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A comparison between different definitions of contrast-induced acute kidney injury for long-term mortality in patients with acute myocardial infarction

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ABSTRACT

Background: Few studies have demonstrated the association between contrast-induced acute kidney injury (CI-AKI) and long-term mortality and explored which definition of CI-AKI accounts for most long-term deaths among patients with acute myocardial infarction (AMI). Therefore, we aimed to evaluate this association and compared the population attributable risks (PARs) of three CI-AKI definitions.
Methods: We analyzed 1300 consecutive AMI patients undergoing angiography in Guangdong Provincial People's Hospital. The endpoint was all-cause mortality. CI-AKI was evaluated according to three definitions: (1) CI-AKI$_A$, with a serum creatinine elevation $\geq$ 50% or $\geq$ 0.3 mg/dL from baseline in the first 72 h after procedure; (2) CI-AKI$_B$, $\geq$ 0.5 mg/dL in 72 h; (3) CI-AKI$_C$: $\geq$ 25% in 72 h; multivariable Cox analysis was conducted to evaluate the association between CI-AKI and long-term mortality. PARs of CI-AKI under different definitions were calculated with their odds ratios and prevalence among our cohort.
Results: During the median follow-up period of 7.0 (5.5; 8.7) years, CI-AKI was significantly associated with poorer outcome regardless of the definition (adjusted hazard ratios: 1.417–2.711). Among the three definitions of CI-AKI, the prevalence was the highest for CI-AKI$_C$ (18.77%), and PAR was the highest for CI-AKI$_A$ (11.62%, 95% CI: 4.99–19.71), followed by CI-AKI$_B$ (9.20%, 95% CI: 4.22–16.00) and CI-AKI$_C$ (7.26%, 95% CI: 0.21–15.62).
Conclusions: Our results suggested that CI-AKI is associated with long-term mortality in patients with AMI irrespective of its definitions. Cardiologists and studies regarding long-term prognosis should pay more attention to the presence of CI-AKI, especially CI-AKI$_A$ with the highest PAR.

1. Introduction

Contrast-induced acute kidney injury (CI-AKI) is a common adverse complication in patients with acute myocardial infarction (AMI) undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI), and may cause prolonged hospitalization, a higher incidence of in-hospital events, and increased mortality [1–4]. However, the challenge is that few studies have demonstrated the association between CI-AKI and long-term mortality in patients with AMI. Some studies suggested that CI-AKI was

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Table 1
Baseline characteristics.

