ORIGINAL

Clinical impact of noncontrast percutaneous coronary intervention in patients with acute coronary syndrome

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Abstract : Purpose : Contrast-induced acute kidney injury (CI-AKI) is one of the common serious complications of percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS). This study aimed to assess the significance of noncontrast strategy in the setting of ACS. Methods : CI-AKI was defined as an increase in serum creatinine of ≥0.5 mg/dL or ≥1.25 times from the baseline. One-year worsening renal function (WRF) was defined as an increase of ≥0.3 mg/dL in serum creatinine from the baseline after PCI. Results : Of 250 ACS patients, 81 were treated with noncontrast PCI. The average doses of contrast medium in the noncontrast and conventional groups were 17 (9–22) ml and 150 (120–200) ml, respectively. CI-AKI was observed in 4 patients (5%) in the noncontrast group and 29 patients (17%) in the conventional group. Noncontrast PCI was associated with a lower incidence of CI-AKI (adjusted odds ratio, 0.26 ; 95% confidence interval [CI], 0.08–0.82). The bootstrap method and inverse probability weighting led to similar results. CI-AKI was associated with a higher incidence of 1-year WRF (adjusted hazard ratio, 2.30 ; 95% CI, 1.12–4.69), while noncontrast PCI was not. Conclusions : Noncontrast PCI was associated with the lower incidence of CI-AKI in ACS patients. J. Med. Invest. 69 : 57-64, February, 2022

Keywords : noncontrast percutaneous coronary intervention, contrast-induced acute kidney injury, worsening renal function, acute coronary syndrome

INTRODUCTION

Contrast-induced acute kidney injury (CI-AKI) is a common and serious complication of percutaneous coronary intervention (PCI) (1), leading to irreversible deterioration of renal function, dependence on dialysis, increased costs, and mortality in patients with acute coronary syndrome (ACS) (2-4). Prevention of CI-AKI may improve such clinical adverse events ; however, effective preventive strategies are limited (5). Although sufficient hydration has been shown to be effective in preventing CI-AKI (4), it is a difficult strategy in emergent and urgent patients. Reducing the amount of contrast medium is expected to have a preventive effect on CI-AKI (6, 7), and such an approach is available even for emergent or urgent PCI patients. Ultimately, PCI without a contrast medium could effectively prevent complications even in patients with severe renal dysfunction, such as a chronic kidney disease stage 4 or 5. Recently, we have reported the feasibility and safety of noncontrast PCI in the setting of ACS for the first time (8) ; however, the association of this strategy with short- and long-term renal function remains unclear as the previous prospective study involved a single-group registry. Therefore, the present study compared the incidence of CI-AKI and long-term clinical adverse events between patients from the previous study and patients who underwent conventional PCI to evaluate the clinical significance of noncontrast PCI in ACS patients.

PATIENTS AND METHODS

Study population

It was a retrospective and single center study designed to assess data on the clinical and procedural characteristics in patients with ACS, including unstable angina pectoris (UAP), non-ST-segment myocardial infarction (NSTEMI), and ST-segment myocardial infarction (STEMI). The study included patients with ACS who underwent PCI. The noncontrast PCI group was extracted from a previous prospective cohort study, which included patients recruited between May 2017 and April 2019 (8). The conventional PCI group was registered as a historical cohort and included patients treated between July 2014 and April 2017 (because the majority of patients with complex backgrounds and lesions were treated with noncontrast PCI from May 2017 to April 2019). In conventional PCI, the amount of contrast medium was not limited. Patients who had undergone hemodialysis or had a life expectancy of <1 year owing to non-cardiac diseases at the time of PCI were excluded from our study. Patients with type 2 AMI were also excluded due to different pathophysiological features from the type 1 AMI (9).

