseline values (before CMA). The diagnostic criterion for CIN was a rise in the sCr level by 25% or more or an absolute increase in the sCr level by 0.5 mg/dl or more compared with the baseline value. The eGFR was calculated using the Cockroft–Gault formula (creatinine clearance [CrCl] = [140 − age] × weight / sCr × 72; $CrCl_{female}$ = CrCl × 0.85 [female sex adjustment]). The results are expressed as mean ± standard deviation (SD), and the data were compared using one-way ANOVA for repeated measurements. All statistical analyses were performed using STATA 14.0 (Stata Corporation, College Station, TX, USA). A p-value ≤0.05 was considered significant.

The study design was approved by the institutional ethics review board, and all patients provided informed consent.

RESULTS

The study included 17 patients. Prior impaired renal function (eGFR <60 ml/min/1.73 m^2) was noted in 41.2% of the patients, and a history of ST-elevation myocardial infarction (STEMI) was noted in 41.2% of the patients. The demographic and clinical characteristics of the study patients are presented in table no. 1.

Table no. 1. Demographic and clinical characteristics of the patients

Parameter	Number (%)
Male	16 (94.1)
Age (mean ± SD), years	61.41 ± 9.007
Hypertension	15 (88.2)
Diabetes mellitus	4 (23.5)
Hypercholesterolemia	6 (35.2)
Smoking history	5 (29.4)
Obesity	4 (23.5)
Prior STEMI	7 (41.2)
Prior non-STEMI	2 (11.8)
eGFR <60 ml/min/1.73 m^2	7 (41.2)

eGFR, estimated glomerular filtration rate; STEMI, ST-elevation myocardial infarction

The time interval between procedures was 24 hours. In patients with a prior eGFR <60 ml/min/1.73 m^2, ICA was performed after an additional 24-hour period. All patients were

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Article received on 24.07.2018 and accepted for publication on 31.08.2018
ACTA MEDICA TRANSILVANICA September 2018;23(3):78-79

intravenously hydrated with 1000 ml sodium chloride (0.9%) per day during hospitalisation. Oral fluid intake was not assessed. Iopromide (769 mg/ml) was used for CCTA, and iohexol (755 mg/ml) was used for ICA.

The mean contrast volume received was 114.11 ± 7.75 ml for iopromide and 129.7 ± 19.24 ml for iohexol.

The sCr levels and eGFRs at baseline, 24 hours after the first CMA (CCTA), and 24 and 48 hours after the second CMA (ICA) are shown in table no. 2.

Table no. 2. Evolution of the serum creatinine (sCr) level and estimated glomerular filtration rate

Parameter	Baseline	24 hours after CCTA	24 hours after ICA	48 hours after ICA
sCr (mean ± SD), mg/dl	0.92 ± 0.28	0.89 ± 0.25	0.92 ± 0.33	0.95 ± 0.08
eGFR (mean ± SD), ml/min/1.73 m^2	95.43 ± 26.69	97.68 ± 23.95	94.48 ± 23.3	91.82 ± 21.84

CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography

There were no significant differences in the mean sCr level and mean eGFR between baseline and 24 hours after ICA (sCr: 0.92 ± 0.28 vs. 0.92 ± 0.33 mg/dl, $F(2.32) = 1.6$, $p = 0.21$; eGFR: 95.43 ± 26.69 vs. 94.48 ± 23.3 ml/min/1.73 m^2, $F(2.32) = 1.22$, $p = 0.29$). The sCr level was significantly higher and the eGFR was significantly lower 48 hours after ICA than at baseline (sCr: 0.95 ± 0.08 vs. 0.92 ± 0.28 mg/dl, $F(3.48) = 3.08$, $p = 0.05$; eGFR: 91.82 ± 21.84 vs. 95.43 ± 26.69 ml/min/1.73 m^2, $F(3.48) = 4.13$, $p = 0.03$). None of the patients met the diagnostic criterion for CIN.