Variables	Total (n = 1300)	CI-AKI$_A$ (n = 163)	non-CI-AKI$_A$ (n = 1137)	p value	CI-AKI$_B$ (n = 77)	non-CI-AKI$_B$ (n = 1223)	p value	CI-AKI$_C$ (n = 244)	non-CI-AKI$_C$ (n = 1056)	p value
Age, y	61.61 ± 12.15	68.77 ± 12.15	60.59 ± 11.80	<0.001	70.78 ± 11.18	61.04 ± 11.98	<0.001	65.31 ± 13.33	60.76 ± 11.70	<0.001
Age > 75, n (%)	220 (16.92)	61 (37.42)	159 (13.98)	<0.001	36 (46.75)	184 (15.04)	<0.001	71 (29.10)	149 (14.11)	<0.001
Female sex, n (%)	208 (16.00)	40 (24.54)	168 (14.78)	0.001	19 (24.68)	189 (15.45)	0.032	62 (25.41)	146 (13.83)	<0.001
Weight, kg	64.92 ± 10.84	62.48 ± 11.1	65.27 ± 10.77	0.003	61.33 ± 10.76	65.15 ± 10.81	0.003	63.16 ± 11.43	65.32 ± 10.67	0.008
SBP, mmHg	121.92 ± 20.25	122.78 ± 26.12	121.8 ± 19.28	0.644	122.17 ± 28.99	121.9 ± 19.59	0.937	122.94 ± 23.87	121.68 ± 19.32	0.445
DBP, mmHg	73.56 ± 11.97	73.8 ± 13.9	73.53 ± 11.67	0.812	73.16 ± 15.4	73.59 ± 11.73	0.809	74.35 ± 13.5	73.38 ± 11.58	0.302
HR, bpm	77.50 ± 15.29	81.92 ± 18.11	76.87 ± 14.75	<0.001	82.84 ± 19.27	77.16 ± 14.95	0.013	80.01 ± 16.86	76.92 ± 14.85	0.009
CHF, n (%)	588 (45.23)	113 (69.33)	475 (41.78)	<0.001	61 (79.22)	527 (43.09)	<0.001	139 (56.97)	449 (42.52)	<0.001
CKD, n (%)	263 (20.23)	73 (44.79)	190 (16.71)	<0.001	45 (58.44)	218 (17.83)	<0.001	59 (24.18)	204 (19.32)	0.088
Hypotension, n (%)	74 (5.69)	26 (15.95)	48 (4.22)	<0.001	20 (25.97)	54 (4.42)	<0.001	30 (12.30)	44 (4.17)	<0.001
LVEF, %	53.81 ± 10.94	49.06 ± 12.32	54.5 ± 10.56	<0.001	48.03 ± 13.11	54.17 ± 10.7	<0.001	51.02 ± 11.73	54.46 ± 10.65	<0.001
LVEF < 40%, n (%)	134 (10.31)	36 (22.09)	98 (8.62)	<0.001	20 (25.97)	114 (9.32)	<0.001	41 (16.80)	93 (8.81)	<0.001
Hypertension, n (%)	646 (49.69)	112 (68.71)	534 (46.97)	<0.001	55 (71.43)	591 (48.32)	<0.001	142 (58.20)	504 (47.73)	0.003
Hyperlipidemia, n (%)	200 (15.38)	19 (11.66)	181 (15.92)	0.158	11 (14.29)	189 (15.45)	0.783	36 (14.75)	164 (15.53)	0.762
Hypoproteinemia, n (%)	606 (46.62)	75 (46.01)	531 (46.7)	0.018	40 (51.95)	566 (46.28)	<0.001	103 (42.21)	503 (47.63)	0.183
Anemia, n (%)	431 (33.15)	76 (46.63)	355 (31.22)	<0.001	36 (46.75)	395 (32.30)	0.008	89 (36.48)	342 (32.39)	0.235
Diabetes, n (%)	267 (20.54)	42 (25.77)	225 (19.79)	0.077	19 (24.68)	248 (20.28)	0.354	50 (20.49)	217 (20.55)	0.984
LDL-C, mmol/L	2.98 ± 1.05	3.09 ± 1.07	2.97 ± 1.05	0.260	2.86 ± 1.18	2.99 ± 1.04	0.459	3.22 ± 1.15	2.93 ± 1.02	0.003
HDL-C, mmol/L	0.96 ± 0.41	0.97 ± 0.27	0.96 ± 0.42	0.630	0.98 ± 0.31	0.96 ± 0.41	0.640	1.03 ± 0.31	0.95 ± 0.42	0.006
HS-CRP, mg/L	31.55 ± 44.29	54.52 ± 53.53	28.19 ± 41.77	<0.001	66.08 ± 55.06	29.32 ± 42.59	<0.001	47.4 ± 54.91	27.8 ± 40.53	<0.001
Lpa, mg/dL	32.69 ± 36.2	31.83 ± 32.65	32.81 ± 36.68	0.750	30.55 ± 30.73	32.81 ± 36.5	0.585	30.77 ± 35.33	33.13 ± 36.4	0.391
SCR, μmol/L	95.49 ± 38.01	119.03 ± 60.8	92.12 ± 32.16	<0.001	140 ± 69.57	92.69 ± 33.20	<0.001	93.43 ± 47.04	95.97 ± 35.61	0.429
eGFR, mL/min/1.73 mm^2	80.22 ± 26.68	67.43 ± 36.36	82.05 ± 24.47	<0.001	54.85 ± 27.72	81.82 ± 25.8	<0.001	85.78 ± 36.92	78.94 ± 23.53	0.006
BUN, mg/dL	5.44 ± 3.05	7.13 ± 4.12	5.2 ± 2.78	<0.001	8.65 ± 4.94	5.24 ± 2.77	<0.001	5.75 ± 3.24	5.37 ± 3.00	0.096
Hemoglobin, g/L	132.47 ± 17.19	126.1 ± 20.82	133.28 ± 16.51	<0.001	123.94 ± 23.14	132.94 ± 16.69	0.008	128.92 ± 20.51	133.17 ± 16.37	0.014
HbA1c, %	6.56 ± 1.50	6.64 ± 1.33	6.55 ± 1.52	0.497	6.57 ± 1.14	6.56 ± 1.52	0.936	6.57 ± 1.39	6.56 ± 1.52	0.892
Serum albumin, g/L	33.22 ± 4.64	31.4 ± 4.57	33.44 ± 4.6	<0.001	29.48 ± 4.61	33.41 ± 4.56	<0.001	32.39 ± 4.23	33.38 ± 4.69	0.011
ACEI/ARB, n (%)	1157 (89.00)	131 (80.37)	1026 (90.24)	<0.001	57 (74.03)	1100 (89.94)	<0.001	210 (86.07)	947 (89.68)	0.142
Beta blocker, n (%)	1064 (81.85)	108 (66.26)	956 (84.08)	<0.001	42 (54.55)	1022 (83.57)	<0.001	185 (75.82)	879 (83.24)	0.018
Statin, n (%)	1284 (98.77)	157 (96.32)	1127 (99.12)	0.002	42 (54.55)	794 (64.92)	0.596	142 (58.20)	694 (65.72)	0.054
PCI, n (%)	836 (64.31)	91 (55.83)	745 (65.52)	0.826	73 (94.81)	1211 (99.02)	0.001	237 (97.13)	1047 (99.15)	0.018
Diuretics, n (%)	404 (31.08)	88 (53.99)	316 (27.79)	<0.001	44 (57.14)	360 (29.44)	<0.001	111 (45.49)	293 (27.75)	<0.001
Metformin, n (%)	17 (1.31)	2 (1.23)	15 (1.32)	0.705	0 (0.00)	17 (1.39)	1.000	3 (1.23)	14 (1.33)	0.745
CV, mL	132.74 ± 53.03	137.06 ± 56.1	132.13 ± 52.57	0.292	138.31 ± 49.05	132.39 ± 53.27	0.310	133.16 ± 56.06	132.65 ± 52.33	0.898
Peri-procedure IABP, n (%)	108 (8.31)	52 (31.90)	56 (4.93)	<0.001	36 (46.75)	72 (5.89)	<0.001	50 (20.49)	58 (5.49)	<0.001

