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Different outcomes between iso-osmolar and low-osmolar contrast media in acute myocardial infarction with renal impairment

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Abstract

Background: *The selection of appropriate contrast media (CM) remains an important issue in terms of renal preservation in patients with acute myocardial infarction (AMI) and renal impairment scheduled for percutaneous coronary intervention (PCI). We compared the clinical outcomes of patients with AMI and renal impairment, depending on the CM type (iso-osmolar CM [IOCM] vs. low-osmolar CM [LOCM]) that was used during PCI.*

Methods: *From the Convergent Registry of Catholic and Chonnam University for Acute Myocardial Infarction, 3174 post-PCI patients with AMI and renal impairment were subdivided into two groups (IOCM [n = 2101] and LOCM [n = 1073]).*

Results: *Regarding in-hospital clinical outcomes, the IOCM group had a higher peak creatinine (Cr) level and lower "Cr differential" than the LOCM group. A higher proportion of dialysis was noted in the IOCM group. In 30-day clinical outcomes, the IOCM group showed higher incidence of new-onset heart failure (HF) but lower incidence of revascularization than the LOCM group. The differences in in-hospital and 30-day clinical outcomes were attenuated after inverse probability of treatment weighting, except for new-onset HF. All other variables in 30-day clinical outcomes, including all-cause death, non-fatal myocardial infarction, cerebrovascular accidents, stent thrombosis, and any dialysis events, were similar between the two groups.*

Conclusions: *IOCM use did not prevent future incidence of dialysis compared to LOCM use in AMI patients with renal impairment.* (Cardiol J 2023; 30, 5: 790–798)

Key words: myocardial infarction, contrast media, renal dialysis, percutaneous coronary intervention, Korea

Introduction

With the increase in the incidence and prevalence of acute myocardial infarction (AMI), the rate of percutaneous coronary intervention (PCI) is gradually increasing in clinical practice [1]. Therefore, patient exposure to contrast media (CM) has substantially increased, highlighting an important issue, i.e., contrast-induced nephropathy (CIN) — an acute decline in kidney function fol-

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lowing CM administration in the absence of other etiologies [2]. It is related to significant morbidity and mortality, including the need for hemodialysis or kidney transplantation [3, 4], and it may develop into persistent renal damage, leading to increased mortality [5]. Therefore, the type and volume of CM plays a crucial role in preventing the development of CIN. It is well-known that the use of low-osmolar CM (LOCM) and iso-osmolar CM (IOCM) causes fewer cardiovascular adverse effects than the use of high-osmolar CM (HOCM) [6, 7]. Compared to HOCM, they were associated with reduced CIN incidence [8]. Thus, both IOCM and LOCM are becoming increasingly popular in various CM-based radiographic procedures.

Although many prospective studies have evaluated the efficacy of iodixanol (IOCM) compared to various types of LOCM in the past decade, it remains controversial whether, compared to LOCM, IOCM is associated with a lower incidence of CIN because of the mixed results of previous studies. In the first comparative study between the two CM types, no significant difference was found in the incidence of CIN [9]. Two randomized controlled trials demonstrated a significantly lower incidence of CIN with iodixanol (IOCM) use compared with iohexol and ioxaglate (LOCM) use [10, 11]. However, other studies have demonstrated no significant difference between IOCM and LOCM [12, 13]. One meta-analysis reported the beneficial effect of IOCM compared to LOCM [14], while some other meta-analyses demonstrated no significant difference between the two [15, 16].

Because it is known that the risk of CIN is substantially increased in patients with renal impairment such as chronic kidney disease [14], the optimal use of CM in reduced renal function is an important medical issue in terms of the prevention of renal-function deterioration. In particular, it is uncertain which CM type will produce better outcomes in patients with AMI and renal impairment (AMI-RI) undergoing PCI. We aimed to determine the CM type (IOCM vs. LOCM) with better clinical outcomes in patients with AMI-RI undergoing PCI.

Methods

Study design and participants

The Convergent Registry of Catholic and Chonnam University for Acute Myocardial Infarction (COREA-AMI) is a large-scale, multicenter registry designed to investigate the real-world characteristics of patients with AMI (including ST-segment elevation myocardial infarction [STEMI] and non-STEMI [NSTEMI]) in the Korean population. COREA-AMI I included patients with AMI undergoing PCI from January 2004 to December 2009. COREA-AMI II included additional patients from January 2010 to August 2014. All consecutive patients with AMI in 9 tertiary institutions were retrospectively included in this registry [17], containing demographic, clinical, and angiographic information, as well as clinical outcome data. These data were collected and stored by an attending physician and a trained clinical research coordinators using a web-based case report form in a clinical data management system.

In the COREA-AMI, 10,719 patients with AMI were initially screened. However, 7545 patients were excluded, including the following: (1) those who had creatinine clearance (CrCl) ≥ 60 mL/ /min/1.73 m^2, (2) those whose CrCl was not measured, (3) those with insufficient CM data, (4) those who received mixed use of both IOCM and LOCM, and (5) those who had received dialysis. A total of 3174 patients were finally enrolled. We further divided this population into an IOCM group (n = 2101) and an LOCM group (n = 1073), depending on the CM type applied during PCI. The study design is summarized in Figure 1.