Noncontrast PCI

A detailed overview of the noncontrast PCI procedure has been described previously (8). Briefly, coronary angiography (CAG) was performed with minimal amount of contrast medium. Interventionists did not use contrast medium during the revascularization and observed culprit lesions using with intravascular ultrasound sonography (IVUS). Balloon/stent position

was determined by IVUS. In a total occluded lesion, a guidewire passed the lesion followed by balloon expansion of a culprit lesion and observation by IVUS. Because information regarding distal from the occlusion was lacking on CAG, culprit vessel was observed as distal as possible by IVUS.

Definition

A successful noncontrast PCI was confirmed when the contrast medium was not injected from guiding catheter engagement to wire removal. Only one attempt of CAG after the PCI was permitted to confirm the final coronary flow. Failed PCI was defined as a failure to obtain a residual stenosis <30% after stent implantation and/or post-PCI TIMI flow grade <3 (10). CI-AKI was defined as an increase in serum creatinine levels of ≥0.5 mg/dL or ≥1.25 times from the baseline, known or presumed to have developed within 72 hours after contrast injection (1). Renal function at 1 year was assessed as worsening renal function (WRF), defined as an increase in serum creatinine of ≥0.3 mg/dL from the baseline after the PCI (11). Periprocedural unstable dynamics was defined as having either of the four following states between 24 hours preceding and post the PCI : ventricular tachycardia/fibrillation, cardiopulmonary arrest, systolic blood pressure <90 mmHg, or heart rate <30 bpm. Major adverse cardiac and cerebrovascular events (MACCE) were defined as the composite of cardiovascular death, ischemic stroke, nonfatal ACS and acute heart failure requiring hospitalization.

Variables

Data on patient characteristics, periprocedural hemodynamics, and angiographical findings, procedural information, and 1-year MACCE were collected by cardiologists. Information regarding medications was gathered at the times of admission and discharge.

Ethical principles

This study protocol conforms to the 1975 Declaration of Helsinki and is in line with the Ethical Guidelines for Epidemiological Research established by the Japanese government. The study was approved by the ethics committee of Kyorin University. According to the guidelines, the study satisfied the conditions for waiving the requirement for informed consent from individual participants.

Statistics

Numerical data are presented as means ± standard deviations if the data followed a normal distribution. Otherwise, data are displayed as medians and interquartile ranges. Categorical variables are expressed as absolute numbers or percentages. Continuous variables were analyzed using the unpaired Student's t-tests or Mann–Whitney U tests, while the Fisher's exact test or chi-squared test was used for categorical variables. The primary endpoint was an incidence of CI-AKI. The secondary endpoints were an incidence of 1-year WRF and MACCE. According to previous studies (1, 8), the incidence of CI-AKI was predicted to be 5% in the noncontrast PCI group and 17% in the conventional PCI group. Assuming 80% power and a significance level of 0.05, 74 patients in the noncontrast PCI group and 148 in the conventional PCI group were required for statistically significant results.

The incidence of CI-AKI was assessed using univariate and multivariate logistic regression analyses and expressed as odds ratios (OR), 95% confidence intervals (CI), and p values. Multivariate logistic regression analysis was conducted with forward stepwise selection. Variables with a p <0.10 in the univariate logistic regression analysis were selected for adjustment. The

nonparametric bootstrap method (resampling with replacement 1000 times on the multivariate model) was used to provide inner validation. Furthermore, inverse probability weighting (IPW) was used to assess the association of noncontrast PCI with CI-AKI. The clinical variables used in IPW included age, sex, hypertension, diabetes mellitus, congestive heart failure, periprocedural unstable hemodynamics, left ventricular ejection fraction, RAS inhibitor use, STEMI, UAP, estimated glomerular filtration rate (eGFR), C-reactive protein levels, uric acid levels, and B-type natriuretic peptide levels. The continuous variables, except for eGFR, were divided into two groups based on the median or mean, as appropriate. eGFR was classified as follows : eGFR ≥ or < 45 ml/min/1.73 m^2, based on the staging of chronic kidney disease (12). The balance between both groups was assessed based on the propensity score distribution and standardized differences. If the absolute value of the standard difference for each variable was <0.1, the model was considered to balance the covariates successfully. Finally, to evaluate possible interactions between noncontrast PCI and eGFR (≥45 or <45 ml/min/1.73 m^2), we compared models with and without the interaction term of 2 variables and calculated the p value using a likelihood ratio test.