Abbreviations: CI-AKI: contrast-induced acute kidney injury; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; CHF: chronic heart failure; CKD: chronic kidney disease; LVEF: left ventricular ejection fraction; LDL-C: low density lipoprotein-C; HDL-C: high density lipoprotein-C; HS-CRP: high sensitive C-reactive protein; SCR: serum creatinine; Lpa: lipoprotein a; eGFR: estimate glomerular filtration rate; BUN: blood urea nitrogen; ACEI: angiotensin-converting enzymes inhibitors; ARB: angiotensin-receptor blockers; PCI: percutaneous coronary intervention; CV: contrast volume; IABP: intra-aortic balloon pump.

an independent predictor of worse long-term prognosis among AMI patients [5–7], while other studies failed to verify this association [8]. One of the reasons for these conflicting results may be the different definitions of CI-AKI, which may also confuse physicians when they are identifying patients at risk [9–11].

The population-attributable risk (PAR) represents the proportion of cases in a population that would not have occurred in the absence of a risk factor [12]. To the best of our knowledge, no studies have quantified the contributions of different definitions of CI-AKI to long-term mortality in patients with AMI.

Therefore, we conducted this study to evaluate the association between CI-AKI and long-term mortality in patients with AMI and to compare the PARs of three different CI-AKI definitions.

2. Method

2.1. Study population

In this study, 1300 consecutive patients with AMI undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI) in Guangdong Provincial People's Hospital were included between January 2010 and December 2013. The inclusion and exclusion criteria were mentioned previously elsewhere [13]. This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of the Guangdong Provincial People s Hospital. All the patients recruited in the study signed written informed consent.

2.2. Protocol

In accordance with standard clinical guidelines, standard guide catheters, guidewires, balloon catheters, and stents were used through the femoral or radial approach [14]. Noninvasive treatment was based on guidelines from the American Heart Association/American College of Cardiology Foundation. Serum creatinine concentrations were measured for all included patients and at 1, 2, and 3 days after contrast exposure.