The present study was conducted in accordance with the ethical principles of the Declaration of Helsinki as revised in 2013. The study protocol of the COREA-AMI was approved by the ethics committee of each participating tertiary institution. All enrolled patients provided written informed consent.

Definitions and study endpoints

Clinical and diagnostic parameters, including demographic data, previous medical history, laboratory data, prescribed medications, and angiographic/echocardiographic profiles, were assessed in all study subjects.

Acute myocardial infarction was defined in accordance with contemporary guidelines [18], which comprise the typical rise and/or fall of cardiac biomarkers in at least one of the following: (1) clinical symptoms or signs suggestive of myocardial ischemia, (2) development of pathological Q-waves in 12-lead electrocardiography (ECG), (3) ECG changes suggesting myocardial ischemia (i.e., ST-segment elevation or depression), and (4) characteristic cardiovascular imaging features suggestive of AMI (i.e., new loss of myocardial viability or newly found regional wall motion abnormality). STEMI refers to AMI with new-onset

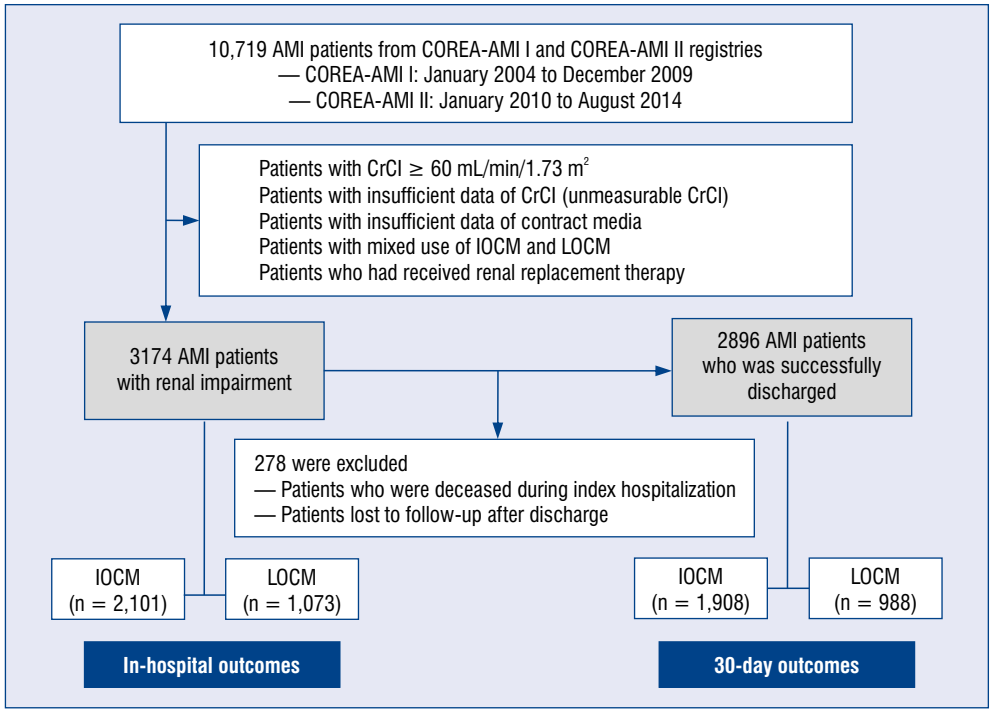

Figure 1. Study population flow chart. Acute myocardial infarction (AMI) patients with renal impairment were enrolled and divided into two groups (IOCM vs. LOCM group) in accordance with the type of contrast media; COREA-AMI — the Convergent Registry of Catholic and Chonnam University for Acute Myocardial Infarction; CrCl — creatinine clearance; IOCM — iso-osmolar contrast media; LOCM — low-osmolar contrast media.

ST-segment elevation of at least 1 mm (0.1 mV) in ≥ 2 contiguous leads or new-onset left bundle branch block on surface ECG [18]. Image-guided PCI refers to the utilization of intracoronary cardiovascular imaging (optical coherence tomography or intravascular ultrasound) during the PCI procedure. Left main coronary artery (LMCA) disease was defined as a ≥ 50% reduction in the intraluminal diameter of the LMCA. Multivessel coronary artery disease (CAD) was defined as significant stenosis in ≥ 2 epicardial coronary arteries (i.e., ≥ 70% stenosis in ≥ 2 epicardial coronary arteries or ≥ 70% stenosis in 1 epicardial coronary artery, with ≥ 50% stenosis of the LMCA). The degree of antegrade intracoronary flow was classified in accordance with the Thrombolysis In Myocardial Infarction (TIMI) flow grade. Image-guided PCI refers to the utilization of optical coherence tomography or intravascular ultrasonography during PCI. The left ventricular ejection fraction (LVEF) was examined using two-dimensional echocardiography.

