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Onset time and prognostic value of acute kidney injury in patients with acute myocardial infarction

Ryota Kosaki [a,b], Kohei Wakabayashi [b,*], Shunya Sato [a], Hideaki Tanaka [a], Kunihiro Ogura [a], Yosuke Oishi [a], Ken Arai [a], Kosuke Nomura [a], Koshiro Sakai [a], Teruo Sekimoto [a], Tenjin Nishikura [a,b], Hiroaki Tsujita [a], Seita Kondo [a], Shigeto Tsukamoto [a], Shinji Koba [a], Kaoru Tanno [b], Toshiro Shinke [a]

[a] Division of Cardiology, Department of Medicine, Showa University School of Medicine, 1–5–8 Hatanodai, Shinagawa-ku, Tokyo 142-8666, Japan
[b] Division of Cardiology, Cardiovascular Center, Showa University Koto-Toyosu Hospital, 5-1-38 Toyosu, Koto-ku, Tokyo 135-8577, Japan

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ABSTRACT

Background: The mechanisms and clinical impact of acute kidney injury (AKI) after acute myocardial infarction (AMI) may differ depending on whether AKI develops during the early or late phase after AMI. The present study assessed the timing of AKI onset and the prognostic impact on long-term outcomes in patients hospitalized with AMI.

Methods: The present study enrolled consecutive AMI survivors who had undergone successful percutaneous coronary interventions at admission. AKI was defined as an increase in the serum creatinine level of ≥0.3 mg/dL above the admission value within 7 days of hospitalization. AKI patients were further divided into two subgroups (early-phase AKI: within 3 days vs. late-phase AKI: 4 to 7 days after AMI onset). The primary endpoint was all-cause death.

Results: In total, 506 patients were included in this study, with 385 men and a mean age of 69.5 ± 13.5 years old. The mean follow-up duration was 1289.5 ± 902.8 days. AKI developed in 127 patients (25.1%). Long-term mortality was significantly higher in the AKI group than in the non-AKI group (log-rank $p < 0.001$). Early-phase AKI developed in 98 patients (19.3%), and late-phase AKI developed in 28 patients (5.5%). In the multivariable analysis, early-phase AKI was significantly associated with all-cause mortality (HR 2.83, 95% CI [1.51–5.29], $p = 0.0012$), while late-phase AKI was not.

Conclusion: Early-phase AKI but not late-phase AKI was associated with poor long-term mortality. Careful clinical attention and intensive care are needed when AKI is observed within 3 days of AMI onset.

1. Introduction

Acute kidney injury (AKI), which occurs in a certain proportion of patients hospitalized with acute myocardial infraction (AMI), is independently associated with increased in-hospital and long-term mortality rates up to 10 years after AMI [1–5]. Recent reports have suggested that even small changes in renal function, as measured by serum creatinine levels, are associated with worse short-term outcomes [6–9]. Based on the existing evidence, an increase in the serum creatinine level is defined as acute kidney injury (AKI). However, the definitions used for the timing of AKI onset has not been consistent in the previous studies, with AKI defined as an increase in serum creatinine levels within 7 or 14 days after admission or at discharge.

In patients with AMI, the mechanisms underlying AKI may be different depending on whether its onset occurs in the early- or the late- phase of hospitalization and whether the inciting insult is the AMI or the primary PCI. In addition, clinical conditions and treatment strategies may influence the development of AKI after AMI. Thus, clinical outcomes might vary depending on the timing of AKI onset. Therefore, the present study classified AKI by its timing at onset and determined the impact of this timing on long-term outcomes in patients hospitalized with AMI.

2. Methods

2.1. Study population

The data of the present study is from a prospective registry which included consecutive AMI patients who underwent emergent percutaneous coronary intervention (PCI) in Showa University

* Corresponding author.
E-mail address: kwaka@live.jp (K. Wakabayashi).

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Hospital. The data was retrospectively analyzed for the purpose of the present study. Patients admitted with a diagnosis of AMI from November 2011 to January 2016 were screened and, if eligible, were prospectively enrolled to the registry. All patients provided written informed consent. The study population included patients who were within 12 h of onset of an AMI and who had successfully undergone a primary PCI. Patients who had experienced cardiopulmonary arrest on arrival or had renal dysfunction on hemodialysis were excluded. In this study, AMIs included both ST-segment elevation myocardial infarctions (STEMI) and non-ST-segment elevation myocardial infarctions (NSTEMI). STEMI and NSTEMI were diagnosed based on general universal definitions [10]. The diagnosis of an AMI was confirmed by coronary angiography in all patients. A successful PCI was defined as a stenosis of less than 25% in the target vessel after reperfusion. When other significant coronary lesions deemed ischemia-inducible were detected, an additional PCI was performed immediately after the primary PCI. The interventional strategy was left to the discretion of the operator. Demographic, clinical, and procedural data, as well as information about in-hospital outcomes, were collected from the medical record and entered into a prospective database. Clinical follow-up data were obtained at office visits or via telephone interviews. This study was approved by the Ethics Committee of Showa University.

