International Journal of Cardiology 273 (2018) 69–73

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Incidence of contrast-induced acute kidney injury in a large cohort of all-comers undergoing percutaneous coronary intervention: Comparison of five contrast media☆

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ARTICLE INFO

Article history:
Received 30 June 2018
Received in revised form 29 August 2018
Accepted 31 August 2018
Available online 1 September 2018

Keywords:
Contrast-induced acute kidney injury
Contrast-induced nephropathy
Percutaneous coronary intervention
Contrast media

ABSTRACT

Background: There is controversy as to whether iso-osmolar contrast media (IOCM) are associated with lower risk of contrast-induced acute kidney injury (CI-AKI), compared with low-osmolar contrast media (LOCM). We aimed to evaluate if a differential risk of CI-AKI exists after percutaneous coronary intervention (PCI) according to different contrast media (CM) types.

Methods: We performed a single-center retrospective study in a cohort of all-comers undergoing PCI between January 2012 and December 2016. CI-AKI was defined as an increase in serum creatinine ≥0.3 mg/dl or ≥50% within 72 h from PCI. IOCM were represented by iodixanol, whereas four different LOCM were utilized (ioversol, iopromide, iomeprol, iobitridol). Multiple-treatment inverse probability of treatment weighting (IPTW)-adjusted logistic regression analysis was performed to identify whether CM type was an independent predictor of CI-AKI.

Results: We included 2648 subjects (ioversol, n = 272; iopromide, n = 818; iomeprol, n = 611; iobitridol, n = 460; iodixanol, n = 487). CI-AKI occurred in 300 patients (11.7%) overall, with no differences across CM groups (ioversol 13.0%, iopromide 11.5%, iomeprol 10.2%, iobitridol 13.9%, iodixanol 11.3%; p = 0.42). CI-AKI requiring dialysis was observed in 8 patients (0.3%) overall (p = 0.50). On IPTW-adjusted analysis, none of the LOCM was associated with a significantly different risk of CI-AKI compared with iodixanol: ioversol OR 0.986 (95% confidence interval [CI] 0.611–1.591), iopromide OR 0.870 (95% CI 0.606–1.250), iomeprol OR 0.904 (95% CI 0.619–1.319), iobitridol OR 1.258 (95% CI 0.850–1.861).

Conclusions: In a large cohort of all-comers undergoing PCI, there were no differences in the adjusted risk of CI-AKI across 4 LOCM, compared with iodixanol.

1. Introduction

Contrast-induced acute kidney injury (CI-AKI) is a frequent and potentially serious complication of percutaneous coronary intervention (PCI) [1]. After a transient phase of vasodilatation, contrast media (CM) induces marked vasoconstriction of the afferent arterioles, with subsequent sustained reduction in renal blood flow, which contributes to renal injury in several ways: release of reactive oxygen species; vacuolization from direct toxic effects of CM on tubular cells, leading to acute tubular necrosis; and ischemia of the outer medulla [1]. There is controversy as to whether the risk of CI-AKI is different according to the type of CM utilized. In fact, some studies did not observe any difference between iso-osmolar (IOCM) and low-osmolar contrast media (LOCM) [2,3], while others found that the IOCM iodixanol is associated with lower risk of CI-AKI compared with LOCM [4,5]. The evidence base for this is derived from meta-analyses including small randomized controlled trials comparing IOCM (iodixanol) with a given LOCM [2–5]. Consequently, possible actual differences in CM-associated renal toxicity might have been undetected due to low sample size, inclusion of low-risk populations, and utilization of two-way comparisons (i.e., iodixanol vs. a specific LOCM).

To the best of our knowledge, no study has so far investigated the risk of CI-AKI across several types of CM in a large cohort of unselected

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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https://doi.org/10.1016/j.ijcard.2018.08.097
0167-5273/

patients undergoing PCI. We therefore performed a single-center retrospective study to ascertain whether a differential risk of CI-AKI exists across five different CM types.

2. Methods

2.1. Patient population

We included all patients undergoing PCI at our institution, for whom both baseline and post-procedural serum creatinine measurements were available, between January 2012 and December 2016. Baseline, procedural and hospitalization data were recorded. All patients signed an informed consent, approved by the local ethics committees, for procedural data collection and for the anonymous use of data for retrospective evaluation.