The follow-up began on the day of discharge. The follow-up was completed 1 year after discharge or the date when an end-point event was observed, depending on what happened first. The risk of WRF or MACCE at 1 year was assessed using univariate and multivariate Cox regression analyses and expressed as hazard ratios (HR), 95% CI, and p values. Variables with a p value <0.10 in the univariate analysis were included in the multivariate Cox regression analysis, with forward stepwise selection to identify the significant factors. Statistical significance was set at p< 0.05. All statistical analyses were carried out using the Stata software, version 14 (StataCorp, College Station, TX).

RESULTS

Patient characteristics

The present study included 250 patients. The patient, angiographic, and procedural characteristics are displayed in Table 1. Noncontrast PCI was performed in 81 patients and was successful in 72 patients (89%). The dose of contrast medium significantly differed between the groups (noncontrast PCI, 17 [9–22] ml ; conventional PCI, 150 [120–200] ml ; p <0.001).

Association of noncontrast PCI with CI-AKI

CI-AKI was observed in 33 patients (4 [5%] in the noncontrast PCI group ; 29 [17%] in the conventional PCI group). The results of univariate logistic regression analysis are shown in Table 2. Noncontrast PCI was associated with a lower incidence of CI-AKI (OR, 0.25 ; 95% CI, 0.09–0.74 ; p = 0.012). Figure 1 demonstrates that these associations did not vary based on renal function, according to the analysis of likelihood ratio test. The association persisted after adjustment (OR, 0.26 ; 95% CI, 0.08–0.82 ; p = 0.022) (Figure 2). The bootstrap method and IPW demonstrated similar results (OR in the bootstrap method, 0.26 ; 95% CI, 0.07–0.90 ; p = 0.033 ; OR in IPW, 0.90 ; 95% CI, 0.85–0.96 ; p = 0.002).

Safety of noncontrast PCI

The incidence of failed PCI was observed 6 (7.4%) in the noncontrast PCI group and 23 (13.6%) in the conventional PCI group, respectively (p = 0.205). Coronary perforation and periprocedural death were not observed in the noncontrast PCI group.