2.2. Definitions of AKI and endpoints

We checked serum biomarkers on admission and within 1 h after the primary PCI. We also monitored serum creatinine (Cr) daily during the first week. Based on the observed changes in the serum Cr level, we divided the patients into two groups, including a non- AKI and an AKI group, in the first week. Several definitions of AKI were used in the previous studies, such as serum creatinine increase cut-off: 0.5 mg/dl, 0.3 mg/dl or 25% [11]. The definition of cut-off: 0.3 mg/dl above the value on admission within 7 days was chosen as same as that of "worsening renal function", because "worsening renal function" was also used in many previous studies [6–9]. AKI patients were further divided into two additional groups, including an early-phase AKI group (onset within 3 days) or a late-phase AKI group (onset within 4 to 7 days after admission). This study's primary endpoint was all-cause death during the long-term follow-up period, which was compared between patients with or without AKI and between patients with early-phase vs. late-phase AKI.

2.3. Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and were compared using the Student's *t*-test or the Wilcoxon rank-sum test depending on their distributions. Categorical variables are presented as numbers with percentages and were compared using the chi-squared test or Fisher's probability test, as appropriate. Hazard ratios (HR) and their 95% confidence intervals (CI) were computed by logistic regression model analysis to clarify the impact of several potentially independent prognostic factors. Variables with $p < 0.1$ on univariate analysis were entered into the multivariable Cox model to adjust for baseline differences. Multivariable analysis was performed with forward–backward stepwise selection methods. The proportion of patients who survived was plotted using Kaplan-Meier curves, and the significance was examined using the log-rank test. Statistical analyses were performed using JMP software version pro 15.0 (SAS Institute Inc, Cary, NC, USA). Statistical significance was defined as $p < 0.05$.

3. Results

Of the 606 patients who underwent a primary PCI for AMI during the study period, 100 patients met the exclusion criteria for this study, including out-of-hospital cardiopulmonary arrests in 65 cases and hemodialysis in 36 cases. The remaining 506 patients were included in this study, with 385 men and a mean age of 69.5 ± 13.5 years. The mean follow-up duration was 1289.5 ± 902.8 days (range 2 to 3118 days). The AMI at presentation was the first cardiovascular event in 429 (84.8%) patients. Seventy-seven