2.2. CI-AKI prophylaxis

All patients received guidelines-recommended [6] CI-AKI prophylaxis, which was based on the intravenous administration of isotonic saline (1.0–1.5 ml/kg/h; 0.5 ml/kg/h in cases of volume overload or left ventricular ejection fraction [LVEF] <45%), started 12 h before PCI (or in the catheterization laboratory for emergency cases) and continued up to 24 h afterwards.

2.3. Contrast media types

At our institution, five CM types were utilized during study period: the IOCM iodixanol (Visipaque 320, GE Healthcare, Chicago, IL) and 4 LOCM. These were: ioversol (Optiray 350, Guerbet, Villepinte, France), iopromide (Ultravist 370, Bayer, Leverkusen, Germany), iomeprol (Iomeron 350, Bracco, San Donato Milanese, MI, Italy), and iobitridol (Xenetix 350, Guerbet). CM choice was not dictated by clinical features, and relative imbalances across CM group sizes are to be ascribed to different moments of CM uptake during study period.

2.4. Definitions

The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation. For stable patients, the most recent pre-procedural serum creatinine value was used. For unstable subjects (acute kidney failure, decompensated heart failure, cardiogenic shock, cardiac arrest, etc.), the last stable known serum creatinine value was utilized. If no prior stable value was known, admission serum creatinine concentration was used.

The Mehran risk score [7] and the contrast-volume-to-creatinine-clearance ratio [8] were calculated to estimate CI-AKI risk. Emergent PCI was defined as PCI indicated for ST-elevation myocardial infarction (STEMI), cardiogenic shock, or cardiac arrest. Complex PCI was defined as total stent length > 60 mm, ≥3 stents implanted, 3 vessels treated, chronic total occlusion (CTO), or rotational/laser atherectomy.

Study outcome was CI-AKI, which was diagnosed, in patients not undergoing dialysis prior to PCI, using the change from pre-procedural to peak serum creatinine levels within 72 h post-PCI. CI-AKI was defined and graded according to the Acute Kidney Injury Network (AKIN) definition [9]: stage 1, increase in serum creatinine of ≥0.3 mg/dl or ≥50% to 100% from baseline; stage 2, increase in serum creatinine >100% to 200% from baseline; stage 3, increase in serum creatinine >200% from baseline or increase in serum creatinine to ≥4.0 mg/dl with an acute increase of ≥0.5 mg/dl. CI-AKI requiring dialysis was defined as the new need for in-hospital renal replacement therapy in patients not undergoing chronic dialysis before PCI.

2.5. Statistical analysis

Continuous variables are presented as mean ± standard deviation and compared with ANOVA. Categorical variables are presented as frequency (percentages) and compared with chi-square test.

To minimize the effect of confounders, we performed propensity score adjustment for multiple treatments. Specifically, inverse probability of treatment weighting (IPTW) was performed using the TWANG (Toolkit for Weighting and Analysis of Nonequivalent Groups) method [10]. The corresponding IPTW (the reciprocals of the propensity scores) were estimated by using generalized boosted regression (a machine-learning approach) through iterative estimation (n = 10,000), entering the following covariates: age, sex, body mass index, diabetes, prior myocardial infarction, prior coronary artery bypass graft surgery, chronic heart failure, peripheral arterial disease, hypotension before/during PCI, baseline hemoglobin, eGFR, heart failure on presentation, LVEF, number of diseased vessels, acute coronary syndrome (ACS), complex PCI, emergent PCI, and vascular access. Balance of the IPTW model was assessed by visually inspecting propensity score distributions, and evaluating, for each covariate, the mean effect size (standardized mean difference) and the mean Kolmogorov-Smirnov statistic (after weighting) across all possible pairwise comparisons. A weighted value <0.20 is considered indicative of good balance for both parameters [10]. As shown in Online Fig. 1 and Online Table 1, satisfactory improvement in balance for all covariates was achieved after IPTW.

Doubly-robust IPTW logistic regression analysis was then performed to ascertain whether CM type was independently associated with CI-AKI after additionally controlling for CM volume. The results of this analysis are provided as odds ratios (OR) and 95% confidence intervals (CI).

Finally, multivariate logistic regression analysis with stepwise backward selection (p-entry = 0.05, p-exit = 0.10) was performed to identify independent predictors of CI-AKI. Candidate predictors were: CM type, CM volume, age, sex, diabetes, prior CABG, eGFR, LVEF, heart failure on presentation, baseline hemoglobin, hypotension during/before PCI, number of diseased vessels, ACS, emergent PCI, complex PCI, and vascular access. The results of this analysis are provided as OR and 95% CI.

