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ORIGINAL ARTICLE

Comparison of Safety of Low Osmolar vs Iso-osmolar Contrast Media for Prevention of CIN in Patients Undergoing Coronary Intervention

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Abstract

Background: *Contrast-induced nephropathy (CIN) is a significant complication following coronary angiography (CAG) and percutaneous coronary intervention (PCI), leading to worsened renal function, prolonged hospital stays and increased healthcare costs. The choice of contrast media used during these procedures play vital role in development of CIN.*

Objective: *To compare the effectiveness of low osmolar contrast media (LOCM) and iso-osmolar contrast media (IOCM) in reducing the incidence of CIN in patients undergoing CAG or PCI.*

Methods: *In this prospective observational study, 60 patients undergoing CAG or PCI were randomized equally into IOCM (n=30) or LOCM (n=30). Serum creatinine (Scr) level and estimated glomerular filtration rate (eGFR) were measured at baseline and 72 hours post-procedure. CIN was defined as a >25% or >0.5 mg/dL increase in Serum creatinine. Logistic regression models were used to identify predictors of CIN*

Results: *CIN incidence was higher in LOCM group (33.3%) than IOCM group (10%) (p=0.03). LOCM usage significantly increased in Scr (p=0.001) and reduced eGFR (p=0.001), whereas IOCM maintained stable eGFR level (p=0.129) and Scr (p=0.023). Diabetes mellitus (OR 13.88, p=0.034), use of LOCM (OR 10.95, p=0.032), and higher contrast volume (OR 1.17, p=0.012) were identified independent predictors of CIN.*

Conclusion: *IOCM was associated with significantly lower CIN risk and more stable renal function compared to LOCM. Considering these findings, IOCM should be preferred in high-risk patients, especially those with diabetes or requiring larger contrast volumes, to minimize the risk of CIN.*

Abbreviations: *CI-AKI = contrast-induced acute kidney injury, CIN = contrast-induced nephropathy, CM = contrast media, eGFR = estimated glomerular filtration rate, LOCM = low-osmolar contrast medium, AR = attributable risk, OR = odds ratio, CAG = coronary angiography, PCI = percutaneous coronary intervention, Scr = serum creatinine, DM = Diabetes mellitus. CKD = chronic kidney disease*

Keywords: *Low osmolar contrast media, Iso-osmolar contrast media, Contrast-induced nephropathy, Coronary intervention.*

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Introduction

Coronary interventions, such as percutaneous coronary interventions (PCI) or coronary angiogram (CAG), play a crucial role in the management of cardiovascular diseases. These procedures include a significant risk of contrast-induced nephropathy (CIN), a leading cause of hospital-acquired renal insufficiency. CIN generally presents within 2 to 3 days after contrast administration and is characterized by either an absolute increase in serum creatinine concentration of at least 0.5 mg/dL or a relative increase of at least 25% from baseline levels (Morcos et al.,1998). Recent research indicates that CIN is the third

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biggest cause of hospital-acquired renal Insufficiency, accounting for 10% (McCullough et al., 2019). Diabetes mellitus (DM) is a well-known risk factor for the development of CIN, particularly in patients undergoing complex PCI, which often involves high contrast volumes and may be associated with hypotension. (Aspelin et al., 2003) showed in the NEPHRIC study that in DM patient IOCM (iodixanol) is much less likely to cause CIN than LOCM (iohexel) Iodine-based contrast media are essential in interventional cardiology for accurate visualization of coronary anatomy and pathology. The osmolality of contrast media potentially effects on renal function and influence CIN risk. IOCM (iodixanol) (vicipack: 290 mOsm/kg H2O), has lower osmolality compared to LOCM (iohexol) (Iopamero: 600-900 mOsm/kg H2O) but it has higher viscosity than monomeric LOCM (e.g., iohexol, iopromide, iomeprol, isovue) which may affect renal perfusion. This presents a practical issue when comparing the more viscous dimeric IOCM with the higher osmolar LOCM. The purpose of this study was to evaluate the comparative safety and efficacy of LOCM and IOCM in preventing CIN during coronary interventions, with the aim of informing optimal contrast media selection.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Department of Cardiology at Bangabandhu Sheikh Mujib Medical University, Dhaka, from 2023 to 2024.

Participants and Intervention

A total of sixty patients, aged 18 to 70 years, with chronic kidney disease (CKD) stage II (eGFR 60–89 mL/min/1.73 m^2), were selected for coronary angiography (CAG) or percutaneous coronary intervention (PCI). Patients with a known contrast media allergy, end-stage renal disease (ESRD), pregnancy, lactation, or involvement in other studies utilizing contrast media were excluded. Eligible patients were randomly allocated to one of two groups: Group A (n=30) received iso-osmolar contrast media (IOCM; iodixanol), and Group B (n=30) received low osmolar contrast media (LOCM; iohexol).

Data Collection and Outcome Measures

Baseline demographic and clinical information, including age, sex, comorbidities, medications, and relevant laboratory and procedural data, was collected for all participants. Serum creatinine (Scr) and estimated glomerular filtration rate (eGFR) were measured before the procedure and again at 72 hours post-contrast administration. Contrast-induced nephropathy (CIN) was defined as either a relative increase of >25% or an absolute increase of >0.5 mg/dL in Scr within 72 hours following the procedure. The primary outcome of the study was the incidence of CIN.