2.3. Endpoint and definitions

The endpoint of this study was long-term all-cause mortality. All eligible patients included were followed up through office visits or telephone interviews 1 month, 6 months and every 1 year after registration until April 2019. CI-AKI was evaluated according to three definitions: (1) CI-AKI$_A$, with a serum creatinine elevation $\geq$ 50% or $\geq$ 0.3 mg/dL from baseline in the first 72 h after procedure; (2) CI-AKI$_B$, $\geq$ 0.5 mg/dL in 72 h; (3) CI-AKI$_C$: $\geq$ 25% in 72 h. The definitions of chronic kidney disease (CKD), anemia and hypotension were the same as those in previous studies [15,16].

2.4. Statistical analysis

We applied the Chi-square test or Fisher's exact test for categorical variables expressed as counts (percentages). Continuous variables were presented as the mean ± SD or median ± IQR, and compared using the *t*-test or Wilcoxon rank-sum test (in the two cohorts, with and without CI-AKI observations). Kaplan-Meier analysis was used to count the cumulative mortality, and the log-rank test was used to assess differences between curves. The association between long-term all-cause mortality and CI-AKI was explored by fitting a multivariable Cox regression model adjusting for other risk factors (e.g., age, heart rate, heart function, renal function, and medication). The adjusted risk factors were selected through univariable Cox regression or based on previous studies and clinical importance [17,18]. Three multivariate Cox proportional hazard regression models were applied for three different definitions of CI-AKI, respectively. PAR was calculated using the equation PAR = P (HR-1)/[1 + P (HR-1)], where P is the prevalence of CI-AKI under different definitions in our database. The standard error of PAR was calculated using the delta method [19]. A two-sided probability value < 0.05 was considered significant. All data analyses were conducted with R software (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Patient characteristics

A total of 1300 patients were included in the analysis. Table 1 details the demographic, clinical and procedural characteristics of the included patients. Suppl. details the baseline characteristics of patients with or without CI-AKI. In general, the mean age was 61.61 ± 12.15 years, and only 16% of the total population was female. A total of 220 patients (16.92%) were older than 75 years. Chronic heart failure (CHF) was present in 588 (45.23%) patients, while CKD was identified in 263 (20.23%) patients.

Irrespective of the definition used, patients complicated with CI-AKI following CAG were older, more often female, with lower weight, worse baseline heart and renal function, and higher incidence of hypertension or hypotension; moreover, they had higher levels of high sensitive C-reactive protein (HS-CRP) and lower levels of hemoglobin (Table 1).

3.2. CI-AKI and in-hospital events

In-hospital events are detailed in Suppl. After the procedure, 27 patients underwent hemodialysis, among whom 22 (28.6%) were complicated with CI-AKI$_B$, 24 (14.7%) with CI-AKI$_A$ and 21 (8.6%) with CI-AKI$_C$. Regardless of the definitions, patients with CI-AKI tended to have hemodialysis after contrast exposure ($p < 0.001$). Moreover, patients with CI-AKI were more likely to develop acute heart failure (AHF) and arrythmia during hospitalization.

3.3. Long-term outcomes

The median follow-up period was 7.0 (5.5; 8.7) years. During the follow-up period, 244 all-cause deaths occurred. The long-term mortality rate was significantly higher in patients with CI-AKI$_B$ (51.9%), followed by CI-AKI$_A$ (37.4%) and CI-AKI$_C$ (26.2%) ($p < 0.001$). Kaplan-Meier curves revealed that patients with CI-AKI demonstrated poorer long-term prognosis than those without CI-AKI (Fig. 1). In addition, after adjusting for age, gender, heart rate, heart and renal function, hypertension, hypotension, diabetes mellitus, anemia, HS-CRP and medications, CI-AKI$_A$ was associated with a 2.049 fold higher risk of long-term death (95% CI: 1.419–2.958), while CI-AKI$_B$ was associated with a 2.711 fold higher risk (95% CI: 1.743–4.217) and CI-AKI$_C$ was associated with a 1.417 fold higher risk (95% CI: 1.011–1.986) (Table 2).

In addition, in a small fraction of our enrolled patients who underwent hemodialysis after the procedure, a higher mortality rate was observed compared with that of those who did not undergo post-procedure hemodialysis (66.67% vs 18.39%, $p < 0.001$). Kaplan-Meier curves also revealed the similar results (Suppl. Fig. 1).