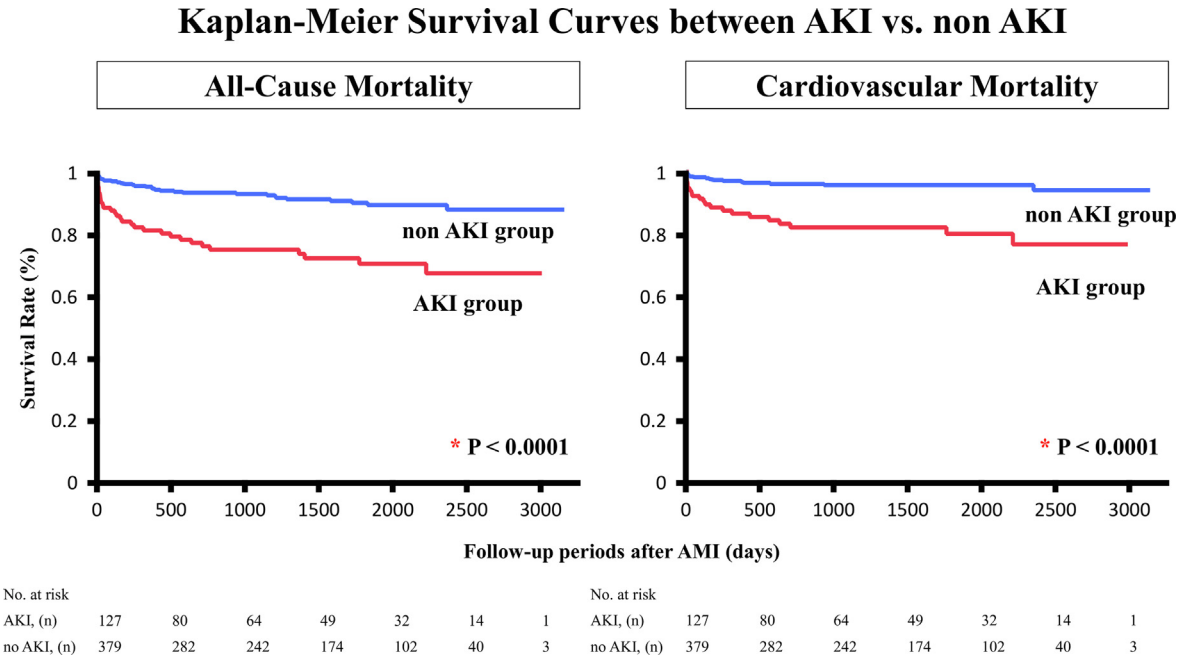

Fig. 1. Distribution of AKI occurrence. The graphs show the incidence of acute kidney injury (AKI) during each day after admission for AMI. The incidence of AKI was the highest during the first day after AMI, and the majority of AKI occurred within the first 3 days, which was defined as early-phase AKI. In contrast, onset at 4 to 7 days after AMI was defined as late-phase AKI.

(15.2%) patients had a history of coronary artery bypass grafts or a previous PCI for an acute or chronic coronary syndrome. In addition, 14.8% of the patients underwent a PCI for another high-risk lesion immediately after the primary PCI. No patients underwent another PCI during the first 7 days after the initial procedure. In total, AKI developed in 127 patients (25.1%), and the distribution of AKI occurrence is shown in Fig. 1. Most cases of AKI occurred within 2 days after admission for AMI.

Baseline characteristics of patients with and without AKI are shown in Table 1. Patients who developed AKI were more likely to be elderly; had higher prevalences of hypertension ($p = 0.0131$), prior MI ($p = 0.0072$), previous PCI ($p = 0.0013$), history of heart failure ($p = 0.0068$), and chronic kidney disease (CKD) ($p < 0.0001$); and had elevated brain natriuretic peptide (BNP) ($p < 0.0001$), initial Cr, CRP (C-reactive protein) ($p = 0.0393$), LDL (low-density lipoprotein) ($p = 0.0063$), and peak Cr levels ($p < 0.0001$). Usage rates of intra-aortic balloon pumping were also higher in the AKI group than in the non- AKI group ($p = 0.0229$). The contrast media volumes and left ventricular ejection fractions (LVEF) were lower in the AKI groups than in the non- AKI group ($p = 0.0002$, $p = 0.0008$). There were no significant differences in multi-vessel disease or cardiogenic shock between patients with or without AKI. All-cause deaths in the entire study population occurred in 67 patients (13.2%) during the follow-up period. Mortality was significantly higher in patients with AKI than in those without AKI (26.0% versus 9.0%, $p < 0.0001$). In the multivariable analysis, AKI was significantly associated with long-term mortality, as shown in Table 2 (HR 2.83, 95% CI [1.51–5.29], $p = 0.0012$). Kaplan-Meier curves showed that mortality was significantly higher in the AKI group (log-rank $p < 0.001$) (Fig. 2). The analysis with another definition of AKI, increase in the serum creatinine level of >0.5 mg/dL, was performed to determine the relation between AKI and long-term mortality. AKI with serum Cre increase >0.5 mg/dl was associated with long-term mortality HR 4.17, 95 %CI 2.01–8.66, p = 0.0001. The HR was higher than HR 2.44 of AKI with serum Cre increase >0.3 mg/dl. The AKI patients were further divided into two subgroups (early-phase AKI [within 3 days] vs. late-phase AKI [4to7day]). Early-phase AKI developed in 98 patients (19.3%), and late-phase AKI developed in 28 patients (5.5%) (Fig. 1). There were no significant differences in baseline variables between these two groups, except for in the prevalence of diabetes mellitus and the hemoglobin A1c (HbA1c), CRP, and peak serum Cr levels (Table 3). The predictors of early-phase AKI and late-phase AKI are as follows. early-phase AKI: CKD; OR 2.41 (1.39–4.19), p = 0.0018, late-phase AKI: CKD; OR 3.48 (1.33–9.10), p = 0.011, respectively.