Kidney function was determined using the CrCl, calculated using the Cockcroft–Gault formula [19]. The CrCl value was the original serum creatinine (Cr) level at the time of admission. In the present study, renal impairment was determined as CrCl < 60 mL/min/1.73 m^2, based on the serum Cr level at the time of admission. Depending on their CrCl value, the patients were divided into three subgroups: (1) CrCl ≥ 40 and < 60 mL/min/1.73 m^2, (2) CrCl ≥ 20 and < 40 mL/min/1.73 m^2, and (3) CrCl < 20 mL/min/1.73 m^2. The body mass index calculation was based on the weight and height at the time of admission. Anemia was defined as hemoglobin level < 12 g/dL.

The CM used during PCI was categorized into two types according to osmolality: IOCM (290 mOsm/kg) and LOCM (600 to 800 mOsm/kg) (**Suppl. Table 1**). Patients who received an IOCM infusion during PCI were included in the IOCM group, and those who received an LOCM infusion were included in the LOCM group.

We examined both in-hospital and 30-day outcomes in the patients. In-hospital outcomes included all in-hospital complications such as in-hospital death, reoccurring MI, new-onset heart failure (HF), cerebrovascular accidents (CVAs), any revascularization, stent thrombosis, peak Cr level, Cr level at discharge, Cr level at discharge minus initial Cr level (ΔCr [discharge – initial]),

peak Cr level minus initial Cr level (ΔCr [peak – initial]), and any adverse event. Thirty-day outcomes included all-cause death, non-fatal MI, new-onset HF, CVA, any revascularization, stent thrombosis, and any dialysis event. New-onset HF refers to any rehospitalization because of clinical symptoms and/or signs of HF, such as shortness of breath, fatigue and general weakness, or swelling in the lower extremities. Any revascularization refers to any repeat PCI or surgical bypass of any anatomical part of the epicardial coronary arteries. Any dialysis event was defined as hemodialysis or peritoneal dialysis.

Statistical analysis

Statistical analysis was performed to evaluate differences in clinical outcomes between the two groups (IOCM vs. LOCM). Continuous variables are expressed as means ± standard deviation and were analyzed using Student's t-test. Discrete variables are described as percentages with numbers and were analyzed using Pearson's χ^2 test or Fisher's two-by-two exact test. Results were considered statistically significant at a p-value < 0.05.

To minimize the effect of selection bias in the analysis of observational data, a propensity score weighting method, i.e., inverse probability of treatment weighting (IPTW) was used. The propensity score was derived by a multiple logistic regression model containing 35 covariates, including CM amount, age ≥ 75 years, sex, final diagnosis, Killip functional classification ≥ II, cardiogenic shock, cardiac arrest, intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), body mass index ≥ 25 kg/m^2, previous medical history, family CAD history, smoking history, laboratory and angiographic parameters, and prescribed medications. Patients with missing data in these covariates or those who were not followed up after hospital discharge were excluded from the analysis with IPTW adjustment.

All analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline clinical and procedural characteristics

The data of 3174 consecutive patients with AMI-RI were included in the analysis, and the baseline characteristics of these patients are summarized in Table 1. Among them, 2101 patients were in the IOCM group and 1073 patients were in the LOCM group. The IOCM group included more male patients and patients with STEMI diagnosis. Although the patients in the LOCM group were older than those in the IOCM group, the proportion of patients ≥ 75 years old was comparable between the groups. Although some severe conditions including Killip functional class ≥ II, cardiogenic shock, and out-of-hospital or in-hospital cardiac arrest were similar in both groups, the patients in the IOCM group received relatively high proportions of IABP and ECMO. Regarding previous history, the patients in the LOCM group had higher prevalence of hypertension, dyslipidemia, and prior PCI history but lower prevalence of prior HF. Although the patients in the IOCM group tended to be more anemic, the proportion of anemia was similar in both groups. The patients in the IOCM group had worse kidney function, showing a higher initial Cr level but lower CrCl. In the CrCl subclasses, CrCl < 20 mL/min/1.73 m^2 was more predominantly found in the IOCM group. The IOCM group showed a higher proportion of LVEF $< 40\%$. Multivessel CAD was more prominently found in the IOCM group. Regarding discharge medications, beta-blockers were more frequently prescribed in the LOCM group. After IPTW adjustment, these differences were well-balanced.

In-hospital outcomes

All in-hospital outcomes are described in Table 2. The peak Cr level was higher in the IOCM group. However, the value of ΔCr (peak – initial) was similar in both groups. The value of ΔCr (discharge – initial) was statistically different between the groups. A higher percentage of patients in the IOCM group received dialysis. After IPTW adjustment, all variables related to the in-hospital outcomes were comparable.

Thirty-day outcomes

After excluding all patients who died during the index hospitalization and those lost to follow-up after discharge, the 30-day outcomes of 2896 consecutive patients were analyzed, as described in Table 3. Clinical outcomes, including all-cause death, non-fatal MI, new-onset HF, CVA, any revascularization, stent thrombosis, and any dialysis event, were determined. Before IPTW adjustment, most outcome variables were similar between the groups, except for new-onset HF and any revascularization. After IPTW adjustment, a similar tendency was observed in new-onset HF, but the difference in any revascularization before IPTW adjustment was statistically attenuated.