A $p < 0.05$ was considered statistically significant. Analyses were performed using SPSS 24 (IBM Corp., Armonk, NY) and R 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Clinical characteristics

During study period, a total of 5788 subjects underwent PCI at our institution, of whom n = 2648 (45.7%) had both baseline and post-procedural serum creatinine measurements available and thus represented the study population (ioversol, n = 272; iopromide, n = 818; iomeprol, n = 611; iobitridol, n = 460; iodixanol, n = 487). As shown in Table 1, demographics and clinical characteristics were in general well-balanced across groups. Patients who received iomeprol had the lowest eGFR, while those treated with iobitridol had the highest, although the absolute difference was minimal. Subjects treated with iodixanol had the lowest prevalence of hypotension during/before PCI. ACS represented the most common indication for PCI in all groups, closely followed by stable coronary artery disease.

3.2. Angiographic and procedural characteristics

As shown in Table 1, patients receiving ioversol and iobitridol were treated more frequently through a transradial access. Subjects receiving iodixanol received the shortest total stent length, and had the lowest prevalence of intravascular imaging, CTO PCI, and emergent PCI. Mean Mehran risk score was lowest in the iodixanol group and highest in the ioversol group. Contrast volume was lowest in the iodixanol group and highest in the iobitridol group. Moreover, contrast volume correlated with complex PCI (OR [per 100-ml increments] 2.60, 95% CI 2.43–2.78, $p < 0.001$), as well as fluoroscopy time (beta coefficient [per 100-ml increments] 10.44, 95% CI 10.11–10.78, $p < 0.001$) and total stent length (beta coefficient [per 100-ml increments] 10.49, 95% CI 9.89–11.10, $p < 0.001$).

3.3. Unadjusted rates of CI-AKI

Serum creatinine measurements were available for 92.9% of patients on day 1 post-PCI, 49.7% on day 2, 38.2% on day 3. Patients for whom post-PCI creatinine was available were older (68.1 ± 11.4 vs. 66.3 ± 9.8 years), had lower eGFR (73.0 ± 28.1 vs. 89.1 ± 23.2 ml/min/1.72 m^2), had higher Mehran risk score (7.4 ± 5.0 vs. 4.4 ± 3.4), and received a higher contrast volume (229 ± 122 vs. 214 ± 95 ml) ($p < 0.001$ for all), compared with those who had no post-PCI creatinine measurements.

As shown in Fig. 1, CI-AKI occurred in 300 patients (11.7%) overall, with no differences across CM groups (ioversol 13.0%, iopromide 11.5%, iomeprol 10.2%, iobitridol 13.9%, iodixanol 11.3%; $p = 0.42$). In the majority of cases, across all groups, stage 1 CI-AKI was diagnosed. CI-AKI requiring dialysis was observed in 8 patients (0.3%) overall ($p = 0.50$).

3.4. Adjusted analyses

Fig. 2 displays the results of IPTW logistic regression analysis for the prediction of CI-AKI, after additionally controlling for CM volume. Compared with the reference IOCM iodixanol, all LOCM were associated with similar adjusted risks of CI-AKI: ioversol OR 0.986 (95% CI 0.611–1.591), iopromide OR 0.870 (95% CI 0.606–1.250), iomeprol OR 0.904 (95% CI 0.619–1.319), iobitridol OR 1.258 (95% CI 0.850–1.861).

Table 1
Clinical and angiographic characteristics, and procedural data.