Ethical Considerations

Written informed consent was obtained from all participants before enrollment. The study protocol was reviewed and approved by the Institutional Review Board (IRB) and Ethics Committee of Bangabandhu Sheikh Mujib Medical University.

Statistical Analysis

Data analysis was performed using SPSS version 26. Continuous variables, including age, HbA1c, Scr, eGFR, and contrast volume, were presented as mean ± standard deviation (SD) and compared between groups using independent t-tests. Categorical variables, such as sex, presence of diabetes, hypertension, dyslipidemia, and CIN incidence, were presented as frequencies and percentages and compared using Chi-square tests. Multivariate logistic regression was used to identify independent predictors of CIN, with adjusted odds ratios (ORs) and 95% confidence intervals (CIs) reported. A p-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics and Contrast Use

A total of 60 patients were enrolled, with 30 assigned to the low-osmolar contrast group and 30 to the iso-osmolar contrast group.

Table-I

Baseline sociodemographic, clinical, and contrast characteristics of participants (n=60)

Variables	Low-osmolar (n=30)	Iso-osmolar (n=30)	P value
Age (years)			
35–45	4 (13.3%)	8 (26.7%)	
46–55	10 (33.3%)	14 (46.7%)	0.058*
56–65	11 (36.7%)	8 (26.7%)	
>65	5 (16.7%)	0	
Sex			
Male	28 (93.3%)	25 (83.3%)	0.424
Female	2 (6.7%)	5 (16.7%)	
Diabetes mellitus	16 (53.3%)	12 (40.0%)	0.301
Hypertension	16 (53.3%)	15 (50.0%)	0.796
Dyslipidemia	9 (30.0%)	21 (70.0%)	0.002*
HbA1c (mean±SD)	7.78±1.2	6.3±0.5	0.034*
Maximum contrast (ml)	357.6±8.4	360.6±10.5	0.222

*Significant at $p<0.05$

Baseline demographic and clinical variables are summarized in Table 1. The age distribution was comparable between groups, although patients aged >65 years were present only in the low-osmolar group (16.7% vs. 0%). Males predominance was observed in both groups (93.3% vs. 83.3%, p=0.424). The prevalence of diabetes mellitus and hypertension did not differ significantly, whereas dyslipidemia was significantly more common in the iso-osmolar group (70.0% vs. 30.0%, p=0.002). Mean HbA1c was significantly higher in the low-osmolar group (7.78±1.2 vs. 6.3±0.5, p=0.034).

The mean maximum contrast volume administered was similar between groups (357.6±8.4 ml vs. 360.6±10.5 ml, p=0.222). When categorized by vessel number, contrast volume increased progressively from single- to triple-vessel procedures, with the highest amount observed in triple-vessel interventions (184.1±40.7 ml, p=0.001).

Renal Function

Table-II

Renal function before and after procedure (n=60)

Variable	Low-osmolar (n=30)	Iso-osmolar (n=30)	P value
Baseline creatinine (mg/dL)	1.2±0.3	1.09±0.19	0.106
Creatinine at 72h (mg/dL)	1.5±0.42	1.16±0.22	0.001*
Baseline eGFR (mL/min/1.73m²)	75.1±20.3	80.5±17.3	0.267
eGFR at 72h (mL/min/1.73m²)	60.6±18	76.7±16.7	0.001*

*Significant at p<0.05

Renal outcomes are presented in Table 2. Baseline serum creatinine and estimated glomerular filtration (eGFR) did not show any significant difference between the groups. At 72 hours post-procedure, the low-osmolar group has shown a significantly higher mean serum creatinine compared with the iso-osmolar group (1.5±0.42 vs. 1.16±0.22 mg/dL, p=0.001). Similarly, eGFR declined significantly in the low-osmolar group (60.6±18 vs. 76.7±16.7 mL/min/1.73m², p=0.001).

Predictors of CIN

Table-III

Multivariate logistic regression for predictors of CIN

Risk factor	Odds ratio	95% CI	P value
Age >65 years	9.58	0.22–423.06	0.242
Diabetes mellitus	13.88	1.22–158.05	0.034*
Undergoing PCI	4.42	0.54–36.22	0.167
Low-osmolar contrast	10.95	1.23–97.92	0.032*
Contrast volume (per ml)	1.17	1.03–1.31	0.012*

*Significant at p<0.05

Multivariate logistic regression identified diabetes mellitus, use of low-osmolar contrast, and higher contrast volume as independent predictors of CIN (Table 3). Age >65 years and undergoing PCI were not significant predictors.

Incidence of CIN

The incidence of CIN was higher in the low-osmolar group compared with the iso-osmolar group, as demonstrated in Figure 1.