Table 1. Baseline characteristics of the patients.

Characteristics	Before IPTW adjustment			After IPTW adjustment		
	IOCM (n = 2101)	LOCM (n = 1073)	P	IOCM (n = 2698)	LOCM (n = 2711)	P
Male patients	1178 (56.1)	537 (50.0)	**0.001**	1460 (54.1)	1457 (53.7)	0.848
Age [years]	73.41 ± 9.15	74.08 ± 8.81	**0.049**	73.55 ± 9.13	73.54 ± 8.94	0.966
Age ≥ 75 years	1012 (48.2)	548 (51.1)	0.122	1315 (48.7)	1319 (48.6)	0.974
STEMI diagnosis	1107 (52.7)	505 (47.1)	**0.003**	1334 (49.5)	1331 (49.1)	0.860
Killip functional class ≥ II	670 (34.7)	363 (34.8)	0.938	916 (34.0)	921 (34.0)	0.999
Cardiogenic shock	186 (8.9)	81 (7.6)	0.212	190 (7.1)	189 (7.0)	0.944
Out-of-hospital or in-hospital cardiac arrest	105 (5.0)	62 (5.8)	0.351	92 (3.4)	98 (3.6)	0.813
Mechanical circulatory support:						
IABP	137 (6.5)	45 (4.2)	**0.008**	130 (4.8)	140 (5.2)	0.747
ECMO	27 (1.3)	5 (0.5)	**0.029**	15 (0.6)	16 (0.6)	0.943
BMI ≥ 25 kg/m^2	438 (21.2)	239 (22.6)	0.380	590 (21.9)	582 (21.5)	0.806
Previous history:						
Hypertension	1,345 (64.0)	734 (68.4)	**0.014**	1,774 (65.7)	1,790 (66.0)	0.893
Diabetes mellitus	815 (38.8)	405 (37.7)	0.566	1,040 (38.5)	1,046 (38.6)	0.988
Dyslipidemia	251 (11.9)	199 (18.5)	**< 0.001**	419 (15.5)	419 (15.4)	0.945
Old MI	106 (5.0)	62 (5.8)	0.383	141 (5.2)	139 (5.1)	0.904
Prior PCI history	180 (8.6)	117 (10.9)	**0.032**	255 (9.5)	252 (9.3)	0.897
Prior CABG history	12 (0.6)	6 (0.6)	0.966	18 (0.7)	17 (0.6)	0.943
Prior HF	62 (3.0)	19 (1.8)	**0.046**	71 (2.6)	77 (2.8)	0.814
Old CVA	246 (11.7)	112 (10.4)	0.284	308 (11.4)	317 (11.7)	0.845
Known CKD with no RRT	10 (0.5)	1 (0.1)	0.112	6 (0.2)	6 (0.2)	0.974
Family CAD history	23 (1.1)	10 (0.9)	0.669	29 (1.1)	34 (1.2)	0.748
Smoking history:			0.763			0.868
Current smoker or ex-smoker	834 (39.7)	420 (39.1)		1,076 (39.9)	1,072 (39.5)	
Non-smoker	1267 (60.3)	653 (60.9)		1,622 (60.1)	1,639 (60.5)	
Hemoglobin [g/dL]	12.63 ± 2.09	12.48 ± 1.95	**0.042**	12.61 ± 2.09	12.60 ± 1.94	0.908
Anemia (hemoglobin < 12 g/dL)	1,058 (50.8)	558 (52.4)	0.374	1357 (50.3)	1362 (50.2)	0.990
Initial Cr level [mg/dL]	1.39 ± 0.93	1.29 ± 0.87	**0.001**	1.33 ± 0.80	1.38 ± 1.10	0.379
Initial Cr ≥ 1.5 mg/dL	548 (26.1)	220 (20.5)	**0.001**	640 (23.7)	647 (23.9)	0.943
CrCl [mL/min/1.73 m^2]	41.63 ± 12.66	43.00 ± 12.07	**0.003**	42.55 ± 12.40	42.27 ± 12.45	0.608
CrCl subclasses:			**0.012**			0.816
CrCl ≥ 40 or < 60 mL/min/1.73 m^2	1260 (60.0)	679 (63.3)		1691 (62.7)	1671 (61.6)	
CrCl ≥ 20 or < 40 mL/min/1.73 m^2	691 (32.9)	344 (32.1)		843 (31.2)	881 (32.5)	
CrCl < 20 mL/min/1.73 m^2	150 (7.1)	50 (4.7)		164 (6.1)	159 (5.9)	
LVEF < 40%	404 (21.0)	176 (17.5)	**0.022**	527 (19.5)	525 (19.4)	0.920
Transfemoral vascular access	1779 (84.7)	892 (83.1)	0.260	2233 (82.8)	2253 (83.1)	0.817
Preprocedural TIMI 0-I	1014 (48.3)	507 (47.3)	0.589	1279 (47.4)	1286 (47.4)	0.988
Multivessel CAD	1465 (69.7)	644 (60.0)	**< 0.001**	1771 (65.6)	1782 (65.7)	0.955
LMCA disease	185 (8.8)	92 (8.6)	0.827	231 (8.6)	232 (8.6)	0.984
Image-guided PCI	403 (19.2)	189 (17.6)	0.284	515 (19.1)	518 (19.1)	0.998
Contrast dose [mL]	301.27 ± ± 193.40	290.10 ± ± 187.85	0.120	304.70 ± ± 194.83	306.12 ± ± 203.83	0.869
Discharge medications:						
ASA	1881 (89.6)	970 (90.4)	0.464	2516 (93.2)	2533 (93.4)	0.860
P2Y12 inhibitors	1874 (89.2)	969 (90.3)	0.332	2507 (92.9)	2520 (93.0)	0.952
Beta-blockers	1534 (73.0)	841 (78.4)	**0.001**	2116 (78.4)	2125 (78.4)	0.991
ACEI/ARB	1442 (68.6)	765 (71.3)	0.123	1965 (72.8)	1969 (72.6)	0.908
Statin	1739 (82.8)	902 (84.1)	0.357	2345 (86.9)	2366 (87.3)	0.802