Patients with early-phase AKI had a high mortality rate (n = 29, 29.6%), while patients with late-phase AKI had a similar mortality rate to the non- AKI group. The early-phase AKI group also had higher cardiovascular mortality during the observation period, as shown by Kaplan–Meier curves (Fig. 3). The early-phase AKI group had the highest long-term mortality, as shown in Supplementary Table 1. A multivariable Cox proportional-hazards model analysis showed that early-phase AKI, age, and the left ventricular ejection fraction were associated with long-term, all-cause mortality (Table 4).

Table 1
Baseline characteristics between AKI vs. no AKI.

	no AKI	AKI	*p* value
	n = 379	n = 127	
Age (y.o.)*	67.8 ± 13.6	74.6 ± 12.0	<0.0001
Male	289 (76.3)	96 (75.6)	0.8796
Body Mass Index (kg/m^2)	23.8 ± 4.3	24.0 ± 4.2	0.2205
Smoker	227 (59.9)	78 (61.4)	0.7615
Hypertension*	261 (68.9)	102 (80.3)	0.0131
Diabetes	150 (39.6)	61 (48.0)	0.0945
Dyslipidemia	308 (81.3)	98 (77.2)	0.3209
Prior MI*	42 (11.1)	26 (20.5)	0.0072
Post CABG	4 (1.1)	2 (1.6)	0.6398
Previous PCI*	45 (11.9)	30 (23.6)	0.0013
History of HF*	13 (3.4)	12 (9.5)	0.0068
History of stroke	42 (11.1)	22 (17.3)	0.0671
CKD	97 (25.6)	77 (60.6)	<0.0001
STEMI	271 (71.5)	93 (73.2)	0.7082
Multi-vessel disease	172 (46.4)	58 (49.6)	0.5440
Cardiogenic shock	21 (5.5)	9 (7.1)	0.5232
IABP*	47 (12.7)	25 (21.2)	0.0229
LVEF (%)*	50.8 ± 10.4	47.1 ± 10.8	0.0008
Contrast media volume (ml)*	189.1 ± 60.9	163.1 ± 71.8	0.0002
BNP (pg/ml)*	187.5 ± 321.8	447.3 ± 667.0	<0.0001
Cr (mg/dl)*	0.79 ± 0.3	1.19 ± 0.78	<0.0001
CRP (mg/dl)*	1.44 ± 3.8	2.06 ± 4.0	0.0393
HDL (mg/dl)	44.7 ± 11.8	42.7 ± 12.2	0.1231
LDL (mg/dl)*	120.4 ± 39.5	109.3 ± 35.9	0.0063
HbA1c (%)	6.36 ± 1.3	6.36 ± 1.3	0.674
peak CK (U/l)	2103.1 ± 2336.0	3319.9 ± 8280.8	0.1
peak Cr (mg/dl)*	0.94 ± 0.3	1.86 ± 1.1	<0.0001

AKI, acute kidney injury; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; HF, heart failure; CKD, chronic kidney disease; STEMI, ST-segment elevation myocardial infarction; IABP, intra-aortic balloon pumping; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; Cr; creatinine; CRP, C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, Hemoglobin A1c; CK, creatine kinase; Values are presented as the mean ± SD or n (%).
* P < 0.05.

4. Discussion

This study assessed the timing of AKI onset and determined the impact of early-phase versus late-phase AKI on long-term outcomes in patients with AMI. The major findings of the present study are as follows: (1) most cases of AKI occurred within 2 days after AMI onset; (2) AKI was associated with worse long-term outcomes after AMI in contemporary clinical practice; (3) patients with early-phase AKI had a higher mortality rate, while patients with late-phase AKI had a similar mortality rate to patients without AKI; and (4) early-phase AKI was an independent predictor of long-term, all-cause mortality.

Monitoring Cr levels during the first few days after AMI simply identify this high-risk patient group. The detection of AKI with early-phase onset and more careful treatment for those high-risk patients are important to improve the clinical outcomes of AMI.

4.1. Previous studies

In high-risk patients, such as those hospitalized with AMI, heart failure, or sepsis or those undergoing cardiac surgery, the incidence of AKI has been reported to be high, ranging from 10% to 25% [12,13]. Emerging evidence suggests that small increases in serum creatinine over a specified period, which is diagnosed as AKI, is associated with mortality not only in heart failure patients but also in AMI patients [8,14]. AKI was defined as serum Cre increase >0.3 mg/dl in the present study. AKI with serum Cre increase >0.5 mg/dl was also associated with long-term mortality HR 4.17, 95 %CI 2.01–8.66, p = 0.0001. The HR was higher than HR 2.44 of AKI with serum Cre increase >0.3 mg/dl. The finding was consistent with the previous study [11]. AKI with serum Cre increase >0.5 mg/dl might be better to find high risk patients.