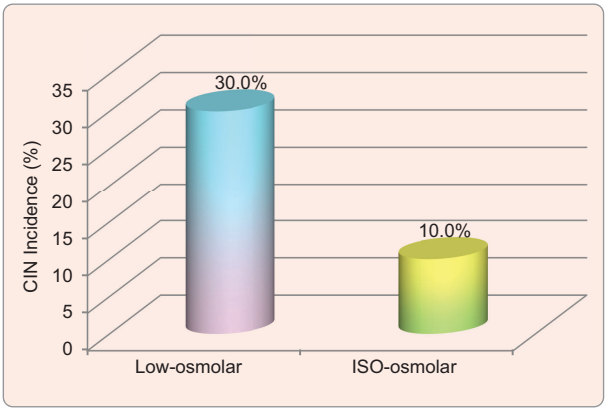

Figure 1: *Incidence of CIN in low-osmolar vs. iso-osmolar contrast groups*

Discussion

This study assessed the effects of low-osmolar contrast media (LOCM) and iso-osmolar contrast media (IOCM) on renal outcomes in patients undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI). The results revealed a significantly higher incidence of contrast-induced nephropathy (CIN) in patients receiving LOCM compared to those receiving IOCM (33.3% vs. 10.0%). Furthermore, multivariate analysis identified diabetes mellitus, the use of LOCM, and increased contrast volume as independent predictors of CIN, while age over 65 years and undergoing PCI did not show statistical significance.

The age distribution in our study group showed that the majority of patients in the LOCM group were between 56–65 years, while in the IOCM group, most patients were aged 46–55 years. This differs slightly from the findings of Bolognese et al. (2011), which reported a mean age of around 65 years in both groups. Our study supports the findings of Bolognese et al. (2011a) and Azzalini et al. (2019), aligning with a higher prevalence of coronary artery disease in men.

With respect to contrast use, the maximum dye volume administered did not differ significantly between groups, which is consistent with the results of Wessely et al. (2009),

Bolognese et al. (2011), and Chua et al. (2014), who similarly observed no significant differences in contrast volume across different media. These findings suggest that the type of contrast, rather than the total amount, may have a more significant impact on renal outcomes.

Renal function analysis revealed that both the LOCM and IOCM groups experienced post-procedural increases in serum creatinine; however, the increase was significantly greater in the LOCM group. This observation coincides with the findings from Mehran et al. (2009), Cho et al. (2010), Chua et al. (2014a), and Wang et al. (2021).These results align with the meta-analysis conducted by McCullough et al. (2006), which indicated that iodixanol (IOCM) was associated with a reduced risk of contrast-induced nephropathy (CIN) in comparison to low-osmolar contrast media (LOCM), particularly among patients with chronic kidney disease. In addition, a more significant decrease in eGFR was observed in patients administered LOCM, whereas renal function was relatively preserved in the IOCM group. Chua et al. (2014a) reported a similar trend, supporting the view that IOCM may be less nephrotoxic.

The role of contrast type as a determinant of CIN has remained controversial. The NEPHRIC trial (Aspelin et al., 2003) showed that iodixanol was associated with a lower risk of CIN compared with iohexol in high-risk patients with diabetes and chronic kidney disease. The RECOVER study (Jo et al., 2006) similarly indicated reduced nephrotoxicity associated with iodixanol in comparison to ioxaglate. The CARE study (Stone et al., 2003) reported no significant difference in the incidence of CIN between iodixanol and iopamidol in patients with moderate renal impairment. Our findings are consistent with the CARE study, indicating that no patients in the IOCM group experienced a significant decline in eGFR. This suggests that the nephrotoxic potential may vary based on the specific LOCM used.

The multivariate logistic regression analysis identified diabetes mellitus, LOCM use, and higher contrast volume as significant predictors of CIN, similar to previously established risk factors (McCullough et al., 2016; Mehran et al., 2009). Although advanced age (>65 years) did not reach statistical significance, the increased odds ratio indicates a potential effect that may not have been detected due to a limited sample size.

Overall, our study supplements the existing evidence that IOCM may be safer than LOCM in terms of renal outcomes, particularly in high-risk groups such as patients with diabetes. However, the variation across studies emphasizes the importance of considering not only the category of contrast medium (LOCM vs. IOCM) but also the specific agent used.

Conclusion:

This study indicates that iso-osmolar contrast media have been associated with a reduced risk of contrast-induced nephropathy (CIN) and improved renal function preservation when compared to low-osmolar agents in patients receiving coronary interventions. The protective effect was particularly pronounced in patients with diabetes and those requiring larger volumes of contrast. The findings highlight the necessity of careful selection of contrast media to reduce post-procedural renal complications.

Limitation:

The study was conducted at a single institution, which may limit the generalizability of the findings to broader populations. The assessment of renal function relied on only serum creatinine and eGFR, which may not fully capture the extent of renal impairment. The follow-up duration of 72 hours may not be sufficient to observe long-term renal effects or recovery patterns.

Recommendations:

For renal function assessment, advancing diagnostic techniques beyond serum creatinine and eGFR may provide a more comprehensive evaluation of kidney health in patients undergoing contrast imaging and incorporating a longer follow-up period would allow for a better understanding of the long-term effects of different contrast agents on renal function. Additionally, multicenter studies with larger and more diverse populations are also needed to confirm the comparative safety of different contrast agents across risk groups.

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