Values are presented as number (percentage) for categorical values and means ± standard deviation for continuous variables. ACEI/ARB — angiotensin converting enzyme inhibitors or angiotensin receptor blockers; ASA — acetylsalicylic acid; BMI — body mass index; CABG — coronary artery bypass grafting; CAD — coronary artery disease; CKD — chronic kidney disease; Cr — creatinine; CrCl — creatinine clearance; CVA — cerebrovascular accidents; ECMO — extracorporeal membrane oxygenation; HF — heart failure; IABP — intra-aortic balloon pump; IOCM — iso-osmolar contrast media; LMCA — left main coronary artery; LOCM — low-osmolar contrast media; LVEF — left ventricular ejection fraction; MI — myocardial infarction; PCI — percutaneous coronary intervention; RRT — renal replacement therapy; STEMI — ST-segment elevation myocardial infarction; TIMI — Thrombolysis In Myocardial Infarction

Table 2. In-hospital outcomes of the patients.

Characteristics	Before IPTW adjustment			After IPTW adjustment		
	IOCM (n = 2101)	LOCM (n = 1073)	P	IOCM (n = 2698)	LOCM (n = 2711)	P
In-hospital death	189 (9.0)	81 (7.5)	0.167	135 (5.0)	122 (4.5)	0.573
Reoccurring MI	12 (0.6)	7 (0.7)	0.779	14 (0.5)	16 (0.6)	0.835
New-onset HF	83 (4.0)	41 (3.8)	0.859	110 (4.1)	91 (3.4)	0.358
Cerebrovascular accident	24 (1.1)	13 (1.2)	0.863	25 (0.9)	38 (1.4)	0.283
Any revascularization	8 (0.4)	4 (0.4)	1.000	13 (0.5)	3 (0.1)	0.080
Stent thrombosis	19 (0.9)	7 (0.7)	0.456	28 (1.0)	22 (0.8)	0.677
Renal outcomes:						
Peak Cr level [mg/dL]	1.685 ± 1.242	1.553 ± 1.409	**0.007**	1.61 ± 1.15	1.64 ± 1.55	0.739
Cr level at discharge [mg/dL]	1.343 ± 0.995	1.278 ± 0.816	0.093	1.28 ± 0.89	1.30 ± 0.84	0.703
ΔCr (peak – initial) [mg/dL]	0.314 ± 0.725	0.288 ± 1.050	0.487	0.30 ± 0.70	0.30 ± 1.03	0.992
ΔCr (discharge – initial) [mg/dL]	–0.062 ± 0.779	0.001 ± 0.720	**0.042**	–0.06 ± 0.68	–0.05 ± 0.87	0.898
Any dialysis event	75 (3.6)	21 (2.0)	**0.012**	82 (3.1)	57 (2.1)	0.199

Values are presented as number (percentage) for categorical values and means ± standard deviation for continuous variables. Cr — creatinine; ΔCr (discharge – initial) — Cr level at discharge minus initial Cr level; ΔCr (peak – initial) — peak Cr level minus initial Cr level; HF — heart failure; IPTW — inverse probability of treatment weighting; IOCM — iso-osmolar contrast media; LOCM — low-osmolar contrast media; MI — myocardial infarction

Table 3. Thirty-day outcomes of the patients after successful discharge.