Table 1.   Patient characteristics

	All	Noncontrast PCI	Conventional PCI	P value
	n = 250	n = 81	n = 169	
Age, years	73 ± 12	75 ± 12	73 ± 12	0.140
Male, n (%)	191 (76)	54 (67)	137 (81)	0.012
Body mass index, kg/m²	23.4 ± 4.0	23.4 ± 3.7	23.3 ± 4.2	0.970
Hypertension, n (%)	186 (74)	62 (77)	124 (73)	0.591
Dyslipidemia, n (%)	139 (56)	50 (62)	89 (53)	0.177
Diabetes mellitus, n (%)	111 (44)	35 (43)	76 (45)	0.793
Congestive heart failure, n (%)	68 (27)	37 (46)	31 (18)	< 0.001
Unstable angina pectoris, n (%)	58 (23)	32 (40)	26 (15)	< 0.001
Non ST-segment elevation myocardial infarction, n (%)	90 (36)	37 (46)	53 (31)	0.027
ST-segment elevation myocardial infarction, n (%)	102 (41)	12 (15)	90 (53)	< 0.001
Periprocedural unstable hemodynamics, n (%)	43 (17)	9 (11)	34 (20)	0.106
Ejection fraction, %	49 ± 13	51 ± 13	49 ± 13	0.257
Laboratory data				
Hemoglobin, g/L	127 ± 20	124 ± 20	129 ± 20	< 0.001
Creatinine, mg/dl	1.0 ± 0.4	1.2 ± 0.8	1.1 ± 0.4	0.063
Estimated glomerular filtration rate, ml/min/1.73m²	56 ± 24	55 ± 25	57 ± 23	0.470
C-reactive protein, mg/dl	0.96 (0.76-1.3)	0.25 (0.08-0.95)	0.97 (0.79-1.23)	0.611
Uric acid, mg/dl	6.2 ± 1.9	6.3 ± 2.0	6.1 ± 1.9	0.614
B-type natriuretic peptide, pg/ml	140 (47-421)	137 (48-475)	142 (47-384)	0.895
HbA1c, %	6.6 ± 1.1	6.5 ± 1.1	6.6 ± 1.2	0.432
Preprocedural medication				
Aspirin, n (%)	240 (96)	73 (90)	167 (99)	0.001
Clopidogrel, n (%)	116 (46)	44 (54)	72 (43)	0.082
Prasugrel, n (%)	126 (50)	36 (44)	90 (53)	0.192
Anticoagulation, n (%)	31 (12)	16 (20)	15 (9)	0.023
Statin, n (%)	121 (48)	57 (70)	64 (38)	< 0.001
Renin-angiotensin system inhibitors, n (%)	99 (40)	35 (43)	64 (38)	0.419
Beta blockers, n (%)	82 (33)	32 (40)	50 (30)	0.118
Furosemide, n (%)	35 (14)	20 (25)	15 (9)	0.001
Postprocedural medication				
Aspirin, n (%)	224 (90)	63 (78)	161 (95)	< 0.001
Clopidogrel, n (%)	129 (52)	59 (73)	70 (41)	0.082
Prasugrel, n (%)	106 (42)	19 (23)	87 (51)	< 0.001
Anticoagulation, n (%)	51 (20)	20 (25)	31 (18)	0.244
Statin, n (%)	217 (87)	73 (90)	144 (85)	0.324
Renin-angiotensin system inhibitors, n (%)	158 (63)	46 (57)	112 (66)	0.146
Beta blockers, n (%)	148 (59)	28 (35)	120 (71)	< 0.001
Furosemide, n (%)	52 (21)	18 (22)	34 (20)	0.701
Angiographical characteristics				
1-vessel disease, n (%)	113 (45)	38 (47)	75 (44)	0.706
2-vessel disease, n (%)	98 (39)	35 (43)	63 (37)	0.369
3-vessel disease, n (%)	35 (14)	6 (7)	29 (17)	0.050
Left main trunk, n (%)	19 (8)	5 (6)	14 (8)	0.621
PCI target lesions *				
Left main trunk, n (%)	14 (6)	3 (4)	11 (7)	0.558
Left anterior descending artery, n (%)	102 (41)	39 (48)	63 (37)	0.102
Left circumflex artery, n (%)	45 (18)	14 (17)	31 (18)	0.838
Right coronary artery, n (%)	94 (38)	25 (31)	69 (41)	0.128
Type A lesion, n (%)	3 (1)	0 (0)	3 (2)	0.553
Type B1 lesion, n (%)	25 (10)	4 (5)	21 (12)	0.074
Type B2 lesion, n (%)	108 (43)	41 (51)	67 (40)	0.104
Type C lesion, n (%)	116 (46)	36 (44)	80 (47)	0.687
Procedural characteristics				
Dose of contrast medium, ml	124 (24-200)	17 (9-22)	150 (120-200)	< 0.001
Successful noncontrast PCI, n (%)	72 (29)	72 (89)	0 (0)	< 0.001
Puncture site				
Radial artery, n (%)	145 (58)	73 (90)	72 (41)	< 0.001
Devices				
Sheath size, Fr	6.3 ± 0.5	6.0 ± 0.3	6.4 ± 0.5	< 0.001
Stent implantation, n (%)	223 (89)	72 (89)	151 (89)	1.000