Variable	Contrast media (n = 2648)					p-value
	Ioversol (n = 272)	Iopromide (n = 818)	Iomeprol (n = 611)	Iobitridol (n = 460)	Iodixanol (n = 487)	
Age (years)	68.0 ± 11.5	67.9 ± 11.3	68.1 ± 11.6	68.1 ± 11.1	68.5 ± 11.4	0.90
Men	220 (81%)	669 (82%)	493 (81%)	368 (80%)	387 (80%)	0.87
Body mass index (kg/m^2)	27.1 ± 3.9	26.7 ± 4.1	26.9 ± 4.2	26.2 ± 3.6	26.8 ± 4.2	0.14
Diabetes mellitus	87 (33%)	275 (34%)	218 (37%)	167 (37%)	172 (36%)	0.61
Dyslipidemia	175 (65%)	486 (60%)	383 (64%)	270 (70%)	275 (57%)	0.09
Hypertension	198 (74%)	599 (74%)	465 (78%)	347 (77%)	376 (78%)	0.25
Current smoker	43 (16%)	146 (18%)	87 (15%)	78 (17%)	75 (16%)	0.53
Prior MI	102 (38%)	290 (36%)	199 (33%)	166 (37%)	163 (34%)	0.64
Prior PCI	117 (43%)	360 (44%)	298 (50%)	206 (45%)	236 (49%)	0.14
Prior CABG	40 (15%)	143 (18%)	84 (14%)	75 (16%)	79 (16%)	0.45
Peripheral arterial disease	72 (27%)	210 (26%)	183 (30%)	134 (29%)	134 (28%)	0.35
Baseline hemoglobin (mg/dl)	13.5 ± 1.8	13.5 ± 2.1	13.3 ± 1.9	13.5 ± 1.8	13.3 ± 1.7	0.11
eGFR (ml/min/1.73 m^2)	71.7 ± 28.3	73.8 ± 27.9	71.2 ± 28.8	75.9 ± 28.2	71.8 ± 27.0	0.05
eGFR < 60 ml/min/1.73 m^2	101 (37%)	263 (32%)	226 (37%)	142 (31%)	180 (37%)	0.07
eGFR < 30 ml/min/1.73 m^2	16 (6%)	40 (5%)	41 (7%)	17 (4%)	16 (3%)	0.06
Dialysis	7 (3%)	12 (1%)	15 (3%)	9 (2%)	9 (2%)	0.65
LVEF (%)	48.2 ± 11.5	49.6 ± 11.7	49.2 ± 11.7	48.6 ± 11.8	49.9 ± 11.6	0.24
LVEF < 50%	105 (41%)	265 (37%)	212 (40%)	163 (39%)	140 (33%)	0.17
Hypotension during/before PCI	19 (7%)	67 (8%)	38 (6%)	27 (6%)	15 (3%)	0.007
Heart failure on presentation	15 (5%)	66 (8%)	40 (7%)	33 (7%)	29 (6%)	0.49
Cardiogenic shock on presentation	9 (3%)	41 (5%)	26 (4%)	19 (4%)	10 (2%)	0.11
Indication of PCI						
Stable CAD	105 (39%)	282 (34%)	236 (39%)	157 (34%)	156 (32%)	0.01
Unstable angina/NSTEMI	57 (21%)	185 (23%)	146 (24%)	111 (24%)	144 (30%)	
STEMI	51 (19%)	158 (19%)	80 (13%)	75 (16%)	61 (13%)	
Shock/cardiac arrest	4 (1%)	28 (3%)	20 (3%)	12 (3%)	13 (3%)	
Heart failure/low LVEF	17 (6%)	27 (3%)	19 (3%)	18 (4%)	21 (4%)	
Complete revascularization	23 (8%)	75 (9%)	64 (10%)	54 (12%)	47 (10%)	
Other	14 (5%)	62 (8%)	44 (7%)	33 (7%)	44 (9%)	
Number of diseased vessels	2.1 ± 0.8	2.1 ± 0.8	2.2 ± 0.8	2.2 ± 0.8	2.2 ± 0.8	0.12
Radial access	172 (77%)	455 (64%)	337 (63%)	275 (74%)	301 (69%)	<0.001
Total stent length (mm)	41.8 ± 30.0	41.1 ± 30.2	39.6 ± 30.6	42.7 ± 29.9	36.4 ± 26.5	0.01
Rotational atherectomy	7 (3%)	26 (3%)	15 (2%)	11 (2%)	14 (3%)	0.90
Intravascular imaging	25 (9%)	74 (9%)	71 (12%)	33 (7%)	28 (6%)	0.01
B2/C type lesion	179 (66%)	521 (64%)	391 (64%)	295 (64%)	286 (59%)	0.25
CTO PCI	43 (16%)	98 (12%)	78 (13%)	51 (11%)	42 (9%)	0.05
Acute coronary syndrome	112 (41%)	371 (45%)	246 (40%)	198 (43%)	218 (45%)	0.34
Emergent PCI	55 (20%)	186 (23%)	100 (16%)	87 (19%)	74 (15%)	0.005
Complex PCI	98 (36%)	281 (34%)	207 (34%)	168 (36%)	147 (30%)	0.29
Mehran risk score	8.0 ± 5.4	7.4 ± 5.2	7.4 ± 5.1	7.3 ± 4.8	6.8 ± 4.4	0.03
Contrast-volume-to-CrCl ratio	4.1 ± 3.2	4.0 ± 2.7	4.1 ± 3.5	4.2 ± 3.5	3.7 ± 3.0	0.30
Contrast volume (ml)	232 ± 113	233 ± 123	228 ± 126	243 ± 129	209 ± 111	0.001
Radiation dose (Gy·cm^2)	133 ± 109	145 ± 118	133 ± 111	139 ± 113	152 ± 134	0.06
Fluoroscopy time (min)	27.0 ± 22.3	25.5 ± 20.4	24.6 ± 23.1	27.0 ± 22.0	20.7 ± 17.1	<0.001