3.4. Pars of three CI-AKI definitions

Among the three definitions of CI-AKI, the prevalence was highest for CI-AKI$_C$ (18.77%), followed by CI-AKI$_A$ (12.54%) and CI-AKI$_B$ (5.92%). For the PARs, it was the highest for CI-AKI$_A$ (PAR:11.62, 95% CI: 4.99–19.71), followed by CI-AKI$_B$ (PAR:9.20, 95% CI:

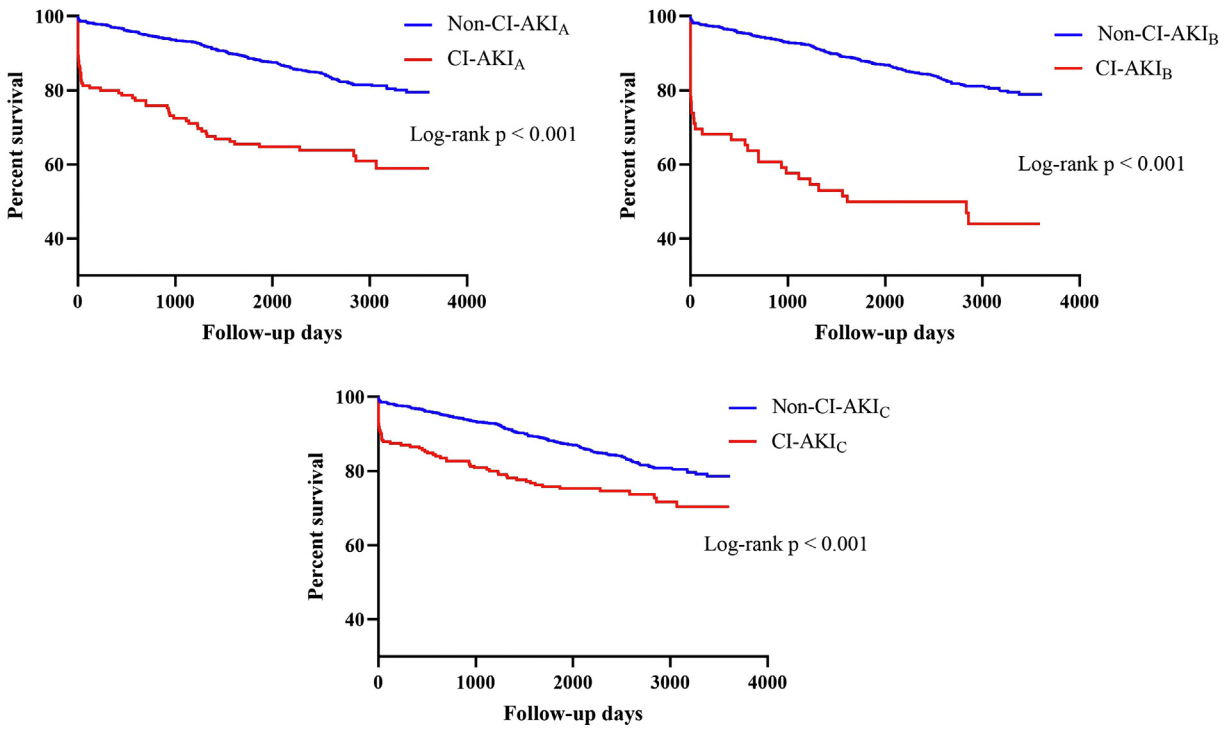

Fig. 1. Association between various definitions of contrast-induced acute kidney injury and long-term mortality in patients with acute myocardial infarction undergoing coronary angiography.

Table 2
Univariable and multivariable analysis of risk factors for long-term mortality.