DISCUSSIONS

CIN affects up to 50% of patients at high risk (3), and it is a clinical reality with high health and economic burdens. In a previous large meta-analysis, James et al. found that the presence of CIN following coronary angiography was associated with increased patient mortality and major cardiovascular events.(5)

The risk of CIN after a second contrast exposure has been investigated in few studies. Trivedi et al. reported a CIN incidence of 14.3% after repeated CMA, even in patients with preserved renal function.(6) On the other hand, Winther et al. performed a study on the effect of repeated CMA in patients with end-stage kidney disease and found a low risk of post-contrast acute kidney injury and long-term complications.(7)

In the present study, we investigated the impact of both intra-venous and intra-arterial CMA on renal function assessed according to the sCr level and eGFR. The important finding of our study was the complete absence of CIN, even in patients with prior impaired renal function. Only 1 patient showed a significant decrease in the eGFR, resulting in a change in the classification of kidney disease from 3a to 3b. However, this patient had other risk factors for kidney disease, such as hypertension and insulin-dependent diabetes mellitus. Interestingly, several patients showed better values of sCr and eGFR at 24 hours after the first CMA, supporting the hypothesis of the correction of pre-renal dysfunction after the initial procedure by intravenous administration of sodium chloride (0.9%). It is known that oral hydration can improve renal function after CMA.(8) However, data on the extent of oral fluid intake before and after CMA were not available.

Our findings appear to confirm previous results indicating the lack of kidney injury after CMA. Sinert et al. compared contrast-exposed patients with contrast-unexposed patients and did not find significant kidney injury after CMA in patients with previously normal renal function. In fact, the incidence of acute kidney injury was greater among patients without CMA than among those with CMA (8.9% vs. 5.7%).(9) Additionally, McDonald et al. did not find a greater risk of nephropathy development in contrast-exposed patients than in contrast-unexposed patients, irrespective of baseline renal function.(10) These findings question whether CMA or other pathological conditions actually cause degradation of renal function.

The present study had several limitations. First, this study had a small sample size. Second, this retrospective study had possible selection bias (oral hydration status and other prophylactic treatments to prevent CIN). Third, the sCr level and eGFR at 72 hours or more after the second CMA were not assessed. Renal function might decline late after CMA. Thus, further studies with a large sample size and long assessment period are needed.

CONCLUSIONS

In conclusion, although the sCr level was high and eGFR was low 48 hours after the second CMA, repeated CMA was not associated with CIN development at this point, even in patients with impaired renal function prior to CMA. Intravenous administration of sodium chloride (0.9%) might help improve renal function before and after CMA.

REFERENCES

1. Alwall N, Johnsson S, Tornberg A, Werko L. Acute renal failure following angiography especially the risk of repeated examination, revealed by eight cases (two deaths). Acta Chir Scand. 1955;109:11-9.
2. Mohammed NM, Mahfouz A, Achkar K, Rafie IM, Hajar R. Contrast-induced nephropathy. Heart Views. 2013;14:106-16.
3. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006;100:S11-5.
4. Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation. 2002;105:2259-64.
5. James MT, Samuel SM, Manning MA, Tonelli M, Ghali WA, Faris P, et al. Contrast-induced acute kidney injury and risk of adverse clinical outcomes after coronary angiography: a systematic review and meta-analysis. Circ Cardiovasc Interv. 2013;6:37-43.
6. Trivedi H, Foley WD. Contrast-induced nephropathy after a second contrast exposure. Ren Fail. 2010;32:796-801.
7. Winther S, Svensson M, Jørgensen HS, Birn H, Bøtker HE, Ivarsen P, et al. Repeated contrast administration is associated with low risk of postcontrast acute kidney injury and long-term complications in patients with severe chronic kidney disease. Am J Transplant. 2016;16:897-907.
8. Yoshikawa D, Isobe S, Sato K, Ohashi T, Fujiwara Y, Ohyama H, et al. Importance of oral fluid intake after coronary computed tomography angiography: an observational study. Eur J Radiol. 2011;77:118-22.
9. Sinert R, Brandler E, Subramanian RA, Miller AC. Does the current definition of contrast-induced acute kidney injury reflect a true clinical entity? Acad Emerg Med. 2012;19:1261-7.
10. 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.