Abbreviations: CAD, coronary artery disease; CABG, coronary artery bypass graft; CrCl, creatinine clearance; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

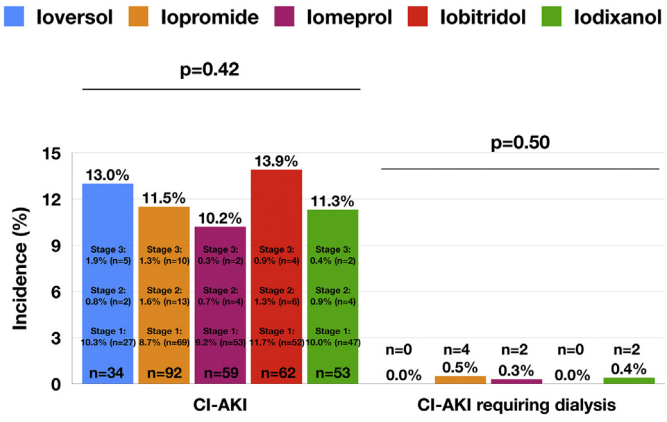

Fig. 1. Rates of CI-AKI and CI-AKI requiring dialysis across contrast media types. For CI-AKI stages definitions, refer to the Methods section.

On multivariable analysis (Table 2), independent predictors of CI-AKI were: age (OR [per 10 years] 1.38, p < 0.001), LVEF (OR [per 10%] 0.64, p < 0.001), baseline hemoglobin (OR [per 1 mg/dl] 0.87, p = 0.001), hypotension during/before PCI (OR 2.62, p < 0.001), ACS (OR 1.95, p < 0.001), and CM volume (OR [per 100 ml] 1.18, p = 0.01).

4. Discussion

Our study findings are: 1) CI-AKI is a common complication of PCI in a cohort of all-comers undergoing PCI; 2) however, the risk of CI-AKI requiring dialysis is very low; 3) on adjusted analyses, there were no differences in the risk of CI-AKI according to any of the four LOCM studied, compared with the benchmark IOCM iodixanol; 4) independent predictors of CI-AKI were age, LVEF, baseline hemoglobin, hypotension during/before PCI, ACS, and contrast volume.

Recently, the scientific community has been extensively debating as to whether CI-AKI really exists, arguing that random fluctuations in serum creatinine, unrelated to CM administration, can result in AKI misclassification [11–14]. For example, Bruce et al. conducted a large retrospective

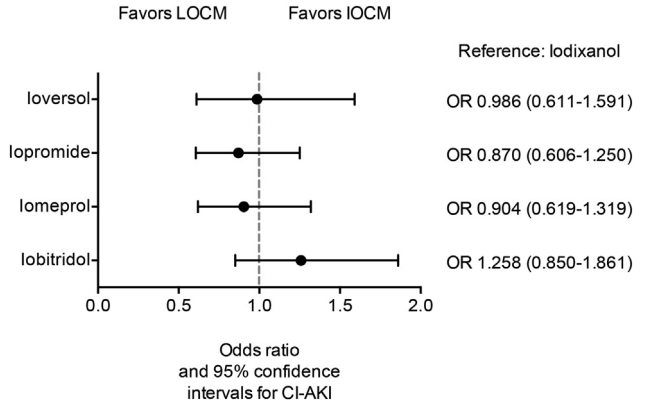

Fig. 2. Forest plot showing adjusted odds ratios (OR) of four low-osmolar contrast media (LOCM) types, compared to the reference iso-osmolar contrast media (IOCM) iodixanol.