* There were duplicated cases.
PCI, percutaneous coronary intervention

Table 2. Logistic regression analysis for CI-AKI

	Univariate		
	OR	95% CI	p value
Age (an increase of 1 year)	1.02	0.99-1.06	0.237
Male	1.45	0.57-3.71	0.434
Body mass index (an increase of 1 kg/m^2)	0.97	0.89-1.07	0.585
Hypertension	0.41	0.19-0.87	0.020
Dyslipidemia	0.72	0.35-1.50	0.379
Diabetes mellitus	2.13	1.01-4.50	0.048
Congestive heart failure	1.40	0.64-3.08	0.397
ST-segment elevation myocardial infarction	2.19	1.04-4.60	0.038
Periprocedural unstable hemodynamics	6.62	3.00-14.63	< 0.001
Ejection fraction (an absolute increase of 10%)	0.58	0.44-0.77	< 0.001
Hemoglobin (an increase of 10 g/L)	0.91	0.76-1.09	0.315
Estimated glomerular filtration rate (an increase of 10 ml/min/1.73m^2)	0.84	0.72-0.99	0.045
C-reactive protein (an increase of 1 mg/dl)	1.43	0.95-2.14	0.087
Uric acid (an increase of 1 mg/dl)	1.22	1.00-1.49	0.051
B-type natriuretic peptide (an increase of 100 pg/ml)	1.06	1.01-1.11	0.028
HbA1c (an absolute increase of 1 %)	1.24	0.93-1.64	0.138
Statin	0.66	0.31-1.38	0.269
Renin-angiotensin system inhibitors	1.14	0.54-2.40	0.722
Beta blockers	1.03	0.47-2.24	0.944
Furosemide	0.83	0.27-2.52	0.739
Noncontrast PCI	0.25	0.09-0.74	0.012
Dose of contrast medium (an increase of 10 ml)	1.06	1.02-1.12	0.008
3-vessel disease	1.44	0.55-3.79	0.459
Left main trunk lesion	5.81	1.87-18.01	0.002
Type C lesion	1.46	0.70-3.04	0.316
The radial artery puncture	0.31	0.14-0.68	0.003
Sheath diameter (an increase of 1 Fr in size)	2.90	1.48-5.68	0.002

CI, confidence interval ; OR, odds ratio ; PCI, percutaneous coronary intervention
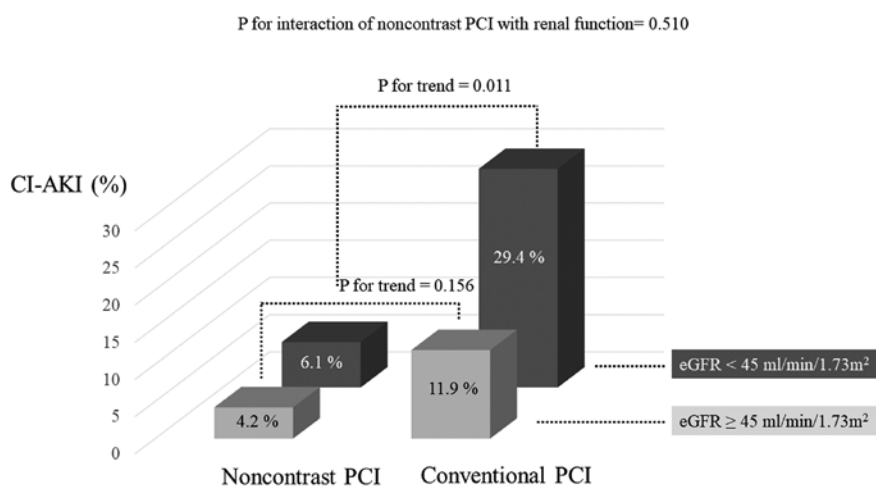