	UNIVARIABLE ANALYSIS				MULTIVARIABLE ANALYSIS											
					CI-AKI$_A$				CI-AKI$_B$				CI-AKI$_C$			
Age	HR	95%CI		p-value	HR	95%CI		p-value	HR	95%CI		p-value	HR	95%CI		p-value
	1.378	1.010	1.881	0.043	0.992	0.978	1.006	0.251	0.992	0.978	1.006	0.265	0.994	0.980	1.008	0.414
Female vs Male	1.480	1.085	2.020	0.013	1.344	0.926	1.953	0.120	1.338	0.922	1.943	0.125	1.317	0.908	1.910	0.147
Weight	0.991	0.979	1.003	0.154												
Heart rate	1.020	1.013	1.027	<0.001	1.016	1.009	1.024	<0.001	1.016	1.008	1.024	<0.001	1.017	1.009	1.025	<0.001
CHF	1.612	1.252	2.076	<0.001	1.026	0.752	1.400	0.873	1.053	0.774	1.433	0.742	1.074	0.790	1.460	0.649
CKD	2.228	1.704	2.914	<0.001	1.370	0.963	1.949	0.080	1.330	0.933	1.895	0.115	1.509	1.068	2.134	0.020
Hypertension	1.344	1.044	1.731	0.022	1.039	0.767	1.409	0.804	1.053	0.776	1.428	0.742	1.061	0.784	1.436	0.700
Hypotension	2.602	1.703	3.975	<0.001	1.916	1.126	3.260	0.016	1.958	1.156	3.315	0.012	1.896	1.114	3.226	0.018
Smoking	0.825	0.642	1.062	0.135												
Hypoproteinemia	0.895	0.659	1.214	0.476												
Anemia	1.574	1.219	2.033	<0.001	1.369	0.999	1.877	0.051	1.378	1.006	1.888	0.046	1.409	1.029	1.929	0.033
HS-CRP, mg/L	1.005	1.003	1.008	<0.001	1.002	0.999	1.005	0.253	1.001	0.998	1.004	0.386	1.002	0.999	1.005	0.222
ACEI/ARB	0.487	0.350	0.677	<0.001	0.671	0.442	1.017	0.060	0.675	0.446	1.022	0.063	0.659	0.435	0.999	0.049
Beta-blocker	0.490	0.371	0.646	<0.001	0.625	0.444	0.880	0.007	0.644	0.457	0.906	0.011	0.613	0.436	0.860	0.005
Diuretic	1.593	1.230	2.062	<0.001												
IABP	3.247	2.328	4.530	<0.001												
Diabetes	1.621	1.226	2.141	<0.001	1.455	1.046	2.024	0.026	1.479	1.063	2.058	0.020	1.488	1.072	2.066	0.018
CI-AKI$_A$	3.098	2.318	4.140	<0.001	2.049	1.419	2.958	<0.001								
CI-AKI$_B$	5.145	3.664	7.225	<0.001					2.711	1.743	4.217	<0.001				
CI-AKI$_C$	1.831	1.376	2.435	<0.001									1.417	1.011	1.986	0.043

Abbreviations: CI-AKI: contrast-induced acute kidney injury; HR: hazard ratio; CHF: chronic heart failure; CKD: chronic kidney disease; HS-CRP: high sensitive C-reactive protein; ACEI: angiotensin-converting enzymes inhibitors; ARB: angiotensin-receptor blockers; IABP: intra-aortic balloon pump.

4.22–16.00), and it was the lowest for CI-AKI$_C$ (PAR:7.26, 95% CI: 0.21–15.62) (Fig. 2).

4. Discussion

Our study evaluated the association between CI-AKI and long-term prognosis in AMI patients, and was the first to compare the PARs for long-term mortality among three different definitions of CI-AKI. In this study, we found that patients with CI-AKI had a higher mortality rate than those without CI-AKI. After adjusting for sociodemographic and cardiorenal risk factors including age, gender, heart rate, CHF, CKD, history of hypertension, history of DM, hypotension, anemia, HS-CRP, and pharmacological therapy, CI-AKI may lead to a 1.417–2.711 fold higher mortality rate depending on the definitions used. Moreover, the highest PAR was found in CI-AKI$_A$, followed by CI-AKI$_B$, and CI-AKI$_C$.