study analyzing the incidence of AKI in patients undergoing contrast-enhanced (with either the LOCM iohexol or the IOCM iodixanol) vs. unenhanced computed tomography. They observed a similar incidence of AKI across the three groups. The authors suggested that the additional risk of AKI accompanying administration of CM (CI-AKI) may be overstated and that much of the creatinine elevation in such patients might be attributable to background fluctuation, underlying disease, or treatment [11]. Similarly, Wilhelm-Leen et al. observed a similar adjusted risk of AKI in patients undergoing CM exposure for a variety of indications (including computed tomography and percutaneous angiography with/without intervention), compared with subjects unexposed to CM [15]. However, the "big data approach" and the retrospective nature of these reports are important limitations: in fact, these studies did not capture variables of critical importance such as administered CM volume [11,15] and serum creatinine values [15], and the temporal sequence between CM administration and AKI development, thus losing precision in the assessment of such a complex phenomenon [12,16].

Although it is not disputed that CM exerts some direct renal toxicity, it has often been erroneously blamed for all cases of renal failure following its administration, *in lieu* of other contributors to AKI development. In fact, AKI following PCI can frequently be traced to a combination of acute procedural factors including hypotension with renal hypoperfusion, atheroma embolization into the renal arteries and bleeding, playing on a background of chronic risk factors (advanced age, diabetes, peripheral arterial disease, preexisting renal dysfunction, etc.) [1,14].

We have observed a moderately high rate of CI-AKI (12.8%), compared with figures from the literature. Valle et al. [17] reported on the NCDR Cath-PCI Registry, including 453,475 patients undergoing PCI. Like in our study, CI-AKI was defined according to the AKIN definition. The incidence of CI-AKI was 8.8%. More recently, Tsai et al. [18] provided data from the same registry, including 954,729 patients. CI-AKI incidence was 7.1%. However, mean contrast volume in Valle et al. [17] and Tsai et al. [18] was 208 and 185 ml, respectively, which is lower than in our cohort (221 ml) and could indicate lower PCI complexity. The incidence of CI-AKI requiring dialysis in Tsai et al. [18] was low (0.3%) and similar to our data (0.2%). Inohara et al. [19] performed a similar study in Japan, including 11,041 patients, and utilizing the AKIN CI-AKI definition as well. CI-AKI was observed in 10.5%, and CI-AKI requiring dialysis in 1.5%, which can be related to possible differences in baseline and procedural characteristics of the study population, biological susceptibility to contrast-mediated renal injury, and practice pattern related to dialysis initiation thresholds.

CM can be classified according to two properties: osmolality and viscosity. Osmolality expresses the ratio between the number of iodine atoms and the number of CM particles. Landmark studies demonstrated a higher incidence of pseudoallergic reactions and direct nephrotoxicity with high-osmolar CM, compared with LOCM [20], which have thereafter become standard of care. Since x-rays attenuation relies on iodine, a lower osmolality (i.e., a higher ratio between the number of iodine atoms and the number of CM particles) will lead to improved visualization. However, osmolality is inversely proportional to viscosity, therefore IOCM are more viscous than LOCM, which might impair their clearance from the tubules, thereby increasing the risk of toxic effects. Accordingly, some meta-analyses did not observe any difference in terms of CI-AKI between IOCM (iodixanol) and LOCM [2,3], while others found a lower risk with the former [4,5]. Importantly, these meta-analyses were based on small randomized trials (most with $n < 200$), conducted over a decade ago, using different CI-AKI definitions, and including populations at low-to-intermediate risk of CI-AKI (e.g., undergoing computed tomography or coronary/peripheral angiography not followed by intervention). Additionally, each of the studies included in those meta-analyses performed pairwise comparisons (iodixanol vs. a LOCM).

Therefore, we decided to conduct the present study for two reasons: 1) provide current real-world data on the incidence and predictors of AKI in a cohort of all-comers undergoing PCI at a tertiary catheterization

Table 2
Univariate and multivariate predictors of CI-AKI.