The incidence of AKI in AMI patients has widely varied in previous studies, with these variations attributable to differences in the definitions used for AKI and the baseline characteristics of patients [15,16]. Amin et al. defined AKI as an increase in the creatinine level during the entire hospitalization of $\geq$0.3 mg/dL above the admission value, with a reported incidence of approximately 19%

Table 2
Univariate and multivariate analysis for predictors of All-Cause Mortality.

	Univariate logistic regression		Multivariate logistic regression	
	Hazard Ratio (95% CI)	*p* value	Hazard Ratio (95% CI)	*p* value
Age (10-year increase)	1.76 (1.41–2.22)	<0.0001	1.39 (1.01–1.95)	0.0469
Male	1.18 (0.67–1.99)	0.5465		
Smoker	1.98 (1.22–3.21)	0.0055		
Hypertension	1.14 (0.67–2.05)	0.6171		
Diabetes	1.03 (0.63–1.68)	0.9187		
Dyslipidemia	1.36 (0.75–2.32)	0.301		
Prior MI	1.99 (1.08–3.44)	0.0283		
Previous PCI	2.26 (1.29–3.82)	0.0057		
History of HF	1.67 (0.58–3.76)	0.3041		
History of stroke	2.43 (1.32–4.23)	0.0055		
CKD	3.56 (2.18–5.92)	<0.0001	1.99 (1.01–3.97)	0.047
STEMI	1.03 (0.61–1.82)	0.9133		
Multi-vessel disease	1.52 (0.86–2.72)	0.1489		
Cardiogenic shock	2.53 (1.11–4.98)	0.0288		
IABP	2.45 (1.31–4.37)	0.0063		
LVEF (10% increase)	0.45 (0.36–0.55)	<0.0001	0.61 (0.45–0.81)	0.0008
AKI (Cr increase ≧ 0.3 mg/dl)	3.28 (2.02–5.30)	<0.0001	2.44 (1.32–4.53)	0.0045

AKI, acute kidney injury; MI, myocardial infarction; PCI, percutaneous coronary intervention; HF, heart failure; CKD, chronic kidney disease; STEMI, ST-segment elevation myocardial infarction; IABP, intra-aortic balloon pumping; LVEF, left ventricular ejection fraction; Cr; creatinine; Values are presented as the mean ± SD or n (%). *P < 0.05.

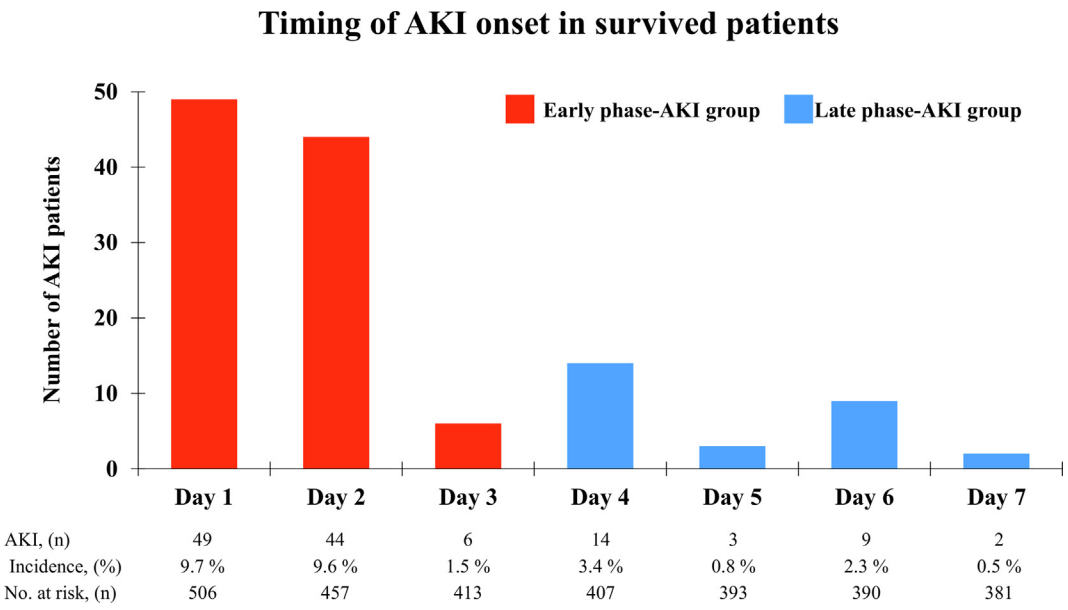

Fig. 2. Kaplan-Meier survival curves for patients with and without AKI. The Kaplan-Meier curves show the cumulative proportions of patients with all-cause mortality and cardiovascular mortality according to acute kidney injury (AKI). The incidences of all-cause mortality and cardiovascular mortality were significantly higher in patients with AKI.