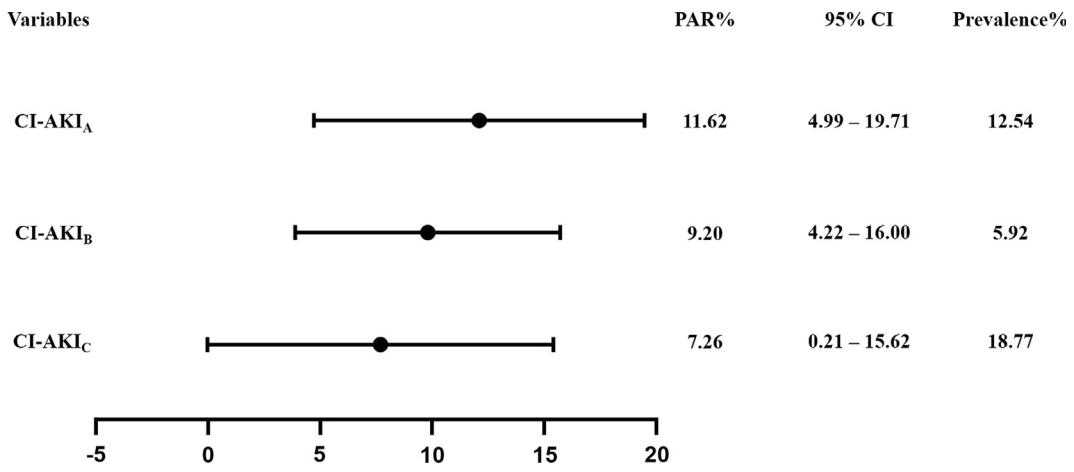

Fig. 2. Population attributable risk of three different definitions of contrast-induced acute kidney injury.

4.1. Findings and comparison with related studies

Our results suggested that CI-AKI was associated with worse long-term outcomes regardless of the definition (adjusted hazard ratios: 1.417–2.711), which was similar to previous results. Centola, M et.al compared two different definitions of CI-AKI in 406 patients with ST-segment elevation myocardial infarction (STEMI). During the median follow-up period of 12 ± 4 months, a significant association was detected between mortality and CI-AKI in both definitions [20]. Our results further verified the previous findings. Indeed, CI-AKI is a marker rather than a mediator of an increased risk of worse long-term outcomes [21]. First, patients who developed CI-AKI following cardiac catheterization tended to have their renal function decline after this acute event [22]. Chalikias G et al. found that AMI patients with acute kidney injury (AKI) during their hospitalization demonstrated a higher rate of deteriorating kidney function (9.5%) than those without AKI (5.1%) during the median follow-up period of 5.6 years [23]. In our cohort, patients with CI-AKI were more likely to have hemodialysis after the procedure and worse baseline renal function, which is similar to previously reported observations [20]. Additionally, deterioration in renal function has long been reported as a strong risk factor for adverse outcomes [18,24]. Second, patients with CI-AKI are prone to hemodynamic instability or comorbidity associated with prognosis [25]. In our study, patients with CI-AKI were more likely to be complicated with CHF and hypotension, and a higher incidence of arrythmia and AHF was also observed in those with CI-AKI. Third, the distant organ effects of AKI, especially the effect leading to cardiac dysfunction, may have a significant impact on prognosis. Potential mechanisms may be endothelial dysfunction, fluid overload, hypercoagulation and myocardial depression activity during ultrafiltration [26].

In our cohort, the incidence of CI-AKI varied from 5.92% to 18.77% depending on the definitions. As reported by previous results, the lack of a long-established definition of CI-AKI resulted in wide variation in the incidence of CI-AKI among patients with AMI [9–11,27]. From July 2006 to June 2007, a study conducted by Jabara et al. enrolled 400 consecutive patients, the incidence of CI-AKI were 3.3% (Scr increase $\geq$ 0.5 mg/dl), 10.2% (Scr increase $\geq$ 25%), 7.6% (eGFR decrease $\geq$ 25%), and 10.5% (the composite), respectively [28]. The incidence of CI-AKI in our cohort was higher than that of Jabara's, which may be due to the difference in the included patients (AMI patients in our study).

In this study, we found that CI-AKI$_A$ (defined as an increase of Scr $\geq$ 0.3 mg/dL or $\geq$ 50% from baseline), which had the highest PAR for long-term mortality, seems to be the most valuable predictor of long-term prognosis in patients with AMI. Previous studies showed that "absolute" criteria (i.e., an increase of 1.0 mg/dL in Scr) neglect a high proportion of patients with small increases in Scr and may lead to underestimation of the incidence of CI-AKI. Actually, a small Scr increase in patients with low baseline Scr may also lead to significant renal impairment [29]. On the other hand, the "relative" criteria (i.e., an increase of 10% in Scr) have a lower discriminative power [28,30,31]. CI-AKI$_A$ was defined as containing both absolute and relative criteria. A PAR of 11.62% for long-term mortality may reflect the appropriate prevalence and hazard ratio of CI-AKI$_A$.