Characteristics	Before IPTW adjustment			After IPTW adjustment		
	IOCM (n = 1908)	LOCM (n = 988)	P	IOCM (n = 2559)	LOCM (n = 2575)	P
All-cause death	59 (3.1)	22 (2.2)	0.180	68 (2.7)	63 (2.5)	0.775
Non-fatal MI	9 (0.5)	8 (0.8)	0.261	14 (0.5)	22 (0.9)	0.318
New-onset HF	28 (1.5)	4 (0.4)	**0.008**	40 (1.6)	12 (0.5)	**0.020**
Cerebrovascular accident	8 (0.4)	4 (0.4)	1.000	10 (0.4)	10 (0.4)	0.949
Any revascularization	9 (0.5)	11 (1.1)	**0.049**	13 (0.5)	30 (1.2)	0.058
Stent thrombosis	5 (0.3)	2 (0.2)	1.000	6 (0.2)	6 (0.2)	0.961
Any dialysis event	6 (0.3)	1 (0.1)	0.434	9 (0.4)	4 (0.1)	0.368

Values are presented as number (percentage) for categorical values. HF — heart failure; IPTW — inverse probability of treatment weighting; IOCM — iso-osmolar contrast media; LOCM — low-osmolar contrast media; MI — myocardial infarction

Discussion

Our study compared clinical outcomes between IOCM and LOCM in real-world patients with AMI-RI. There were more male patients and patients with STEMI in the IOCM group, and the proportion of mechanical circulatory support was higher in this group than in the LOCM group. Hypertension, dyslipidemia, and prior PCI history were more prevalent in the LOCM group, whereas prior HF was more prevalent in the IOCM group. The initial kidney function and LVEF were lower in the IOCM group. There was a higher proportion of multivessel CAD in the IOCM group. Regarding discharge medications, beta-blockers were more frequently prescribed in the LOCM group. These differences were well-balanced after IPTW adjustment.

Regarding in-hospital outcomes, the IOCM group showed a higher peak Cr level but similar ΔCr (peak – initial) value. Considering that the IOCM group had higher initial Cr level, kidney function tended to worsen proportionally to the initial Cr level, but there was no significant differ-

ence in the change in Cr level between the groups. The value of ΔCr (discharge – initial) was statistically lower in the IOCM group, suggesting that both groups showed similar Cr levels at discharge regardless of the significant difference in initial Cr level between the groups. Notably, the incidence of any dialysis event was higher in the IOCM group. Given that the patients in the IOCM group had worse kidney function at initial presentation and higher peak Cr level, the former had undergone dialysis at a higher frequency than the latter, owing to the higher likelihood of kidney-function deterioration. Nevertheless, these differences in in-hospital outcomes were attenuated post-IPTW because of the balancing of the covariates.

In 30-day outcomes, a higher incidence of new-onset HF in the unadjusted analysis was noted in the IOCM group, possibly because of selection bias owing to differences in baseline characteristics. The IOCM group included more male patients. Regarding previous medical history, more patients in the IOCM group had prior HF. Furthermore, the patients had higher Cr levels and lower CrCl, and a higher proportion had CrCl < 20 mL/min/1.73 m^2, indicating worse kidney function. Patients in the IOCM group also had lower LVEFs, with a considerable proportion of patients with LVEF < 40%. Regarding discharge medications, beta-blockers, which are known to reduce infarct size and early mortality, were less frequently prescribed in the IOCM group. Additionally, a higher proportion of patients in the IOCM group had multivessel CAD and STEMI. These multi-faceted factors may contribute to the occurrence of new-onset HF within a 30-day follow-up interval [20–25]. Furthermore, this worse outcome was not attenuated after adjustments with IPTW, with the between-group difference remaining significant.

The rates of dialysis tended to be higher in the IOCM group, although this trend was attenuated after IPTW adjustment. Although the requirement of dialysis does not directly signify the presence of CIN, our results seem somewhat similar to or different from those of some previous studies. A literature review reported several studies that compared IOCM and LOCM groups [11, 14–16, 26]. Some studies showed a similar incidence of CIN between the groups [15, 16, 26], while other studies demonstrated a beneficial effect of IOCM on lowering the CIN risk [10, 11, 14]. Meanwhile, only one clinical study from the Swedish Coronary Angiography and Angioplasty Registry (SCCAR) demonstrated lower incidence of kidney failure in ioxaglate-treated patients compared to IOCM-treated patients [27], which suggests that IOCM can lead to the deterioration of kidney function compared to LOCM. Given that only unadjusted results were considered in our study, the results of the SCCAR study seem consistent with those of our study. However, SCCAR was a non-randomized observational registry, and the survival analyses of the study results were not adjusted for covariates. Moreover, two subsequently published randomized controlled trials produced contradictory results, demonstrating that IOCM was less nephrotoxic than LOCM [10, 11]. Furthermore, the in-hospital outcomes, including the incidence of in-hospital dialysis, were statistically attenuated after IPTW adjustment.

In 30-day outcomes, most variables including all-cause death, non-fatal MI, CVA, stent thrombosis, and any dialysis event were similar between the groups. According to a study conducted in China, both CMs had similar 2-year all-cause death [5], which is consistent with our post-discharge outcomes. Naturally, there are several differences between that study and the present one. The study included all patients undergoing elective PCI, whereas the present study targeted patients with AMI-RI undergoing emergent or urgent PCI. Moreover, the study showed the 2-year outcomes of patients from a single institution, while our study showed clinical outcomes over a relatively short period of time of patients from multiple medical centers.