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% confidence interval	p-value	Odds ratio	95% confidence interval	p-value
Contrast media type (reference: iodixanol)			0.51			
Ioversol	1.19	0.76–1.85	0.45			
Iopromide	1.02	0.72–1.44	0.93			
Iomeprol	1.08	0.75–1.56	0.69			
Iobitridol	1.33	0.91–1.94	0.14			
Age (per 10 years)	1.33	1.20–1.49	<0.001	1.38	1.18–1.60	<0.001
Male sex	0.54	0.42–0.70	<0.001			
Diabetes	1.32	1.04–1.69	0.02			
Prior CABG	0.94	0.68–1.30	0.70			
eGFR (per 10 ml/min/1.73 m^2)	0.88	0.84–0.92	<0.001	0.95	0.89–1.01	0.10
LVEF (per 10%)	0.61	0.55–0.67	<0.001	0.64	0.57–0.72	<0.001
Heart failure on presentation	5.51	3.98–7.64	<0.001			
Baseline hemoglobin (per 1 mg/dl)	0.80	0.75–0.85	<0.001	0.87	0.80–0.94	0.001
Hypotension during/before PCI	5.84	4.17–8.18	<0.001	2.62	1.63–4.23	<0.001
Number of diseased vessels	1.06	0.92–1.22	0.41			
Acute coronary syndrome	2.15	1.70–2.72	<0.001	1.95	1.43–2.67	<0.001
Emergent PCI	2.17	1.68–2.80	<0.001			
Complex PCI	0.86	0.67–1.10	0.24			
Femoral access	1.82	1.41–2.34	<0.001			
Contrast media volume (per 100 ml)	0.96	0.88–1.06	0.44	1.18	1.04–1.34	0.01

Abbreviations: CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection rate; PCI, percutaneous coronary intervention.

laboratory specialized in complex interventions; 2) ascertain whether a differential risk of CI-AKI exists according to several CM utilized during study period. In particular, to the best of our knowledge, ours is the first cohort study performing a five-way comparison across 4 LOCM and iodixanol. To this regard, so far the only available evidence derived from the network meta-analysis by Biondi-Zoccai et al. [21], who also found a similar risk of CI-AKI among patients treated with iodixanol, iomeprol, iopamidol, and ioversol. The strengths of our study stem from its large sample size, all-comer nature, including a large proportion of patients undergoing complex PCI. Additionally, we performed solid adjustment utilizing a novel machine-learning approach (generalized boosted regression), which takes advantage of the computational power of modern workstations. Multiple-treatment IPTW-adjusted logistic regression has very recently been proposed as a sound method for minimizing confounding and residual selection bias in observational studies [22]. Advantages, compared with traditional logistic regression, include the ability of the algorithm to model non-linear relationships and interactions, and perform variable selection in a data-adaptive fashion, thus achieving better balance between treatment groups on pre-treatment covariates, reducing bias in treatment effect estimates, and producing more stable propensity score weights [10].

We have identified age, LVEF, baseline hemoglobin, hypotension during/before PCI, ACS, and CM volume as independent predictors of CI-AKI. These associations had been previously reported in the literature [1,7,18,23], which confers strength to our findings.

Our study has some limitations. First, our study is not a randomized trial, although our propensity score model achieved excellent adjustment, minimizing the risk that residual bias could confound our results. Second, being a real-world registry, post-procedural creatinine was not available for all patients (but only in 45.7%), although this problem is commonly found also in national registries (e.g., 60% in the NCDR Cath-PCI Registry). Patients for whom post-PCI creatinine values were not available had a lower CI-AKI risk profile, so that the actual CI-AKI incidence might have been overestimated, if anything, making our estimates more conservative. Finally, post-PCI creatinine measurements were not performed in equal proportions on post-procedural day 1, 2, and 3. Since this biomarker already starts rising within 24 h after CM exposure in cases who will develop CI-AKI [24], it is likely that the vast majority of those subjects were detected promptly and followed with repeated creatinine measurements on the following days.

5. Conclusions

In this large cohort of all-comers undergoing PCI, the risk of CI-AKI was independent of the type of CM utilized. Specifically, ioversol, iopromide, iomeprol, and iobitridol were associated with similar risk of CI-AKI compared with iodixanol. In the absence of large randomized studies comparing several different CM types in a contemporary population at high risk for CI-AKI, our report provides reassuring data regarding the safety profile of five currently used CM.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.08.097.

Funding

None.

Conflict of interest

Dr. Azzalini received honoraria from Guerbet, Terumo, and Sahajanand Medical Technologies; and research support from ACIST Medical Systems, Guerbet, and Terumo. The other authors have no disclosures.

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