Figure 1. Association between noncontrast PCI and the incidence of CI-AKI based on renal function
Noncontrast PCI was significantly associated with a lower incidence of CI-AKI in patients with an eGFR of <45 ml/min/1.73 m^2. The incidence in patients with an eGFR of ≥45 ml/min/1.73 m^2 was lower in the noncontrast PCI group ; however, the difference was not significant. Notably, according to the likelihood ratio test, the relationship between noncontrast PCI and the lower incidence of CI-AKI persisted regardless of renal function.
CI-AKI, contrast-induced acute kidney injury ; eGFR, estimated glomerular filtration rate ; PCI, percutaneous coronary intervention
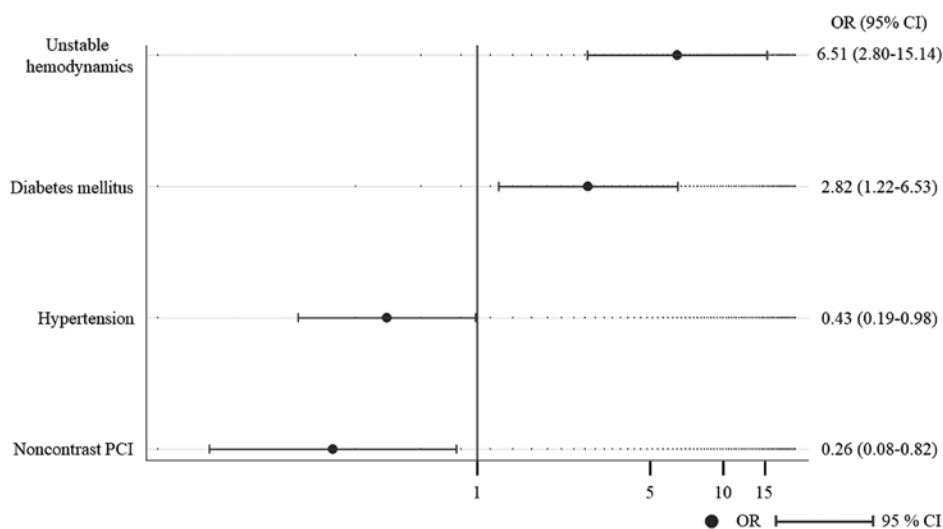
Figure 2.   Multivariate logistic regression analysis for CI-AKI
Noncontrast PCI was associated with a lower incidence of CI-AKI after adjustment for periprocedural unstable hemodynamics, diabetes mellitus, and hypertension.
CI, confidence interval ; CI-AKI, contrast-induced acute kidney injury ; OR, odds ratio ; PCI, percutaneous coronary intervention

One-year prognosis and renal function

In-hospital mortality was observed in 20 patients (8.0%), and 230 patients were analyzed for long-term endpoints. The follow-up duration was 365 (224–365) days. WRF and MACCE at 1 year were documented in 53 patients (23%) (the noncontrast PCI group, 15 [19%] ; the conventional PCI group, 38 [25%]) and 31 patients (13%) (the noncontrast PCI group, 13 [17%] ; the conventional PCI group, 18 [12%]), respectively. The recurrence of nonfatal ACS, one of MACCE, did not differ between the groups (6 [8%] in the noncontrast PCI group and 3 [2%] in the conventional PCI group [p = 0.064]). The results of the univariate and multivariate Cox regression analyses concerning 1-year WRF and MACCE are demonstrated in Table 3. Noncontrast PCI was related to neither the incidence of 1-year WRF nor that of 1-year MACCE. CI-AKI was related to 1-year WRF (adjusted HR, 2.30 ; 95% CI, 1.12–4.69) and was not to 1-year MACCE.

DISCUSSION

To the best of our knowledge, this is the first study to demonstrate the association of the noncontrast PCI strategy with a lower incidence of CI-AKI. Different from noncontrast PCI for chronic total occlusion (13), the strategy in the setting of ACS is feasible even for interventionists without board certification (8). Our study revealed some challenges other than contrast medium to prevent CI-AKI.