Iodinated CM is mainly excreted by the kidneys, with a biologic half-life of < 60 min in individuals with normal kidney function [28]. Naturally, if kidney function is compromised, this half-life may be lengthened, increasing the likelihood of CM retention in the human body and worsening kidney function. Because all study subjects had RI, it seems plausible that they might have been more prone to nephrotoxicity compared to AMI patients with preserved kidney function. Given that the in-hospital dialysis rate was different but the 30-day dialysis rate was similar in the groups, the CM type does not appear to have a long-lasting effect on kidney function as expected. Because iodixanol is traditionally believed to be less harmful to the kidneys than most other CM, our results are remarkable.

Given that the PCI rates of AMI in South Korea were reported to be quite high [1] compared to those from other regions of the world [29], this investigation in Korean patients with AMI is important. Nevertheless, there is a paucity of this type of study on renal outcomes between

IOCM and LOCM. We found only one randomized controlled trial that compared IOCM and ioxaglate in patients with renal insufficiency undergoing angiography [11]. This study, however, did not target patients with AMI who required emergent PCI. To our knowledge, our study is the first to evaluate clinical outcomes in patients with AMI-RI, depending on the CM type used during PCI, in a Korean population.

Limitations of the study

Our study has several limitations that should be considered in the interpretation of the results. First, the COREA-AMI registry only included 9 tertiary centers with high volumes of patients with AMI. Therefore, it is difficult to generalize the real-world characteristics and all clinical outcomes of the two study groups. Second, although this study was based on a large-scale, multicenter, and observational registry, it was non-randomized, introducing selection bias in the statistical analysis. Moreover, we excluded patients who received mixed use of both IOCM and LOCM. Thus, although the propensity score weighting method was performed to minimize the selection bias, conducting a multicenter randomized controlled trial would be preferable in the future.

Conclusions

Despite previous studies having reported favorable effects of IOCM use on the development of CIN, and our traditional and common belief that, compared to LOCM, IOCM is associated with more favorable renal outcomes in patients with AMI undergoing PCI, the present study demonstrated that IOCM use did not prevent future incidence of dialysis compared to LOCM use in patients with AMI-RI.

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References

1. Kim Y, Jeong MHo, Ahn Y, et al. Results of a 10-year experience in Korea using drug-eluting stents during percutaneous coronary intervention for acute myocardial infarction (from the Korea acute myocardial infarction registry). Am J Cardiol. 2018; 122(3): 365–373, doi: 10.1016/j.amjcard.2018.04.026, indexed in Pubmed: 30041888.
2. Thomsen HS, Morcos SK, Thomsen HS, et al. Contrast media and the kidney: European Society of Urogenital Radiology (ESUR) guidelines. Br J Radiol. 2003; 76(908): 513–518, doi: 10.1259/bjr/26964464, indexed in Pubmed: 12893691.
3. McCullough PA, Wolyn R, Rocher LL, et al. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med. 1997; 103(5): 368–375, doi: 10.1016/s0002-9343(97)00150-2, indexed in Pubmed: 9375704.
4. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation. 2002; 105(19): 2259–2264, doi: 10.1161/01.cir.0000016043.87291.33, indexed in Pubmed: 12010907.
5. Du M, Jiang L, Tang X, et al. Contrast induced nephropathy and 2-year outcomes of iso-osmolar compared with low-osmolar contrast media after elective percutaneous coronary intervention. Korean Circ J. 2021; 51(2): 174–181, doi: 10.4070/kcj.2020.0307, indexed in Pubmed: 33525073.
6. McClennan BL. Low-osmolality contrast media: premises and promises. Radiology. 1987; 162(1 Pt 1): 1–8, doi: 10.1148/radiology.162.1.3786748, indexed in Pubmed: 3786748.
7. Thomsen HS, Dorph S. High-osmolar and low-osmolar contrast media. An update on frequency of adverse drug reactions. Acta Radiol. 1993; 34(3): 205–209, indexed in Pubmed: 8489830.
8. Barrett BJ, Carlisle EJ. Metaanalysis of the relative nephrotoxicity of high- and low-osmolality iodinated contrast media. Radiology. 1993; 188(1): 171–178, doi: 10.1148/radiology.188.1.8511292, indexed in Pubmed: 8511292.
9. Chalmers N, Jackson RW. Comparison of iodixanol and iohexol in renal impairment. Br J Radiol. 1999; 72(859): 701–703, doi: 10.1259/bjr.72.859.10624328, indexed in Pubmed: 10624328.
10. Aspelin P, Aubry P, Fransson SG, et al. Nephrotoxic effects in high-risk patients undergoing angiography. N Engl J Med. 2003; 348(6): 491–499, doi: 10.1056/NEJMoa021833, indexed in Pubmed: 12571256.
11. Jo SH, Youn TJ, Koo BK, et al. Renal toxicity evaluation and comparison between visipaque (iodixanol) and hexabrix (ioxaglate) in patients with renal insufficiency undergoing coronary angiography: the RECOVER study: a randomized controlled trial. J Am Coll Cardiol. 2006; 48(5): 924–930, doi: 10.1016/j.jacc.2006.06.047, indexed in Pubmed: 16949481.
12. Briguori C, Colombo A, Airoldi F, et al. Nephrotoxicity of low-osmolality versus iso-osmolality contrast agents: impact of N-acetylcysteine. Kidney Int. 2005; 68(5): 2250–2255, doi: 10.1111/j.1523-1755.2005.00683.x, indexed in Pubmed: 16221226.
13. Solomon RJ, Natarajan MK, Doucet S, et al. Investigators of the CARE Study. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. Circulation. 2007; 115(25): 3189–3196, doi: 10.1161/CIRCULATIONAHA.106.671644, indexed in Pubmed: 17562951.
14. McCullough PA, Bertrand ME, Brinker JA, et al. A meta-analysis of the renal safety of isosmolar iodixanol compared with low-osmolar contrast media. J Am Coll Cardiol. 2006; 48(4): 692–699, doi: 10.1016/j.jacc.2006.02.073, indexed in Pubmed: 16904536.
15. Heinrich MC, Häberle L, Müller V, et al. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. Radiology. 2009; 250(1): 68–86, doi: 10.1148/radiol.2501080833, indexed in Pubmed: 19092091.