Our results also indicated that prevention of CI-AKI$_B$ defined as an increase of Scr $\geq$ 0.5 mg/dL from baseline may avert 9.20% of long-term mortality in patients with AMI, which was derived from both the prevalence and the magnitude of its association with long-term mortality. Patients with an absolute Scr increase $\geq$ 0.5 mg/dL were evaluated as high risk, which is broadly consistent among previous studies. Guillon et al found that patients with an increase in Scr $\geq$ 0.5 mg/dL had higher based complications. After adjusting for related risk factors, this group (6.9%) had a 2.9-fold increase in 6-month mortality [10]. Budano et al reported a similar finding in 755 patients undergoing contrast exposure [32]. However, this criterion may be too strict and lead to a lack of prognostic value.

In this research, CI-AKI$_C$ was identified in 18.77% of the subjects, but its HR value was the lowest among all three CI-AKI definitions, which is quite similar to the result of a large sample randomized CI-AKI trial (HORIZON-AMI) [7]. In addition, CI-AKI$_C$ had the lowest PAR, which may only explain 7.26% of the long-term mortality. Its lowest ranking among all three CI-AKI definitions was not unexpected. One explanation may be the inclusion of low risk patients and heterogeneity [33–35]. This seems to suggest that interventions targeting patients with CI-AKI$_C$ may cost the most but generate the lowest effect in reducing long-term mortality in patients with AMI.

4.2. Limitations

First, our study was a sub-study of an observational cohort of unselected patients conducted in a single center located in South China; thus, the prevalence of CI-AKI may not be representative. However, our cohort is one of the largest CI-AKI databases regarding AMI patients. In particular, PAR can only be calculated based on observational data. Second, due to the observational design, we could only indicate that preventing CI-AKI may eliminate 5–11% of long-term all-cause death rather than directly prove it. However,

our study evaluated the harm caused by CI-AKI from a new dimension (PAR) and first compared the differences in PAR between three various definitions. Third, some patients were discharged within 72 h after the CAG/PCI and did not have their creatinine level measured thereafter, and it is quite difficult to collect details regarding subsequent kidney insults over a follow-up period as long as 7 years. Therefore, we may not be able to report follow-up renal outcomes (normalization or deterioration) or renal insulting events, which are important for worse outcomes. However, the association between CI-AKI and long-term mortality was adjusted by various important prognostic factors from the TIMI and GRACE scores. Finally, the Scr assay in our laboratory was performed by the Jaffe method, which may have been abated by the others.

5. Conclusions

Our results suggested that CI-AKI is associated with long-term prognosis in patients with AMI irrespective of the definition used. Cardiologists as well as future studies exploring long-term prognosis should pay more attention to the presence of CI-AKI, especially CI-AKI$_A$ with the highest PAR.

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CRediT authorship contribution statement

Li Lei: Methodology, Formal analysis, Investigation, Writing - original draft, Data curation, Writing - review & editing. **Yan Xue:** Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Zhaodong Guo:** Methodology, Investigation, Writing - original draft, Writing - review & editing. **Bowen Liu:** Methodology, Investigation, Writing - original draft, Writing - review & editing. **Yibo He:** Investigation, Validation, Writing - review & editing. **Feier Song:** Investigation, Validation, Writing - review & editing. **Jin Liu:** Methodology, Data curation, Writing - review & editing. **Guoli Sun:** Investigation, Data curation, Writing - review & editing. **Liling Chen:** Investigation, Writing - review & editing. **Kaihong Chen:** Investigation, Resources, Writing - review & editing. **Zhidong Huang:** Writing - original draft, Investigation, Writing - review & editing. **Ming Ying:** Writing - original draft, Investigation. **Liyao Zhang:** Writing - original draft, Investigation. **Zhiqi Su:** Writing - original draft. **Li Pan:** Writing - original draft. **Shiqun Chen:** Conceptualization, Methodology, Formal analysis, Writing - review & editing. **Jiyan Chen:** Conceptualization, Methodology, Resources, Supervision, Funding acquisition, Writing - review & editing. **Yong Liu:** Conceptualization, Methodology, Resources, Supervision, Funding acquisition, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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