As ad-hoc PCI is unavoidable in many patients with ACS, noncontrast PCI involves the use of small amounts of contrast medium for CAG. The extremely low dose of contrast medium (as low as 10–20 ml) might not be harmful for renal function. Indeed, Figure 1 shows that the incidence of CI-AKI is similar regardless of renal function in the noncontrast PCI group. The development of CI-AKI might owe to periprocedural unstable hemodynamics in the noncontrast PCI group. However, it has been unclear whether such small amounts of the contrast medium may lead to vasoconstriction and subsequent sustained reduction in renal blood flow, contributing to renal injury (4). It would be impossible to conduct noncontrast CAG and PCI

with the current standard of care. In the setting of UAP and NSTEMI, coronary magnetic resonance angiography (14,15) may be acceptable instead of CAG. Noncontrast CAG and PCI may be feasible under the specific conditions.

It is not surprising that periprocedural unstable hemodynamics was strongly correlated with a higher incidence of CI-AKI, which has been previously reported(16). As well as contrast medium, unstable hemodynamics contribute to the reduction of renal blood flow and lead to AKI. AKI is a common and well-known predictor for worse prognosis among patients with shock state such as septic shock (17) and cardiogenic shock(18). The results of our study suggest that the maintenance of hemodynamics should be the most important countermeasure for CI-AKI in a critical setting. Although various types of equipment exist, such as intra-aortic balloon pumping (IABP), VA extra-corporeal membrane oxygenation, and Impella® (Abiomed, Danvers, MA), it has been unknown whether these devices improve renal prognosis. For instance, IABP neither improves nor impairs renal function in AMI patients with cardiogenic shock (19). Currently, it is difficult to resolve the problems regarding unstable hemodynamics.

Diabetes mellitus has been reported to be correlated with the development of CI-AKI (20). Diabetes mellitus contributes to the development of chronic kidney disease through various mechanism, including accumulation of advanced glycation end-products and microinflammation (21, 22). Hypertension also contributes to renal impairment (23) ; however, the morbidity was related to a lower incidence of the renal complication in our study. Patients with hypertension are not as likely to be in a shock state as patients without hypertension. It is noted that the left main trunk (LMT) lesions and radial artery puncture were significantly associated with the incidence of CI-AKI in the univariate analysis, but such associations were not observed after adjustment. The LMT lesion was strongly related to the higher prevalence of unstable hemodynamics (data has not been shown in the Result section : 64% in the LMT lesions vs 14% in non-LMT lesions ; p <0.001). RA puncture indicated the similar relation (data has not been shown in the Result section : 6% in the RA puncture vs 32% in non-RA puncture ; p <0.001). Femoral puncture seemed to be selected for patients with more