in AMI patients [8]. In the present study, the incidence of AKI was approximately 25%. Compared with this previous study, some factors associated with AKI were higher, including the average age, the prevalence and severity of CKD, and the occurrence of a STEMI.

It has been reported that patients with transient AKI have a greater risk of death after AMI during long-term follow-up, even if their renal function is completely recovered at discharge [17]. Thus, it is known that AKI is a reliable marker of long-term mortality. However, there is limited information about the clinical implications of the timing of AKI onset in patients with AMI. Therefore, this study determined the effect of the timing of AKI onset on long-term outcomes after AMI.

4.2. Impact of early-phase AKI on long-term mortality

The overall 3-year, all-cause mortality rate was 13.2% in this study, which is consistent with the findings of previous reports [18,19]. In order to assess the effects of AKI timing on clinical outcomes, we divided AMI patients with AKI into two groups, including an early-phase AKI group and a late-phase AKI group. The majority of cases of AKI occurred within the first 3 days, or the early-phase, after AMI. The distribution of the AKI occurrence was consistent with a previous study. Recently, Moriyama et al. have reported that early-phase AKI is associated with higher rates of in-hospital, all-cause death, although they did not assess long-term outcomes [20]. To our best knowledge and research, the present study is the first one to report that early-phase AKI is associated with higher long-term mortality. These patients had a poorer prognosis than those with late-phase AKI. The mechanisms underlying early-phase versus late-phase AKI may be different, and the corresponding prevention and management strategies should likely be different between the two groups as well. Thus, differences in the mechanisms of AKI occurrence in the early- versus late- phase should be explored.

Table 3
Baseline characteristics between early-phase AKI vs. late-phase AKI.

	Early-phase AKI n = 98	Late-phase AKI n = 28	*p* value
Age (y.o.)	74.4 ± 13.6	75.5 ± 14.5	0.2909
Male	75 (75.8)	21 (75.0)	0.9343
Body Mass Index (kg/m^2)	23.5 ± 3.8	23.3 ± 5.0	0.7072
Smoker	61 (61.6)	17 (60.7)	0.9310
Hypertension	80 (80.8)	22 (78.6)	0.7927
Diabetes*	53 (53.5)	8 (28.6)	0.0196
Dyslipidemia	78 (78.8)	20 (71.4)	0.4127
Prior MI	22 (22.2)	4 (14.3)	0.3581
Previous CABG	2 (2.0)	0 (0.0)	0.4484
Previous PCI	25 (25.3)	5 (17.9)	0.4160
History of HF	11 (11.1)	1 (3.6)	0.2285
History of stroke	19 (19.2)	3 (10.7)	0.2953
CKD	60 (60.6)	17 (60.7)	0.9917
STEMI	69 (69.7)	24 (85.7)	0.0910
Multi-vessel disease	48 (53.3)	10 (37.0)	0.1374
Cardiogenic shock	8 (8.1)	1 (3.6)	0.4116
IABP	21 (23.1)	4 (14.8)	0.3562
LVEF (%)	46.7 ± 10.8	48.3 ± 11.0	0.4399
Contrast media volume (ml)	168.3 ± 76.3	146.0 ± 51.5	0.1702
BNP (pg/ml)	505.3 ± 727.8	246.5 ± 325.1	0.1041
Cr (mg/dl)	1.27 ± 0.9	0.93 ± 0.3	0.0718
CRP (mg/dl)*	2.28 ± 4.5	1.30 ± 3.1	0.0083
HDL (mg/dl)	42.4 ± 11.2	43.7 ± 15.3	0.6562
LDL (mg/dl)	109.3 ± 36.6	109.5 ± 34.2	0.9120
HbA1c (%)*	6.51 ± 1.4	5.86 ± 0.8	0.0044
peak CK (U/l)	3637.1 ± 954.4	2232.1 ± 1771.6	0.9833
peak Cr (mg/dl)*	2.00 ± 1.2	1.33 ± 0.3	0.0025

AKI, acute kidney injury; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; HF, heart failure; CKD, chronic kidney disease; STEMI, ST-segment elevation myocardial infarction; IABP, intra-aortic balloon pumping; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; Cr; creatinine; CRP, C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, Hemoglobin A1c; CK, creatine kinase; Values are presented as the mean ± SD or n (%).
* P < 0.05.