16. Reed M, Meier P, Tamhane UU, et al. The relative renal safety of iodixanol compared with low-osmolar contrast media: a meta-analysis of randomized controlled trials. JACC Cardiovasc Interv. 2009; 2(7): 645–654, doi: 10.1016/j.jcin.2009.05.002, indexed in Pubmed: 19628188.
17. Shin DIl, Chang K, Ahn Y, et al. Impact of occluded culprit arteries on long-term clinical outcome in patients with non-ST-elevation myocardial infarction: 48-month follow-up results in the COREA-AMI Registry. J Interv Cardiol. 2014; 27(1): 12–20, doi: 10.1111/joic.12078, indexed in Pubmed: 24147831.
18. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018; 39(2): 119–177, doi: 10.1093/eurheartj/ehx393, indexed in Pubmed: 28886621.
19. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976; 16(1): 31–41, doi: 10.1159/000180580, indexed in Pubmed: 1244564.
20. McCallum W, Tighiouart H, Kiernan MS, et al. Relation of kidney function decline and NT-proBNP with risk of mortality and readmission in acute decompensated heart failure. Am J Med. 2020; 133(1): 115–122.e2, doi: 10.1016/j.amjmed.2019.05.047, indexed in Pubmed: 31247182.
21. Bergström A, Andersson B, Edner M, et al. Effect of carvedilol on diastolic function in patients with diastolic heart failure and preserved systolic function. Results of the Swedish Doppler-echocardiographic study (SWEDIC). Eur J Heart Fail. 2004; 6(4): 453–461, doi: 10.1016/j.ejheart.2004.02.003, indexed in Pubmed: 15182771.
22. Brophy JM, Joseph L, Rouleau JL. Beta-blockers in congestive heart failure. A Bayesian meta-analysis. Ann Intern Med. 2001; 134(7): 550–560, doi: 10.7326/0003-4819-134-7-200104030-00008, indexed in Pubmed: 11281737.
23. Klingbeil AU, Schneider M, Martus P, et al. A meta-analysis of the effects of treatment on left ventricular mass in essential hypertension. Am J Med. 2003; 115(1): 41–46, doi: 10.1016/s0002-9343(03)00158-x, indexed in Pubmed: 12867233.
24. He J, Ogden LG, Bazzano LA, et al. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. Arch Intern Med. 2001; 161(7): 996–1002, doi: 10.1001/archinte.161.7.996, indexed in Pubmed: 11295963.
25. Tsai IT, Wang CP, Lu YC, et al. The burden of major adverse cardiac events in patients with coronary artery disease. BMC Cardiovasc Disord. 2017; 17(1): 1, doi: 10.1186/s12872-016-0436-7, indexed in Pubmed: 28052754.
26. From AM, Al Badarin FJ, McDonald FS, et al. Iodixanol versus low-osmolar contrast media for prevention of contrast induced nephropathy: meta-analysis of randomized, controlled trials. Circ Cardiovasc Interv. 2010; 3(4): 351–358, doi: 10.1161/CIRCINTERVENTIONS.109.917070, indexed in Pubmed: 20647563.
27. Liss P, Persson PB, Hansell P, et al. Renal failure in 57 925 patients undergoing coronary procedures using iso-osmolar or low-osmolar contrast media. Kidney Int. 2006; 70(10): 1811–1817, doi: 10.1038/sj.ki.5001887, indexed in Pubmed: 17003814.
28. Bettmann MA. Frequently asked questions: iodinated contrast agents. Radiographics. 2004; 24 (Suppl 1): S3–S10, doi: 10.1148/rg.24si045519, indexed in Pubmed: 15486247.
29. Ui S, Chino M, Isshiki T. Rates of primary percutaneous coronary intervention worldwide. Circ J. 2005; 69(1): 95–100, doi: 10.1253/circj.69.95, indexed in Pubmed: 15635211.