Table 3.   Cox regression analysis for long-term outcomes

	1-year worsening renal function						1-year MACCE					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Age (an increase of 1 year)	1.02	1.00-1.05	0.088	NA			1.04	1.00-1.07	0.059	NA		
Male	1.47	0.74-2.92	0.277	NA			2.23	0.78-6.38	0.134	NA		
Body mass index (an increase of 1 kg/m^2)	0.95	0.88-1.02	0.128	NA			0.96	0.88-1.05	0.400	NA		
Hypertension	1.92	0.91-4.08	0.089	NA			1.08	0.46-2.50	0.861	NA		
Dyslipidemia	0.90	0.52-1.54	0.690	NA			0.79	0.39-1.59	0.508	NA		
Diabetes mellitus	1.33	0.77-2.28	0.304	NA			2.41	1.17-4.98	0.017	1.98	0.95-4.13	0.068
Congestive heart failure	2.60	1.50-4.49	0.001	NA			4.16	2.05-8.45	< 0.001	2.73	1.28-5.81	0.009
Ejection fraction (an absolute increase of 10%)	0.67	0.55-0.81	< 0.001	NA			0.67	0.52-0.86	0.002	NA		
ST-segment elevation myocardial infarction	1.24	0.72-2.16	0.437	NA			0.84	0.40-1.79	0.653	NA		
3-vessel disease	1.31	0.66-2.60	0.444	NA			1.03	0.40-2.69	0.949	NA		
CI-AKI	4.30	2.15-8.61	< 0.001	2.30	1.12-4.69	0.022	2.66	1.02-6.95	0.045	NA		
Laboratory data at discharge												
Hemoglobin (an increase of 10 g/L)	0.68	0.58-0.79	< 0.001	0.86	0.73-1.02	0.084	0.76	0.62-0.93	0.008	NA		
Estimated glomerular filtration rate (an increase of 10 ml/min/1.73m^2)	0.61	0.54-0.70	< 0.001	0.67	0.58-0.77	< 0.001	0.72	0.61-0.84	< 0.001	0.80	0.67-0.95	0.010
Medication at discharge												
Statin	0.42	0.21-0.81	0.010	NA			1.13	0.34-3.72	0.837	NA		
Renin-angiotensin system inhibitors	1.36	0.75-2.48	0.309	NA			0.71	0.35-1.45	0.352	NA		
Beta blockers	1.13	0.65-1.98	0.665	NA			0.89	0.44-1.82	0.754	NA		
Furosemide	2.54	1.46-4.45	0.001	NA			3.20	1.58-6.51	0.001	NA		
Noncontrast PCI	0.79	0.43-1.43	0.428	NA			1.48	0.72-3.02	0.282	NA		

CI, confidence interval ; CI-AKI, contrast induced acute kidney injury ; HR, hazard ratio ; NA, not applicable ; MACCE, major adverse cardiac and cerebrovascular events ; PCI, percutaneous coronary intervention

severe conditions. Namely, LMT lesions and RA puncture were confounding factors of unstable hemodynamics.

Noncontrast PCI was correlated with a lower incidence of CI-AKI, which was related to a higher incidence of 1-year WRF ; however, a direct association of noncontrast PCI with the long-term renal prognosis was not observed. The result might be due to a small difference in the adverse events between the groups. According to the multivariate Cox regression analysis, some factors other than CI-AKI, such as hemoglobin and eGFR, predicted the incidence of WRF at 1 year. Some previous studies indicated that anemia was correlated with WRF (24, 25). Hypoxia caused by anemia stimulates the renin-angiotensin-aldosterone system and contributes to renal vasoconstriction. These factors further exacerbate proteinuria by increasing protein in the renal tubules (26). The association of lower eGFR with the higher incidence of WRF was consistent with a previous study (27). It would be easy to understand that patients with chronic kidney disease are likely to develop WRF in the subsequent clinical course.

According to the results of our study, periprocedural unstable hemodynamics was the most strongly correlated with the incidence of CI-AKI. As proposed previously (28), CI-AKI may be an incorrect technical term and contrast-associated AKI may be more appropriate to characterize the adverse event. Unless a new radiopaque substance without potential risks of AKI

is developed, noncontrast PCI is the best way to mitigate the adverse effects of the contrast medium on renal function. Therapeutic approach aiming at stabilizing hemodynamics should be the future challenge to overcome the CI-AKI and improve both short- and long-term prognosis. A technological advancement will be necessary to achieve this goal.

LIMITATIONS

The present study included some limitations. First, the correlation between noncontrast PCI and CI-AKI was determined by various statistical techniques. The observed biases were appropriately adjusted. However, as this was a retrospective observational study, unidentified biases would present. Second, there were some differences in medication and procedural characteristics between the groups owing to different treatment periods. Patients who were treated more recently may demonstrate better prognosis. However, as far as we know, there are no breakthrough that contribute to improve hemodynamics and reduce the incidence of CI-AKI during the period.

CONCLUSIONS

Noncontrast PCI was significantly associated with a lower incidence of CI-AKI in ACS patients. However, even if the contrast medium was not injected, CI-AKI would not disappear in a critical setting. Treatment for the most important contributing factor, unstable hemodynamics, should be developed in future studies to prevent CI-AKI.

CONFLICT OF INTERESTS

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