4.3. Mechanism of early-phase AKI

There were no significant differences in baseline variables between patients with early- vs. late-phase AKI, except for in the prevalence of diabetes mellitus and the HbA1c, CRP, and peak serum Cr levels. Thus, these factors may play a role in the differences between the mechanisms underlying early- versus late-phase AKI.

Many studies demonstrated the relation between contrast volume and AKI in AMI patients [21,22], although some studies suggested AKI after AMI was not associated with the volume of contrast. Thus, the impact of contrast volume on AKI in AMI is still controversial. The definition of CIN is generally serum creatinine increase more than 0.5 mg/dl or 25% during 48–72 h after contrast use. It is similar to the definition of early-phase AKI in the present study. Thus, the mechanism of majority of early-phase AKI might be CIN. Early-phase AKI patients more frequently had diabetes mellitus than late-phase AKI. Diabetes mellitus is a strong predictor and one of risk score for CIN that Mehran R et al. advocated. In the early-phase AKI group, diabetes was more frequent, and the HbA1c level was significantly higher. The flow reserve of the kidney may be less in diabetic patients with uncontrolled serum glucose levels. Microvascular dysfunction might reflect the poor prognosis [23]. Furthermore, it is well known that CIN is the predictor for long-term mortality after PCI. It could be the one of explanation why early-phase AKI patients had higher mortality in the present study.

Cosentino et al. demonstrated that admission high-sensitive CRP was closely associated with AKI development and severity, and with in-hospital outcomes in AMI [24]. Early-phase AKI patients had higher CRP on admission than late AKI patients in the present study. In patients with AMI, it has been documented those inflammatory factors and activation of neurohormonal systems, such as the renin-angiotensin-aldosterone system, by AMI might aggravate renal dysfunction, increase catecholamine pro-

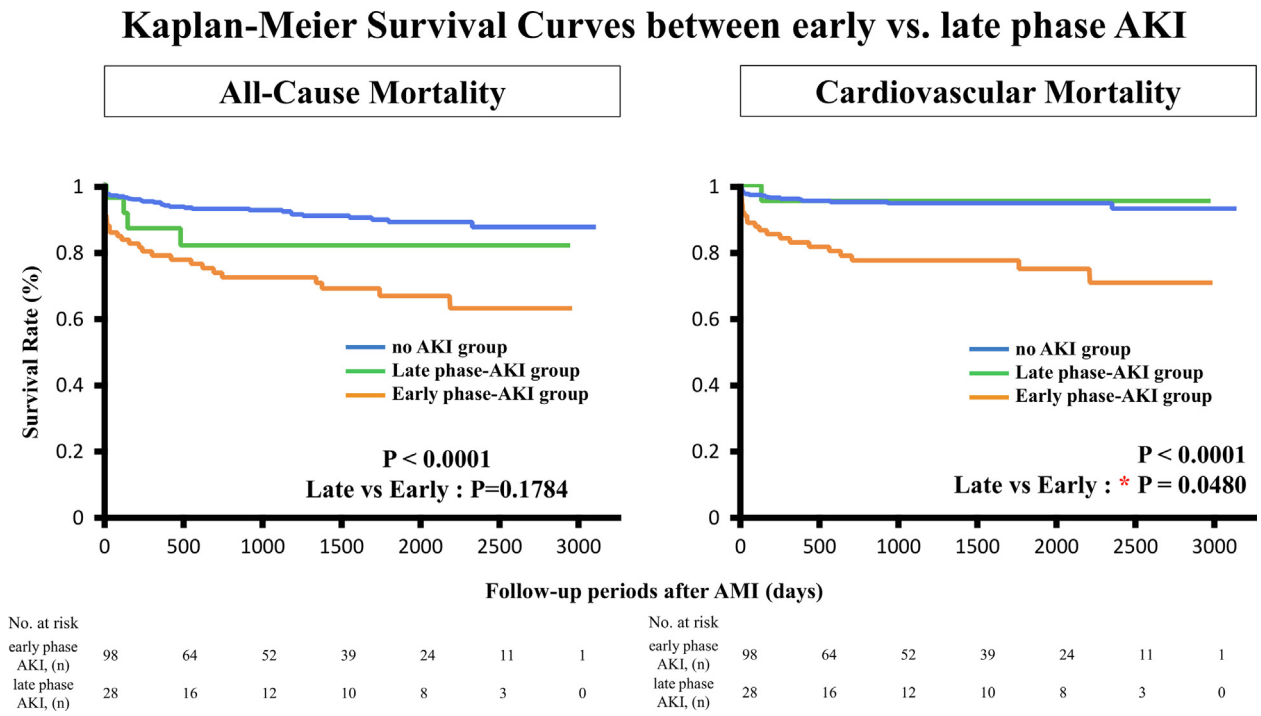

Fig. 3. Kaplan-Meier survival curves in early-phase versus late-phase AKI. Kaplan-Meier survival curves show that patients with early-phase AKI had the worst all-cause mortality. The early-phase AKI group had a significantly higher incidence of cardiovascular mortality than either the non- AKI or the late-onset AKI groups.

Table 4
Univariate and multivariate analysis for predictors of All-Cause Mortality.

	Univariate logistic regression		Multivariate logistic regression	
	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value
Age (10 year increase)	1.76 (1.41–2.22)	<0.0001	1.43 (1.03–2.00)	0.0306
Male	1.18 (0.67–1.99)	0.5465		
Smoker	1.98 (1.22–3.21)	0.0055		
Hypertension	1.14 (0.67–2.05)	0.6171		
Diabetes	1.03 (0.63–1.68)	0.9187		
Dyslipidemia	1.36 (0.75–2.32)	0.301		
OMI	1.99 (1.08–3.44)	0.0283		
Previous PCI	2.26 (1.29–3.82)	0.0057		
History of HF	1.67 (0.58–3.76)	0.3041		
History of stroke	2.43 (1.32–4.23)	0.0055		
CKD	3.56 (2.18–5.92)	<0.0001	2.15 (1.08–4.25)	0.0277
STEMI	1.03 (0.61–1.82)	0.9133		
Multi-vessel disease	1.52 (0.86–2.72)	0.1489		
Cardiogenic shock	2.53 (1.11–4.98)	0.0288		
IABP	2.45 (1.31–4.37)	0.0063		
LVEF (10% increase)	0.45 (0.36–0.55)	<0.0001	0.60 (0.45–0.80)	0.0006
Early-phase AKI	3.50 (2.14–5.66)	<0.0001	2.83 (1.51–5.29)	0.0012
Late-phase AKI	1.22 (0.37–2.95)	0.7092		

OMI, old myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; HF, heart failure; CKD, chronic kidney disease; STEMI, ST-segment elevation myocardial infarction; IABP, intra-aortic balloon pumping; LVEF, left ventricular ejection fraction; AKI, acute kidney injury; Values are presented as the mean ± SD or n (%). *P < 0.05

duction, and elevate endothelin [25–28]. These neurohormonal alterations may lead to renal arteriolar vasoconstriction and a reduction in renal perfusion pressure, which may result in poor clinical outcomes. Although assessing the impact of these factors on AKI onset is difficult with AMI, they may represent key factors.

The factor such as hemodynamic abnormalities might be also related with the cause of early-phase AKI. The mechanism of early-phase AKI may be multifactorial. The incidence of late-phase AKI was lower than that of early-phase AKI. The mechanism of late-phase AKI might be drug-induced or transient dehydration, not resulting in serious condition later. Further studies are needed to determine the mechanism of early-phase and late-phase AKI in AMI.

5. Study limitations

This study had several limitations. First, though we tried to adjust for confounding factors via a multivariate logistic regression analysis, we cannot exclude the possibility of residual contributing factors resulting from the presence of an unmeasured confounder or measurement errors in the included factors. Second, because of methodologic limitations in this retrospective analysis, we cannot identify etiologic factors for AKI in patients with MI.

Although the predictors for early- and late-phase AKI were individually analyzed, the analyses of predictors for each group may be underpower. Finally, the initial Cr level might have been affected by hemodynamic or metabolic statuses at presentation. Thus, it is difficult to ascertain an approximation of baseline renal function in all patients.

6. Conclusion

Early-phase but not late-phase AKI was associated with poor long-term mortality. Monitoring Cr levels during the first few days after AMI is a simple method to identify this high-risk patient group. Careful clinical monitoring and intensive care are needed in patients with AMI and AKI, particularly for those with early-phase onset.

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Author contributions

None.

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

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2021.100826.

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